Virchows Arch (2015) 467 (Suppl 1):S1–S279
DOI 10.1007/s00428-015-1805-9

ABSTRACTS

ESP Abstracts 2015

Oral Free Paper Sessions

Sunday, 6 September 2015, 08.30 – 12.00, Meeting Room 6/I
OFP-01 Oral Free Paper Session Digestive Diseases Pathology I

OFP-01-001
Colorectal mucinous adenocarcinoma: Proposal of a novel grading system

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Objective: To explore the inter-observer reproducibility and prognostic significance of a grading system based on the counting of poorly differentiated clusters (PDC) of tumour cells in mucinous adenocarcinoma (MAC) of the colon and rectum.
Method: Grading based on the counting of PDC was assessed in 108 surgical colorectal MACs. PDC represented clusters composed of ≥ 5 cancer cells with no glandular formation in the tumour stroma and at its invasive edge. MACs with <5, 5 to 9, and ≥10 clusters were classified as G1, G2 and G3 by two independent pathologists blinded to the clinico-pathological data. The inter-observer agreement and prognostic significance of PDC grade were compared with those of a grading system based on glandular differentiation.
Results: PDC grade was more reproducible and significantly associated with disease progression ($P = 0.0089$) as well as with death from MAC ($P = 0.0035$), as compared to the grade based on glandular differentiation which was not associated with any of the clinico-pathological variables. Moreover, PDC grade emerged as a significant, independent prognostic factor of recurrence free survival ($P = 0.0198$) and cancer specific survival ($P = 0.0293$) in MAC.
Conclusion: PDC grading is feasible, reproducible and prognostically relevant in MAC, which may support its use in routine practice.

OFP-01-002
Overall Tumour Budding (OTB) for prognostication in colorectal cancer

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Objective: In colorectal cancer (CRC), tumour budding at the invasion front (peritumoral budding, PTB) and within the tumour (intratumoral budding, ITB) has significant prognostic value. Since ITB and PTB are highly correlated, we aimed to assess the clinical relevance of an 'overall' tumour budding (OTB) score.
Method: Pan-cytokeratin stained slides from 156 well-characterized stage I-IV CRC patients were evaluated: OTB was scored as 10 densest out of 20 high-power fields (HPF) of ITB and PTB. OTB scores were correlated with clinicopathological features and survival using a ROC curve based cut-off (10 buds/HPF; high/low-grade OTB) and continuous OTB counts.
Results: High-grade OTB was associated with higher pT, pN, distant metastasis, lymphatic invasion and advanced TNM-stage (all $p < 0.05$). Continuous OTB counts significantly correlated with higher pT ($p \leq 0.01$), pN ($p \leq 0.01$), distant metastasis ($p \leq 0.01$), lymphatic invasion ($p \leq 0.0001$), venous invasion ($p \leq 0.01$), tumour grade ($p \leq 0.01$) and advanced TNM-stage ($p \leq 0.05$). OTB scores independently correlated with poor survival outcome (HR (95 %CI): 1.02, CI: 1.0002–1.04, $p = 0.03$) when adjusted for TNM-stage and adjuvant therapy.
Conclusion: OTB is a strong adverse prognostic parameter, capturing associations with metastasis and survival. It includes the densest regions of tumour budding irrespective of intra- or peritumoral location and simplifies the 10HPF/1HPF scoring system.

OFP-01-003
Dysplastic colonic adenomas are useful samples for Lynch syndrome immunohistochemical screening

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Objective: To assess the usefulness of colonic adenomas as samples for the study of mismatch repair (MMR) protein expression loss when trying to identify individuals with suspected Lynch syndrome (LS).
Method: We studied a series of 61 colonic adenomas from 22 proven mutation carriers (8 females and 14 males) belonging to 16 LS families. Germline mutations were present in MLH1 in 6 cases, MSH2 in 8, MSH6 in 1, and EPCAM in 1. Formalin-fixed, paraffin-embedded tissue sections were used. MMR protein expression was assessed with the aid of anti-hMLH1, anti-hMSH2, and anti-hMSH6 mouse monoclonal antibodies.
Results: Twenty-seven conventional adenomas (CAs), 22 sessile serrated adenomas (SSAs), 4 traditional serrated adenomas (TSAs), and eight hyperplastic polyps (HPs) measuring 0.1–2.2 cm were studied. High-grade dysplasia (HGD) was observed in 33 cases. Loss of MMR protein expression was identified in 34 cases and, in agreement with underlying germline mutations, it involved MLH1 in 9 instances, MSH2 in 24, and MSH6 in 1. Of these 34 informative polyps, 25 (74 %) showed HGD ($p = 0.001$).
Conclusion: Colonic adenomas are useful samples for the assessment of MMR protein expression when LS is suspected. Results are particularly rewarding when colonic adenomas exhibit high-grade dysplasia.

OFP-01-004
P38 expression in colorectal adenomas: Relationship to morphological features and stem cell protein Cd133

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Objective: The P38 protein is known to be expressed in colorectal adenomas. Colon tumorigenesis of adenoma type is promoted in mouse

models with P38 deletion. We aimed to study the expression patterns of P38 in human colorectal adenomas.
Method: We have studied the immunohistochemical expression of P38 in colorectal adenomas on tissue microarrays. Protein expression was studied with regard to morphological adenoma features and, to the expression of Ki67 and CD133 by the Kendall rank-correlation test.
Results: P38 was expressed in 81.6 % of colorectal adenomas. Nuclear P38 correlated to male gender ($p < 0.01$/tau = 0.157), to a decreased stromal component (0.02/−0.140), to low-grade dysplasia (<0.01/−0.254) and to decreased size (<0.01/−0.267). Nuclear and/or cytoplasmic P38 (global P38) correlated to presence of multiple adenomas (<0.01/0.198), low-grade dysplasia (<0.01/−0.158), decreased mucosecretion (0.01/−0.143) and to a decreased extent of the stromal component (0.02/−0.131). Nuclear and cytoplasmic P38 were correlated (<0.01/0.315). Nuclear P38 correlated to nuclear or cytoplasmic CD133 (<0.01/0.213 and <0.01/0.293).
Conclusion: The results of this study showing a correlation between P38 and a decreased adenoma size, as well as low-grade dysplasia, suggest a role for P38 in the initial steps morphogenesis of colorectal adenomas. The correlation to the stem-cell-marker CD133, known to belong to the quiescent cell compartment, are in agreement with an interference with tumour dormancy.

OFP-01-005
Improving margin analysis in ESD specimens

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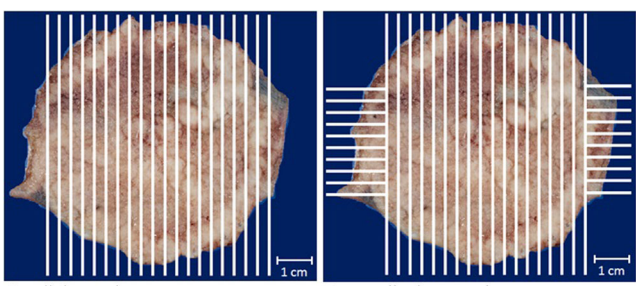
Objective: Endoscopic submucosal dissection (ESD) allows en-bloc resection of superficial gastro-intestinal tumours, providing qualitatively excellent specimens. Macroscopic processing usually uses parallel lateral sections. We recently developed an approach using perpendicular lateral sections, hypothesizing that it decreases false positive lateral margins. We aimed to test false positive rates of lateral margins in a series of colorectal ESD, depending on section method.
Method: We studied 182 ESD specimens. Parallel section was used from 2006 to 2009 ($n = 55$). Perpendicular lateral section was used from 2010 to 2014 ($n = 127$). We recorded the number of positive margins, along with grade of dysplasia or carcinoma. Patient outcomes (local recurrence and disease-free survival) were also observed.
Results: 29/55 (52.7 %) margins were positive for parallel sections. Of these, 5 cases harbored high grade dysplasia (HGD), and one carcinoma. In contrast, perpendicularly cut margins were significantly less frequently positive: 38/127 (29.9 %) ($p = 0.003$). Two had HGD and none carcinoma. Overall, no patients showed local recurrence during long-term follow-up, thereby defining all positive margins as false positives.
Conclusion: Our specimen handling method, with perpendicular section of lateral margins, appears to significantly decrease false positive rates in colorectal ESD specimens. While this technique may require complex handling, it may reduce unnecessary surgeries.

Margin technique:



Parallel margins Perpendicular margins

OFP-01-006
Indications for a strategic role of the stromal cells in the tumour progression of pancreatic cancer

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Objective: Pancreatic-ductal-adenocarcinoma (PDAC) remains a highly lethal malignancy characterized by a rich stromal component. Here we focus on the role of stromal-cells in the tumour progression.
Method: Factors involved in Epithelial-Mesenchymal-Transition (EMT) (including SNAIL1, ZEB1, ZEB2) and tumour-suppressors (SMAD4 and PTEN) were assessed by mRNA-in-situ-Hybridization (mRNA-ISH) and immunostaining on multipunch tissue-microarrays containing 120 well-characterized PDACs with special attention to stromal-cells. Additionally, microRNA-profiling after RNA-isolation from material obtained from juxta-tumoural and tumour-remote stroma after Laser-Capture-Microdissection by using qRT-PCR for specific microRNA-sequences was undertaken.
Results: Stromal-cells surrounding EMT-Type-tumour-budding-cells express high-levels of SNAIL1, ZEB1 and ZEB2 and show frequent PTEN-loss and chromosome-10 deletion, this being associated with distant metastasis ($p = 0.0045$). High-levels of SMAD4 in stromal-cells are associated with larger tumour size ($p = 0.0112$) and worse overall-survival ($p = 0.021$). miRNA-profiling shows a differential expression between juxta-tumoural and tumour-remote stroma concerning miR-21, miR-210, miR-203 and miR-200b.
Conclusion: Stromal-cells seem to play an important role in PDAC progression, especially by supporting EMT-type-tumour-budding and distant metastasis. We could additionally show that juxta-tumoural stroma differentially regulates miRNA in addition to harboring genetic changes in tumour-suppressor genes. Better understanding of the role of the cancer stroma will be detrimental in developing novel targeted and individualized therapeutic approaches.

OFP-01-007
Microsatellite instability as a prognostic factor in mucinous colorectal cancer

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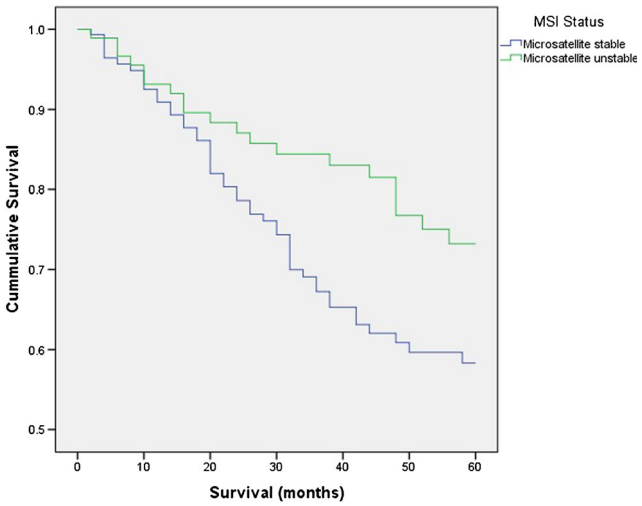
Objective: Mucinous colorectal (CRC) adenocaricnoma has been associated with worse outcomes. It is controversial whether all mucinous tumours are high grade, or whether a high pathological grade show only be conferred on microsatellite stable mucinous carcinoma. We investigated whether MSI was associated with improved survival outcomes in CRC patients with mucinous histology.
Method: In a cohort of 264 patients with mucinous CRC treated at our institution during the period 1998–2011, 5-year survival rates were compared for MSI and microsatellite stable tumours. We also calculated hazard ratios (HR) and 95 % confidence intervals (CI) for mortality using Cox regression, adjusting for age, gender, tumour grade and MSI.
Results: Mean age was 74 years (range 20–103 years), and 107 (40.5 %) were male. MSI was found in 95 (36.0 %) of mucinous tumours. The 5-year survival rate was significantly higher in patients with MSI compared with those with microsatellite stable tumours (73 % versus 58 %, $p = 0.035$). In a multivariate analysis, age (HR 1.05, 95 %CI 1.03–1.07, $p < 0.0001$) and tumour grade (HR 2.31, 95 %CI 1.30–4.12, $p = 0.004$) predicted increased mortality, whereas MSI was associated with decreased mortality (HR 0.61, 95 %CI 0.38–0.98, $p = 0.043$).

Conclusion: We conclude that MSI may be a positive prognostic factor in mucinous CRC.

Figure 1: 5-year survival in 264 mucinous CRC patients by MSI status:



OFP-01-008

Tissue expression of CEA, CA19-9, and CA125 serum markers in pseudomyxoma peritonei

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Objective: Our aim was to study tissue expression of serum tumour markers CEA, CA19-9, and CA125 in pseudomyxoma peritonei (PMP), i.e. peritoneal mucinous carcinoma.
Method: We analyzed CEA, CA19-9, and CA125 protein expression immunohistochemically from 92 appendix-derived PMPs. CA19-9 negative/weak cases were further sequenced for the mutational hotspot positions of the biosynthetic enzyme fucosyl transferase 3 (FUT3).
Results: All tumours were CEA immunopositive. The staining was predominantly apical, but in five aggressive high-grade tumours containing signet ring cells, an intense immunostaining was found in all tumour cell membranes. The preoperative serum CEA levels of these cases were normal and the patients died within 5 years after diagnosis. CA19-9 showed strong positive staining in most of the tumours (90 %). From the negative/weak cases, the mutational status of the FUT3 gene was confirmed by DNA sequencing. CA125 was infrequently expressed by PMP tumour cells, but in most of the cases (79 %) adjacent nonneoplastic mesothelial cells showed immunopositivity.
Conclusion: CEA is invariably expressed by PMP tumour cells, whereas CA125 seems to be mostly expressed by adjacent mesothelium. Importantly, we found five aggressive PMP tumours showing intense CEA immunostaining without increase in serum levels. This may limit the prognostic value of serum CEA measurements.

OFP-01-009

Sizing of colorectal adenomas: Pathology is more accurate than endoscopy

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Objective: Colorectal adenoma size is an important parameter in guidelines used to stratify patients for surveillance colonoscopy, with size ≥10 mm indicating an advanced adenoma, meriting a shorter interval before next colonoscopy. Guidance on how to measure adenomas is lacking. Our aim was to compare endoscopy and pathology sizing in a large series of adenomas.
Method: Endoscopy and pathology sizes available from intact adenomas removed at colonoscopies performed as part of the Northern Ireland Bowel Cancer Screening Program, from 2010 to 2014, were included in this study. Chi-squared tests were applied to compare size categories in relation to clinicopathological parameters.
Results: 2352 adenomas from 1465 individuals were included. Significantly greater size rounding or 'terminal digit preference' was evident in endoscopy v. pathology sizing (30 % v. 19 %, $p < 0.001$). There was a trend towards larger endoscopy than pathology sizing in four of the five study centers. Applying a 10 mm cut-off, 6.9 % of all adenomas, and 27.2 % of those 8–12 mm in size, had discordant endoscopy and pathology sizes, with consequent change in surveillance stratification for 8.8 % of individuals.
Conclusion: Pathology size of adenomas is more accurate than endoscopy size and should be used to determine appropriate surveillance intervals. Use of endoscopy size increases the burden on surveillance colonoscopy.

OFP-01-010

The role of the JAK/STAT pathway in gallbladder cancer

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Objective: Since cholelithiasis and cholecystitis are main risk factors for gall bladder carcinoma (GBC), inflammation-driven signaling pathways such as the Janus kinase (JAK) and signal transducer and activator of transcription (STAT) pathways might be of interest for investigating the carcinogenesis of GBC.
Method: Several members of the STAT pathway were analyzed by immunohistochemistry on tissue micro-arrays (TMAs) containing 396 gallbladder carcinomas and 137 non-neoplastic tissue samples. Furthermore the STAT pathway was analyzed by Western blot using eight different gallbladder cancer cell lines. Furthermore in vivo experiments with Xenograft mouse models were conducted.
Results: Our data highlight a potentially clinically significant association between an IL-6/IL-6R- and STAT3-mediated signaling cascade as the nuclear expression of STAT3 revealed staining of high intensity in more than 40 % of all cases investigated. Most of our study cases coprised GBCs with a high positive cytoplasmic staining intensity for IL-6R (99 %). STAT1 was upregulated in a small fraction of the cohort.
Conclusion: An IL-6/IL-6-R- and STAT3-driven signaling cascade is suggested as being critically involved in the development of GBC. Thus, STAT3, especially phosphorylated STAT3, might serve as reliable predictor for an IL-6- or STAT3-targeted therapy of GBC patients.

OFP-01-011

Barrett's esophagus related neoplasia: Goblet cells are present in the columnar lined mucosa with early neoplastic lesions irrespective of the phenotype

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Objective: It has been proposed that oesophageal adenocarcinoma may arise in columnar lined mucosa (CLM) without goblet cells (GC). However data on association of GC and oesophageal glandular neoplasia is limited. We aim to assess the presence of GC within early neoplastic CLM and the associated phenotype in endoscopic resection (ER) specimens.

Method: 78 ERs from 50 Australian patients were reviewed. Semi-quantitative assessment of presence and extent of GC was done by dividing length of CLM on each hematoxylin & eosin stained section into 1 mm segments as estimated by a 20x objective field. Fields with GCs were aggregated per case as a percentage of the total length of all segments of CLM examined. The extent of GC was correlated with the neoplastic phenotype and grade.
Results: 96 % (48/50) of patients and 91 % (71/78) of specimens showed GC. GC were present in 90 % (10/11), 95 % (38/40), 86 % (18/21) of intestinal, mixed and foveolar morphologic phenotypes respectively. Average extent of GC in intestinal, mixed, and foveolar morphologic phenotypes was 57, 46 and 23 % respectively. Immunophenotype was concordant with morphologic examination in 59 % (23/39) patients. Average extent of GC in low grade intraepithelial neoplasia, high grade intraepithelial neoplasia and intramucosal adenocarcinoma/oesophageal adenocarcinoma was 40, 42 and 42 % respectively.
Conclusion: The majority of early neoplastic lesions arise in the columnar lined mucosa with goblet cells. Goblet cells are present irrespective of phenotype or grade of neoplasia.

OFP-01-012

The expression of serotonin and serotonin transporter in intestinal mucosal biopsies in patients with Irritable Bowel Syndrome (IBS)

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Objective: Irritable bowel syndrome (IBS) is characterized basically by altered gut motility. Serotonin is a signaling molecule that plays a critical role in regulation of gastrointestinal motility. This study was performed to investigate the serotonin-positive cell count as well as serotonin-selective reuptake transporter (SERT) expression in the colon of IBS patients.
Method: The study included 40 IBS patients, 14 were diarrhea-predominant (IBS-D), 20 were constipation-predominant (IBS-C) and 6 had mixed symptoms (IBS-M). In addition, 20 healthy subjects were included as controls. Colonoscopy was performed on all patients and controls. Biopsies were immunostained for serotonin and SERT.
Results: Mean serotonin-positive cell count in biopsies of total IBS patients, IBS-D, IBS-C and IBS-M was 27.93 ± 6.455, 31.92 ± 7.065, 25.40 ± 5.5 and 27 ± 2.966 cells/10 HPF respectively, while that of control was 43.05 ± 8.54 cells/10 HPF. Serotonin-positive cell count was significantly lower in total IBS patients than control subjects ($p = 0.001$). SERT immunoreactivity score was significantly lower in the colonic biopsies of total IBS patients, IBS-D, IBS-C and IBS-M than control subjects ($p = 0.021$, 0.0115, 0.017 and 0.008 respectively).
Conclusion: The reduced serotonin-positive cell count as well as SERT expression in the colon of all subtypes of IBS patients points to their possible contribution to the pathogenesis of IBS.

OFP-01-013

Prognostic value of high c-Met expression in patients with poor prognosis pancreatic adenocarcinoma following surgical resection: Comparison of three c-Met scoring methods and exploration of underlying mechanisms of c-Met overexpression

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Objective: The HGF/c-Met pathway is a hypoxia-inducible pathway involved in tumour-stroma interactions and invasion in pancreatic ductal adenocarcinoma (PDAC). We aimed to assess the prognostic value of c-Met overexpression in PDAC and the underlying mechanisms.

Method: Patients with resected PDAC without perioperative chemotherapy/radiotherapy were retrospectively selected. c-Met immunostaining was graded using a simplified score (high c-Met≥ 20 % of cancer cells with strong staining) and compared to other visual scales. Hypoxia was assessed by HIF-1α/CA9 immunostaining, necrosis and automated microvascular density [MVD]. c-Met gene copy number was assessed by FISH. c-Met mRNA levels were quantified by RT-PCR.
Results: Thirty-seven patients were analyzed. The simplified c-Met score displayed the best prognostic value and reproducibility. High c-Met (7/37) was associated with shorter DFS (6.3 vs. 33.0 months, HR = 3.456, $p = 0.0035$) and OS (10.8 vs. 39.0 months, HR=4.257, $p = 0.0006$). In multivariate analysis, high c-Met was independently associated with DFS and OS. There was no correlation between hypoxia-related markers and c-Met expression. c-Met gene was not amplified. c-MET expression appeared to be transcriptionally activated in PDAC.
Conclusion: c-Met is an independent prognostic marker in resected PDAC. High c-Met expression (RNA and protein) was not associated with hypoxia or gene amplification. Comparative transcriptomic analysis of c-MET high/low tumours will be presented.

OFP-01-014

Somatostatin receptor 2A expression is not restricted to well differentiated neuroendocrine tumours but also occurs in poorly differentiated neuroendocrine carcinomas of pancreatic and extrapancreatic origin

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Objective: A large number of neuroendocrine tumours (NETs) express somatostatin receptors (SSTRs), especially SSTR2A. However, the SSTR-status in poorly differentiated NENs (neuroendocrine carcinomas, NECs) and NETs with an elevated Ki67-index ("NETs G3") is unclear. This study investigates the immunohistochemical SSTR2A and SSTR5 profiles of NECs and NETs G3 including their molecular TP53 status.
Method: Surgical resection specimens of 33 NECs (Ki67-index >20 %) of different origin (pancreas/ampulla, colorectum, bladder, parotid gland, merkel cell carcinoma of the skin) and 6 NETs G3 (Ki67-index >20 %) of pancreatic ($n = 4$) and colorectal ($n = 2$) origin were examined by immunohistochemistry (synaptophysin, chromogranin A, Ki-67, CD56, p53, progesterone receptor, CK20, SSTR2A, SSTR5). Molecular analysis (TP53, exon 5-9, by direct sequencing) was done in 24 NECs and 4 NETs G3.
Results: 4/6 NETs G3 and 5/33 NECs are SSTR2A positive. 22/33 NECs are p53 positive. SSTR2A positive NETs G3 are p53 negative. 2/4 NETs G3 and 12/24 NECs are TP53 mutated.
Conclusion: SSTR2A expression occurs also in NECs, however rarely. Pancreatic and colorectal NETs with a Ki67-index greater than 20 % ("NETs G3") retain their SSTR2A expression. SSTR2A positive NECs do not harbor TP53-mutations. In our small series, TP53-mutations occur mostly in NECs.

OFP-01-015

Histology of endoscopic ultrasound assisted fine needle biopsy is highly accurate in diagnosing submucosal lesions

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Objective: Submucosal lesions (SML) such as GIST tumours are regarded difficult to sample by endoscopic ultrasound-assisted FNA (EUS-FNA). Fine needle biopsy (FNB) is an alternative approach. The aim of this prospective, randomized study was to compare the diagnostic accuracy of FNA and FNB on SML lesions.

Method: Patients referred to our endoscopy unit for EUS on an SML were enrolled September 2012–October 2014. SMLs were punctured with both FNA and FNB. If available, a cytotechnician was present on-site (ROSE). The adequacy of target lesion material, immunohistochemistry (IHC) and tumour proliferation indexing (GIST only, Ki67 %) was assessed. McNemar's test and Fischer's exact was used for statistical comparison.
Results: 62 cases were enrolled and 45 out of those were punctured with FNA and FNB. Distribution of tumours in Table 1. FNB was superior to FNA in fetching target lesion material ((23/26, 89 %) vs (17/26, 65 %), $p = 0.03$, producing tumour material for IHC ((23/26, 89 %) vs (13/26, 50 %), $p = 0.002$) and for Ki67 %-indexing (18/26 (69 %) vs 6/26, 23 %, $p < 0.001$). The sensitivity of FNA was however higher if ROSE was available compared to non-ROSE (14/16, 88, vs 3/10, 30 %, $p = 0.002$).
Conclusion: Fine needle biopsy is highly accurate and can be recommended as the first line approach when performing EUS-assisted sampling on submucosal lesions. Access to ROSE however considerably improves the results of FNA.

Table 1 Distribution of lesions:

LESION	FREQUENCY, n (%)	FNA+FNB
GIST	26 (42)	26/26
Leiomyoma	15 (24)	15/15
Lipoma	10 (16)	1/10
Benign ectopic tissue	6 (10)	3/6
Benign submucosal cyst	4 (6)	0/4
Submucosal ectatic vessel	1 (2)	0/1
Sum	62	45/62

Sunday, 6 September 2015, 14.30–16.30, Meeting Room 6/I
OFP-02 Oral Free Paper Session Digestive Diseases Pathology II

OFP-02-001
Expression of Common Lymphatic Endothelial and Vascular Endothelial Receptor-1 (CLEVER-1) by peritumoural endothelium is associated with adverse histological features in hepatocellular carcinoma
O. Cain*, S. Shetty, S. Hübscher
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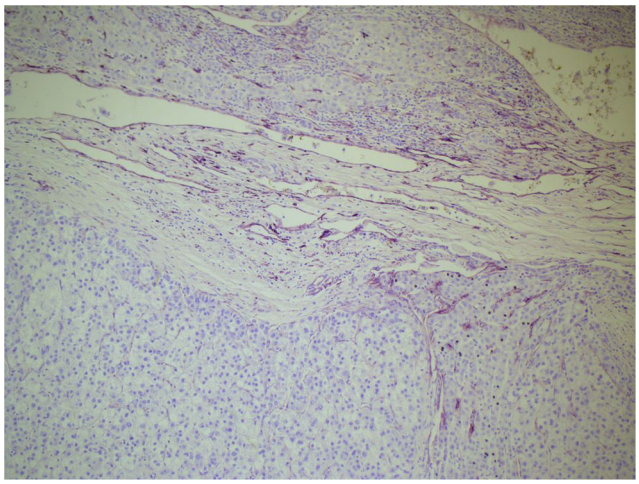
Objective: The lymphocyte recruitment molecule CLEVER-1 is expressed by sinusoidal endothelial cells in the normal liver and by continuous endothelium in inflammatory liver conditions. This study aimed to characterize its pattern of expression and prognostic significance in HCC.
Method: Liver tissue from 48 cirrhotic patients with a single nodule of HCC who had undergone liver transplantation was studied. Immunohistochemistry for CLEVER-1 was semi-quantitatively scored and correlated with established histological markers of poor prognosis.
Results: CLEVER-1 was expressed by sinusoidal vessels within the tumour and by blood vessels in the immediately adjacent stroma (peritumoural vessels). CLEVER-1 expression in peritumoural vessels correlated significantly with vascular invasion ($p = 0.024$) and with tumour grade ($p = 0.017$). There was no association between the expression of CLEVER-1 in tumoural vessels and adverse histological features. In some cases CLEVER-1 expression was also noted in a subset of stromal cells within peritumoural fibrous septa.
Conclusion: This is the first study to demonstrate an association between CLEVER-1 expression and adverse histological features in HCC. Further studies are needed to identify the mechanism of this association and to determine the nature and significance of CLEVER-1 expression in peritumoural stromal cells.

Immunohistochemical staining of CLEVER-1 in peritumoural vessels:



OFP-02-002
p62 (SQSTM1) expression in human liver disease: Preliminary results
D. Tiniakos*, L. Burnett, R. Hussain, L. Mulcahy, M. Karanikolas, Y. Bury, N. Cooper
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Objective: p62 (SQSTM1), a stress-inducible "hub-protein" that shuttles between nucleus and cytoplasm, is overexpressed in impaired autophagy. We assessed the cellular/subcellular topography and correlation of p62 expression with clinico-pathological parameters in human liver disease.
Method: 92 liver specimens (69 needle biopsies,7 surgical,8 explant,8 autopsy) with various liver diseases or hepatocellular carcinoma-HCC ($n = 9$) were prospectively immunostained with anti-p62 for diagnostic purposes and semi-quantitatively evaluated. Four control normal livers were used.
Results: In normal liver, <1 % of hepatocytes showed mild cytoplasmic or zone 1 nuclear p62 immunostaining; biliary epithelial cells (BEC) were negative. Panacinar strong nuclear p62 was only observed in autopsy livers while zone 1 nuclear positivity was more frequent in surgical specimens ($p < 0.0001$), independent of disease type. Mild/moderate cytoplasmic p62 was most frequent in steatohepatitis ($p = 0.01$) while isolated strong cytoplasmic immunoreactivity characterized acute hepatitis ($p < 0.0001$). Diffuse strong cytoplasmic p62 immunostaining was only observed in HCC. BEC showed occasional mild cytoplasmic p62 immunoreactivity independent of specimen/disease type.
Conclusion: p62 subcellular topography shows diversity depending on specimen type or liver disease. Panacinar hepatocyte nuclear p62 in autopsy liver maybe a death-related phenomenon while strong isolated cytoplasmic p62 in acute hepatitis may indicate underlying acute cell stress. Diffuse strong cytoplasmic p62 immunoreactivity maybe a marker for malignancy.

OFP-02-003
PTEN aberrations in different tissue compartments of pancreatic cancer are associated with adverse features and worse prognosis
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Objective: PTEN inactivation is a frequent event in cancer. Here we explore the mechanisms and the significance of PTEN aberrations in pancreatic-ductal-adenocarcinoma (PDAC).
Method: PTEN aberrations were assessed in a well-characterized PDAC-cohort ($n = 120$) by immunohistochemistry, mRNA- and fluorescent-in-situ-hybridization (mRNA-ISH and FISH), multiple-ligation-dependent-probe-amplification (MLPA) for loss of heterozygosity (LOH) and microRNA detection using qRT-PCR after RNA extraction from laser-capture-microdissected material.
Results: PTEN-protein/-mRNA-loss paralleled the path of carcinogenesis (normal>PanIN>PDAC) ($p < 0.0001$). PTEN-loss in tumour-cells correlated with higher tumour grade ($p = 0.0338$) and in stromal-cells with distant metastasis ($p = 0.0045$). PTEN-LOH was detected by MLPA and FISH in 51 % of all cases and in 73.5 % of cases with PTEN-protein/mRNA-loss and was associated with higher tumour grade ($p = 0.0412$), vascular invasion ($p = 0.0176$), distant metastasis ($p = 0.0082$) and decreased overall-survival ($p = 0.0127$). Epithelial-mesenchymal-transition-type-cells at the invasive-front (EMT-type-tumour-budding-cells) showed, additionally to LOH, an overexpression of microRNA-21. Stromal-cells also showed gross deletions of chromosome 10 and microRNA-21-overexpression.
Conclusion: We find significant heterogeneity regarding the mechanisms of PTEN-loss in PDAC. PTEN deletion is a major cause of PTEN-loss, correlates with aggressive tumour characteristics and is an adverse prognostic factor in PDAC. Stromal cells contribute to the PTEN-loss by both monosomy of chromosome 10 and/or microRNA-21-overexpression. EMT-type-tumour-budding-cells enhance PTEN-loss by expressing high levels of microRNA-21.

OFP-02-004
SMAD proteins in pancreatic cancer: A two sided story

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Objective: Defects in TGFβ-signaling promote tumour growth and molecules in this pathway, including SMADs, are suspected tumour suppressors. Here we explore the role of different SMAD-proteins in tumour progression of pancreatic-ductal-adenocarcinoma (PDAC).
Method: SMAD2/3, SMAD4 and pSMAD were assessed by mRNA-in-situ-Hybridization (mRNA-ISH) and immunostaining in main-tumour, epithelial-mesenchymal-transition-type-cells (EMT-type-budding-cells) and stromal-cells on multipunch tissue-microarrays containing 120 PDACs and associated with the clinico-pathological features.
Results: SMAD4 was significantly reduced in PDAC-tissues (main-tumour, EMT-type-budding-cells and lymph-node-metastases) compared with normal epithelia and precursor lesions (PanIN) ($p < 0.001$). SMAD4-loss was marginally associated with metastatic disease ($p = 0.0665$). However, retained SMAD4-expression in PDAC-cells correlated with EMT-type-tumour-budding ($p = 0.0068$) and shorter disease-free-survival ($p = 0.0073$). Moreover, SMAD4-expression in tumour-stroma correlated with larger tumour size ($p = 0.0112$) and worse overall-survival ($p = 0.021$). Loss of pSMAD in PDAC-tissues correlated with distant metastasis ($p = 0.0168$), higher tumour grade ($p = 0.0176$), venous invasion ($p = 0.0094$) and marginally with worse outcome ($p = 0.06$). SMAD2/3-loss correlated with metastatic disease ($p = 0.0081$).
Conclusion: SMAD2/3 and pSMAD seem to exert a tumour-suppressing role in PDAC. The role of SMAD4-loss seems more contradictory, on the one hand favoring tumour progression, while on the other hand being associated with reduced EMT-type-tumour-budding. We thus conclude that the tumour-promoting role of SMAD4-loss seems to be independent of EMT-type-tumour-budding in PDAC.

OFP-02-005
Morphological and immunohistochemical profile of hereditary diffuse gastric cancer

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Objective: Hereditary Diffuse Gastric Cancer (HDGC) encompasses a spectrum of precursor and invasive lesions. We aimed to characterize the morphology of early and advanced HDGCs and investigate the relationship between morphology and biomarkers of cell-adhesion, proliferation, anoikis, epithelial-mesenchymal-transition and cancer cell stemness.
Method: Twenty-one lesions from 17 HDGC patients encompassing 12 intramucosal carcinomas (pT1a) and 9 widely invasive carcinomas (pT>1) were analyzed by immunohistochemistry for E-cadherin, Ki67, Bcl-2, p53, pSrc and ALDH1A.
Results: All pT1a lesions showed typical signet ring cells (SRCs), absence of p53 and Ki-67 expression. In contrast, pT>1 carcinomas were composed by a mixture of SRCs and pleomorphic cells, characterized by high Ki-67 proliferation index (89 %) and p53 overexpression (56 %) in the pleomorphic component. E-cadherin immunoexpression was heterogeneous, from absent/decreased to cytoplasmic. Expression of ALDH1 and pSrc decreased from early (100 and 58 %, respectively) to advanced carcinomas (44 and 33 %, respectively). Bcl-2 was expressed only in one case.
Conclusion: We verified that early HDGCs present with an "indolent" phenotype (SRCs; Ki67-; p53-), while advanced carcinomas display an "aggressive" phenotype (pleomorphic cells; Ki67+; p53+). This is the first evidence of phenotypic heterogeneity in HDGC lesions and may help define predictive biomarkers of progression from indolent to widely invasive carcinomas.

OFP-02-006
SOD2 and SOD3 common polymorphisms are associated with colorectal cancer prevalence

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Objective: Reactive oxygen species (ROS) are consequence of aerobic respiration. Oxidative stress induces high levels of ROS that damage DNA. Superoxide dismutases (SOD) are a group of enzymes responsible for ROS detoxification. SOD2 and SOD3 polymorphisms are associated with ROS levels and may influence colorectal carcinoma (CRC) development. This study aimed to evaluate the association between common polymorphisms of SOD2 and SOD3 genes and CRC.
Method: FFPE non-tumoural colonic mucosa of 100 CRC biopsies was compared with blood samples of 100 healthy controls as a case-control study. SOD2 V16A and SOD3 H63R polymorphisms were genotyped by PCR-SSP, through commercially available kits.
Results: Our results showed that SOD2 16A (58 vs 40 %, $P < 0.01$; OR = 2.1; 95 % CI 1.2 to 3.6) and SOD3 63R (60 vs 43 %, $P < 0.05$; OR = 2.0; 95 % CI 1.1 to 3.5) mutated alleles were prevalent among CRC cases while the normal alleles where prevalent among control group.
Conclusion: SOD2 and SOD3 mutated forms were related with enzymatic activity decrease which correlates with ROS levels increase and consequently CRC higher risk. Our results corroborate the potential role of oxidative stress in CRC development and provide insight into the potential pathogenesis of SOD2 and SOD3 common polymorphisms in CRC predisposal.

OFP-02-007

hENT1 testing in pancreatic ductal adenocarcinoma: Are we ready yet? A multimodal evaluation of hENT1 status

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Objective: Human equilibrative nucleoside transporter 1 (hENT1) may predict survival in resected pancreatic adenocarcinoma treated by gemcitabine but the method of evaluation remains controversial.
Method: A murine (10D7G2) and rabbit (SP120) anti-hENT1 antibodies were applied on the same TMA of 471 tumours from 5 centers. Three additional hENT1 antibodies were tested on 251 cases. hENT1 RNA expression was assessed by affymetrix chips and qPCR on a subset of patients (86 and 100 respectively). Immunochemistry and RNA expression were compared and correlated with progression free (PFS) and overall survival (OS).
Results: The murine antibody was the only one to have a predictive value in gemcitabine-treated patients (PFS: HR = 0.44 [0.31–0.62] $p < 0.05$). There was no correlation between hENT1 high cases using the murine and the other antibodies. High hENT1 RNA expression was associated or nearly associated with a longer PFS in gemcitabine-treated patients (HR = 0.5298 [0.2672–1.0505], $p = 0.07$ w/affymetrix chip and HR = 0.4599 [0.2046–1.0334], $p = 0.05$ w/qPCR in patients from centre 2). RNA expression was not associated with hENT1 expression assessed by immunochemistry.
Conclusion: The murine (10D7G2) hENT1 antibody is the only one with a predictive value; unfortunately it is not commercially available. hENT1 RNA expression may represent an alternative to select patients.

OFP-02-008

Histologic evaluation of resection specimens in patients with esophageal neoplasia: Type of lesion does not reliably predict histology and staging

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Objective: It remains controversial whether the macroscopic classification of the esophageal lesions according to the Japanese criteria has a prognostic value with regard to endoscopic therapy. The aim of this prospective, single-center study was to evaluate the clinical role of macroscopic classification in patients with early esophageal neoplasia.
Method: A total of 69 patients with 78 suspect lesions undergone endsoscopy with targeted biopsies prior to endoscopic resection/dissection included assessment of the macroscopic type according to the Japanese classification. Histology was correlated with macroscopic assessment.
Results: The distribution of the lesions by gross type was: Is, $n = 6$ (8 %); IIa, $n = 34$ (44 %); IIb, $n = 29$ (37 %); IIc, $n = 4$ (5 %); IIa+b, $n = 3$ (4 %); IIa+c, $n = 2$ (2 %). Histology revealed no neoplasia in 8 lesions, low grade dysplasia (LGD) in 18, high grade dysplasia (HGD) in 13, early adenocarcinoma (EAC) in 35 and early squamous carcinoma (ESC) in 4 lesions. The distribution of macroscopic types was: LGD-Is 0 %, IIa 22 %, IIb 72 %, IIc 0 %, IIa+b 6 %; HGD-Is 15 %, IIa 31 %, IIb 38 %, IIc 8 %, IIa+c 8 %; EAC+ESC-Is 8 %, IIa 56 %, IIb 23 %, IIc 5 %, IIa+b 5 %, IIa+c 3 %. Macroscopic type did not predict advanced cancers (G2 or 3, $n = 8$) and penetration to the submucosa ($n = 9$). Histology of ER/ESD specimens led to a change in diagnosis in 43 % of the focal lesions and a relevant change in the management in 26 % of patients.
Conclusion: Macroscopic type does not predict histology, grading and penetration depth. Targeted biopsies of focal lesions are not accurate enough for precise diagnosis.

OFP-02-009

Molecular alterations underlying Crohn's Disease associated colorectal neoplasia

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Objective: Crohn's disease (CD) is a special type of chronic inflammatory bowel disease that – depending on the duration, extent and severity of colorectal inflammation – is associated with an increased risk for developing colorectal cancer (CRC). While it has been demonstrated that chromosomal instability is the leading form of genomic instability in ulcerative colitis-associated CRCs, it remains vague for CD-associated CRCs.
Method: We applied microsatellite PCR, mismatch repair protein immunohistochemistry, high-resolution array comparative hybridization (aCGH) and targeted next generation sequencing to formalin-fixed paraffin-embedded CRC samples from 17 different patients suffering from CD. If available, we included precursor lesions and inflamed mucosa.
Results: All 17 patients were diagnosed with CRC at a relatively young age (mean 47 years) compared to what one would expect in sporadic colorectal carcinogenesis and had a long history of CD. Histologically the CD-associated CRCs were adenocarcinomas, frequently displaying mucinous and/or signet ring cell components. While CRCs with this phenotype are often located in the right-sided colon and are typically microsatellite instable, all analyzed CD-associated CRCs were – despite their mucinous histology – microsatellite stable. Consistently, aCGH data showed chromosomal aberration patterns similar to those known from sporadic CRC following the chromosomal instability pathway.
Conclusion: While a high percentage of mucinous CRCs demonstrates microsatellite instability, none of the CD-associated CRCs was microsatellite instable. Accordingly, genomic profiling of CD-associated CRCs argues for an active chromosomal instability pathway. A detailed molecular analysis showed major differences between sporadic mucinous CRCs and CD-associated CRCs.

OFP-02-010

Plasma miR 17 host gene protein in patients with chronic hepatitis C virus infection: Relation to hepatic expression of PTEN and NFkB

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Objective: This work was designed to evaluate the plasma levels of miR 17 host gene (MIR17HG) protein, encoded by the miR-17~92 cluster host gene, in patients with chronic hepatitis C virus (HCV) infection, and to investigate its relation to hepatic expression of PTEN and NFkB.
Method: The study included 30 treatment-naïve patients with chronic HCV infection and 15 healthy subjects. Plasma levels of MIR17HG protein were determined using ELISA kit. Core liver biopsies obtained from patients were evaluated immunohistochemically for the expression of PTEN and NFkB.
Results: Plasma MIR17HG protein levels were significantly higher in patients with chronic HCV infection than in healthy subjects ($P = 0.012$), and in patients with cirrhosis than in patients with chronic hepatitis C without cirrhosis ($P = 0.001$). Also, plasma MIR17HG protein levels correlated inversely with hepatic PTEN expression ($P = 0.002$), and correlated positively with hepatic NFkB expression ($P = 0.013$). PTEN expression correlated inversely with NFkB expression ($P = 0.006$).
Conclusion: Activation of the miR-17~92 cluster may play a role in the pathogenesis of HCV-related liver disease through inhibition of PTEN and activation of NFkB. This is probably the first study to use the plasma MIR17HG protein levels as an index of miR-17~92 cluster activation.

OFP-02-011

Eukaryotic translation initiation factors are overexpressed in colorectal carcinoma compared to -normal colorectal mucosa: Impact on the RTK/PI3K/Akt-mTOR pathway and putative therapeutic targets

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Objective: Colorectal cancer (CRC) is the third most common cancer in Western countries. Some eukaryotic translation initiation factors (eIFs) are increased in CRC compared to normal mucosa. eIFs are involved in the regulation of protein synthesis and functionally linked to the MAPK and the mTOR signaling pathways, which are major targets for cancer therapy. We aimed at analyzing the relationship between mTOR and eIFs in CRC and non-neoplastic colorectal mucosa (NNCRM).
Method: Paired CRC and NNCRM from 80 individuals on tissue microarrays (TMAs) were studied by immunohistochemistry with eIF subunits 1, 2α, 3B, 3H, 3M, 4G, 4E and 6. The protein expression levels of eIFs and mTOR pathway members were determined by Western Blot and qRT-PCR.
Results: Western Blot and qRT-PCR of CRC revealed a significant up-regulation of eIF subunits 2α, 3a, 3b, 3j, 4B, 4G and 5 compared to NNCRM ($p < 0.001$). We observed higher expression of phospho-mTOR, mTOR, phospho-PTEN, PTEN, phospho-4e-BP1 and 4e-PB1 compared to NNCRM. IHC revealed up-regulation of eIF2α, eIF4e and eIF4g as well as variable expression patterns of eIF6.
Conclusion: Our findings show an altered expression of eIFs in CRC with influence on the mTOR pathway. eIFs need to be further validated as prognostic/ predictive biomarkers.

Sunday, 6 September 2015, 17.00–19.00, Meeting Room 6/I
OFP-03 Oral Free Paper Session Cytopathology

OFP-03-001

Primary HPV screening in Tampere City: Colposcopy and histology follow-up

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Objective: Primary HPV testing has been implemented for cervical cancer screening in the city of Tampere, Finland since 2012 in 35–60 aged females. Conventional screening arm included females from Pirkanmaa region of about same population.
Method: HPV was assessed with Abbott RealTime High Risk HPV test detecting 14 HPV high-risk genotypes including16 and 18. Both HPV test and Pap smear were taken, but only HPV positive slides were analyzed. HPV, cytology, colposcopy and LEEP results from 2012 screening year are summarized.
Results: Out of 8076 invited females, 5647 screening participants were HPV tested. Control cytology arm included 9500 invited and 6563 participated females in the same age group. HPV arm revealed 6.3 % HPV positivity with 5.6 % NILM or ASC-US cytology. LSIL or severe cytology (0.9 %) was followed by colposcopy and the diagnoses of 9 cases of CIN3 and 1 case of adenocarcinoma in situ were diagnosed. Cytology arm ASC-US rate was 5.6 % and LSIL or severe referral for colposcopy rate was 1.3 %. Cytology arm revealed 6 cases of CIN3.
Conclusion: The attendance rate was similar in both arms. The colposcopy rate was comparable, but CIN3 detection in HPV arm was almost doubled per 1000 females. Primary HPV screening seems to be more sensitive for CIN3 detection than conventional screening.

OFP-03-002

Combining color and morphology improves identification of low-grade urothelial cancer cells

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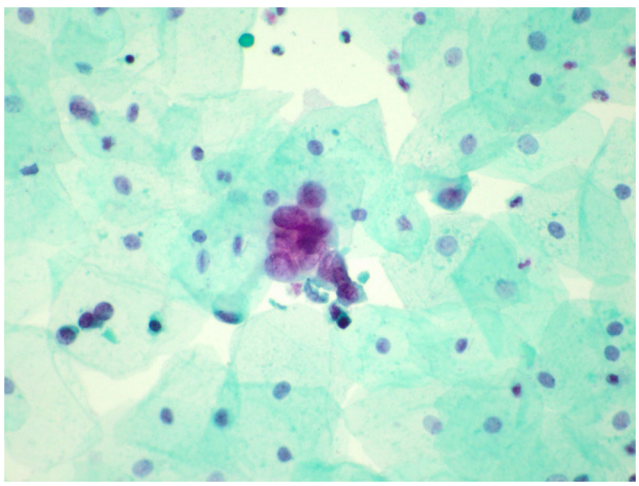
Objective: CellDetect® is a unique histochemical-stain enabling color and morphological discrimination between malignant and benign cells. In an open-label study, we showed the capability of CellDetect® to accurately identify urothelial carcinoma (UC) in urine smears. The objective of the current study was to validate the findings in blinded settings.
Method: The study was conducted in nine hospitals enrolling patients monitored for history of UC. 217 urine smears, including 96 positive and 121 negative cases, were recruited for the study. Smears were blindly observed by at least two cytology experts, and diagnoses were compared to biopsy in positive cases and to cystoscopy/biopsy in negative cases.
Results: The sensitivity of CellDetect® was 84.4 % with a specificity of 82.7 %. Notably, this high sensitivity was observed regardless of cancer stage as 84.7 % of early stages, non-muscle-invasive cancers were detected. Moreover, the accuracy of detecting low-grade tumours was also relatively high (78 %).
Conclusion: This study validates the capability of CellDetect® in identifying UC recurrence. Of special importance is that the high sensitivity was maintained throughout all cancer grades and stages. The data suggests that CellDetect® can be further developed to provide a non-invasive alternative to cystoscopic surveillance.

CellDetect® staining of urothelial cancer cells:



OFP-03-003

The evaluation of miRNAs panel on liquid based cytology of thyroid lesions: The role of miR-375 in follicular lesions

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Objective: Fine needle aspiration cytology (FNAC) plays a major role for the evaluation of thyroid nodules although 25 % are follicular neoplasms(FN) with varying malignant risk. MicroRNA(miRNA) may reshape FNs as long as they are negative gene expression regulators involved in tumour development. Scant data explored miRNAs in thyroid FNAC.
Method: From January to April 2015, 27prospective FNs with histology were enrolled. Thirteen benign lesions(BL) and 19positive for malignancy(PM) were selected as controls. FNs resulted at histology in

14malignancies (1Follicular Carcinoma-FC,7Papillary thyroid carcinoma-PTC and 6Follicular variant of PTC-FVPC) and 13Follicular adenomas (FA). The 19PMs included 9FVPC, 8PTC, 2medullary carcinomas (MTC). MiRNAs were extracted from liquid based cytology (LBC), quantified by real time PCR, analyzed for 5miRNAs(10b, 92a, 221, 222 and 375).
Results: Only MiR-375 was over-expressed in the FNs and PMs diagnosed as thyroid carcinoma. A cut-off of 12 miR-375/miR-U6 relative ratio recognized 100 % benign lesions regardless of categories and 93.4 %PMs. Specifically in each FNAC category, FVPCs showed higher values than PTCs. For miR-375, we reported 97.1 %sensitivity, 100 %specificity, 96.3 %NPV, 98.3 % Diagnostic accuracy.
Conclusion: LBC is suitable for miRNAs evaluation. MiR-375, over-expressed in all malignant FNs and 93.4 %PMs, may represent a valid marker in ruling out BLs and supporting PTCs and/or FVPCs.

OFP-03-004
Fine needle aspiration cytology of male breast lesions: A retrospective study over a 13 year period
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Abstract: FNAC is a very accurate tool for the diagnosis of male breast lesions. It is highly sensitive and specific with good cytohistologic correlation. To reduce the high rate of surgical biopsies of benign male breast masses, we conclude that FNAC should be performed as a standard procedure in the clinical evaluation of male breast lesions Data on male breast FNAC, performed from 2001 to 2014, were collected from the records of our cytology laboratory. FNAC diagnosis were categorized as benign, malignant, atypical/suspicious for malignancy and inadequate/unsatisfactory. Cytohistologic correlation was done with data from histopathology records. Over these 13 years 122 patients with palpable breast lumps underwent Fine needle aspiration (FNA) at our hospital. The age ranged from 17 to 84 years. Diagnostic aspirates were obtained in all 122 cases. The diagnoses were as follows: 63 benign (gynecomastia 47, miscellaneous 16) (52 %), 10 malignant (8 %), 32 atypical/suspicious for malignancy (26 %) and 17 non-diagnostic/unsatisfactory (14 %). Hence, we strongly recommend the use of FNAC as the first-line investigation in the clinical evaluation of male breast lumps.

OFP-03-005
Axillary lymph node fine needle aspiration in breast cancer: A four-year retrospective study with cytohistological correlation
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Objective: Fine needle aspiration cytology (FNAC) is performed in axillary lymph nodes (ALN) for breast cancer staging prior to neoadjuvant-chemotherapy or surgical treatment. We aim to correlate ALN FNAC with histology results to evaluate FNAC's diagnostic accuracy.
Method: All ALN FNAC cases that underwent surgical resection in our Institution between January 2010 and December 2013 were reviewed. FNAC results were correlated with ALN incisional/excisional biopsies and axillary dissections.
Results: FNAC was performed in 625 patients that underwent ALN excision (622 females, 3 males, mean age: 56,5 years-old), 156 following neoadjuvant-chemotherapy. FNAC results were set as positive (n = 330), negative (n = 184), suspicious for malignancy (n = 16) or insufficient for diagnosis (n = 95). Insufficient cases were excluded. Suspicious and neoadjuvant-chemotherapy cases were analyzed separately. Cytohistological correlation was found in 334 non-treated patients. Forty-nine cases were discrepant. The only 2 false-positive FNAC were reviewed and interpreted again as positive (corresponding to isolated tumour cells (ITC) or micrometastases). Ten false-negatives were found to be micrometastases or ITC. The sensitivity was 82,7 %; specificity 98, 2 %; positive predictive value 99,1 %; negative predictive value 69,9 %.
Conclusion: In our Institution, ALN FNAC has high specificity and positive predictive value, remaining a useful pre-therapeutic diagnostic tool. Additional sampling should minimize insufficient and false negative cases.

OFP-03-006
Cytological, clinical and radiological findings in 32 cases of suspected breast cancer recurrence after lipofilling
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Objective: To describe the cytological, clinical and radiological findings in patients with suspected breast cancer recurrence after lipofilling.
Method: We included all patients who underwent fine needle aspiration at our Institution from January 2009 to December 2014 with a clinical and/or radiological suspicion of breast cancer recurrence after lipofilling.
Results: Thirty-two breast lesions were studied from 27 patients (mean age: 52,8 ± 8,5) who underwent lipofilling after mastectomy (81,2 %) or wide local excision (18,1 %). Suspicious lesions appeared after a mean period of 5,2 years after surgery, were mostly located under the previous scar and measured 3–60 mm in diameter (mean diameter: 16,2 mm). Six out of 23 lesions were detected at mammography; 31/32 lesions were detected at ultrasound and 5/5 lesions were detected at MRI. At cytological examination most cases showed steatonecrotic debris (75 %), variably associated to macrophages both isolated (59,3 %) and/or in clusters (28,1 %), adipocytes (43 %), multinucleated giant cells (25 %), and lipophages (18 %). Atypical epithelial cells were described in 4/32 cases (12,5 %), however only in 2/4 cases a diagnosis of cancer was confirmed on histology.
Conclusion: The cytological diagnosis of breast cancer recurrence after lipofilling is challenging, since clusters of epithelioid macrophages could be easily misdiagnosed as atypical epithelial cells.

OFP-03-007
Diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration cytology of pancreatic lesions
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Objective: Endoscopic ultrasound-guided fine needle aspiration cytology (EUS-FNAC) is the most common procedure to obtain cytological specimen of pancreas nowadays. It is minimally invasive, safe and cost-effective. However, discrepancy in cytological and histologic diagnosis sometimes happens. This study was aimed to evaluate the diagnostic accuracy of EUS-FNAC of pancreas.
Method: A retrospective study was performed on 191 cases of pancreatic lesions initially diagnosed by EUS-FNAC with following histological diagnosis between 2010 and 2012 in Department of Pathology, Seoul National University Hospital. Cytologic and surgical diagnoses were categorized into five groups: 'Negative', 'benign', 'atypical', 'malignant' and 'insufficient for diagnosis (IFD)'. Subsequently, 167 cases with diagnosis in both examinations were statistically analyzed for the correlations.
Results: In comparison with surgical diagnosis, cytologic diagnosis were true-positive in 103 cases (61.7 %), true-negative in 28 cases (16.8 %), false positive in 9 cases (5.4 %) and false negative in 27 cases (16.1 %). The diagnostic accuracy was 78.4 %, sensitivity was 79.2 % and specificity was 75.7 %. Although negative predictive value was 50.9 %, positive predictive value was 92.0 %.
Conclusion: Though several limitations exist, EUS-FNAC is a useful and reliable diagnostic tool for evaluation of pancreas lesion.

OFP-03-008

Thyroid versus parathyroid fine needle aspiration cytology: Is there a role for birefringent crystals?

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Objective: In fine needle aspiration cytology, distinguishing a parathyroid pseudofollicular pattern from a follicular thyroid pattern may be challenging, especially without ancillary techniques. Histological studies have described birefringent crystals of calcium oxalate within thyroid follicles and documented their absence in parathyroid specimens; our aim is to assess these findings in cytological samples.
Method: The department database was surveyed from 2005 to 2014. Thyroid and parathyroid (Giemsa and Papanicolau) cytology slides were examined under polarized light microscopy, following confirmatory review of available histology or PTH immunocytochemistry slides. Birefringent crystals were identified and described. Statistical analysis was performed.
Results: We revised 15 parathyroid and 42 thyroid cytology cases (14 follicular neoplasms, 12 follicular lesions of undetermined significance and 16 benign). Birefringent crystals were identifiable in 93 % of parathyroid and on all thyroid slides. Thyroid crystals were broadly distributed and heterogeneous in size and conformation, with larger polyhedral fractured shapes forming aggregates in 38 %. In the parathyroid, miniature shapes prevailed (53 %), scattered over cell nests, and demanding high power observation to detail their round contour.
Conclusion: Despite being present in comparable extent in thyroid and parathyroid cytological specimens, the difference in distribution, size and conformation of birefringent crystals may offer an additional feature to distinguish both.

OFP-03-009

Use of FTA cards for the storage of breast cancer nucleic acid on fine needle cytology samples

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Objective: Storage of nucleic acids is important for DNA-molecular techniques. FTA cards are filter papers that immobilize and stabilize nucleic acids and can be stored at room temperature. The objective of this study was to evaluate whether nucleic acids of breast cancer (BC) cells, obtained by FNC in a clinical setting, may be collected, stored and preserved on FTA cards.
Method: 30 BC, 5 non-Hodgkin Lymphoma (NHL) and 5 benign reactive lymph node (BRH) FNC cells were stored at −80°C and on FTA cards. DNA extraction and PCR were performed on cells at -80°C and on 2 punched disks on the FTA cards. Fifty nanograms of DNA from both stored cells types were used to amplify exon 14 of Jak2 gene.
Results: The means of extracted DNA from BC cells were 28,19 ng/ul for −80 °C and 3,28 ng/ul for the FTA cards. Useful DNA was extracted in 29 cases (97 %) by both methods. DNA extracted from all NHL and all BRH were 37,54 ng/ul and 4,28 ng/ul, respectively. Significant differences were found between −80°C and FTA cards ($p < 0{,}0001$), but no differences were detected between 260/280 nm ratios in BC and NHL/BRH.
Conclusion: FTA cards can be conveniently used for the storage of BC cells obtained by FNC, providing a reliable alternative to traditional methods.

OFP-03-010

Small biopsies in the diagnosis of Langerhans cell histiocytosis

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Objective: Small biopsies, fine needle aspiration biopsy (FNAB) and core needle biopsy (CNB), have emerged as important sampling methods in the diagnosis of musculoskeletal tumours. The clinical presentation and images of Langerhans cell histiocytosis (LCH) may be confused with malignant bone neoplasm and tissue examination is required to make a correct diagnosis. The aim of this study was to test the utility of small biopsies in the diagnosis of LCH.
Method: Nine patients who presented with LCH in the skeleton were initially examined by small biopsies, two by FNAB alone and seven by FNAB and CNB. Five FNAB specimens were prepared as cell blocks for immunocytochemical examinations. Cytological smears, cell block and CNB sections were re-evaluated and correlated to ancillary tests and the final diagnoses.
Results: A correct diagnosis was rendered in seven patients examined by FNAB complemented by immunocytochemical staining on cell block and/or by simultaneously performed CNB. In two patients examined by FNAB alone and without ancillary tests, the cytological diagnoses were inconclusive.
Conclusion: The small biopsies obtained by FNAB in conjunction with CB or/and CNB and complemented by ancillary studies allow a confident diagnosis of LCH and are equal in diagnostic value to open surgical biopsies.

OFP-03-011

Cytohistological correlation of suspicious for malignancy and follicular lesion of undetermined significance of the thyroid gland: A multi-institutional study for assessment of malignancy risk

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Objective: The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) standardizes diagnostic terminology and provides management algorithms for thyroid nodules. The "Follicular Lesion of Undetermined Significance" (FLUS) and "Suspicious for Malignancy" (SM) categories comprehend heterogeneous lesions and entail malignancy in 5–15 and 60–75 %, respectively. This study aimed to assess the risk of malignancy in these categories, through cytohistological correlation.
Method: The databases of 5 institutions were searched for a 2-year period (2013–2014). Fine-needle aspiration (FNA) and corresponding surgical pathology reports were reviewed. Statistical analysis was performed.
Results: A total of 192 FNAs with subsequent thyroidectomy were retrieved, 95 FLUS and 97 SM. Among FLUS, 60 % were neoplasms of follicular epithelium (33 malignant neoplasms with 28 papillary carcinomas, follicular variant - PCFV) and 40 % benign lesions (inflammatory and hyperplastic). Of the SM, 13 % were low grade follicular neoplasms, 68 % malignant neoplasms and 19 % benign lesions.
Conclusion: In our series, the rate of malignancy in SM was comparable to the BSRTC ascribed risk, whereas FLUS cases yielded a higher value than predicted, mainly due to PCFV (29 %). These data imply that FLUS may have a higher risk of malignancy than commonly believed and address the need to research new markers for this category.

OFP-03-012

Fluorescence lifetime imaging in routine cytology

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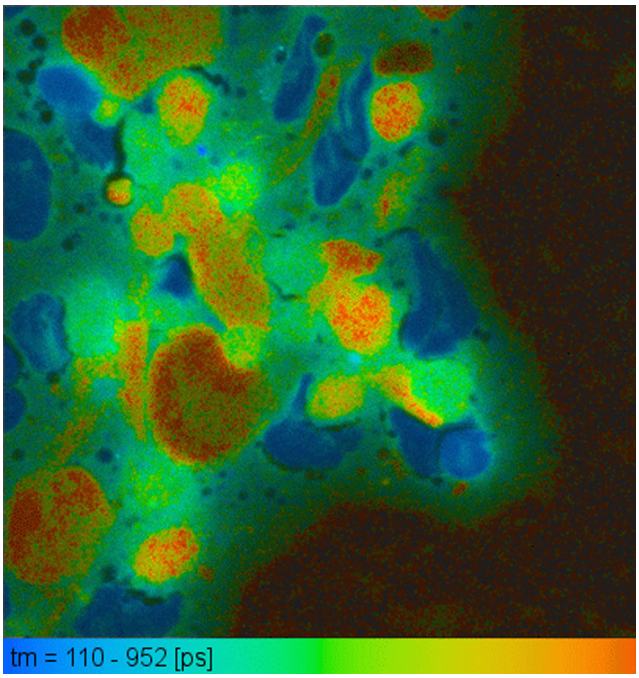
Objective: Fluorescence-lifetime imaging microscopy (FLIM) creates the image contrast with the help of the fluorescence lifetime values transformed in pseudocolors at each pixel of the two-dimensional computerized microscopic image and does not need any staining. The aims of this pilot study was to investigated the utility of the FLIM technique for the examination of unstained cytologic material.

Method: We used tumour imprints or routine bone marrow smears of 20 patients after fixation with formaldehyde vapor. Images were obtained with a confocal microscope equipped with a HPM-100-40 Hybrid detector and 405 nm pulsed diode laser.
Results: In all cases we obtained highly contrasted FLIM images, with clearly distinguishable cellular elements. The obtained shapes and textures permitted to recognize the different cell types. Red blood cells were characterized by the short lifetimes of their hemoglobin component. Cytoplasm and the protein background showed intermediate lifetime values. Fluorescence lifetime of the nuclei of the granulopoetic precursors was considerably longer than in nuclei of erythroblasts. Leukemic blasts of several types of acute leukemia showed considerable variation, generally long lifetime values. In one case of Chediak-Higachi disease, the pathologic cytoplasmic granula were clearly distinguishable. Moreover in that case, intracytoplasmic bacteria could be identified, which were not well visible in the routine cytologic preparations.
Conclusion: The FLIM technique can be applied in routinely acquired unstained cytologic material. The images are contrasted and permit to identify cellular elements. Different lifetime values of nuclear chromatin suggest physicochemical differences of the nuclear organization.

Unstained imprint of oat cell carcinoma:



Monday, 7 September 2015, 08.30–12.00, Meeting Room 6/I
OFP-04 Oral Free Paper Session Breast Pathology

OFP-04-001
Expression of Epithelial to Mesenchymal Transition - related transcription factor ZEB1 in phyllodes breast tumours: An immunohistochemical study
I. Akrida*, V. Bravou, S. Nikou, I. Petrou, S. Kounelis, V. Zolota, H. Papadaki
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Objective: Phyllodes breast tumours consist of epithelial and mesenchymal components. Epithelial-mesenchymal transition (EMT) has been implicated in carcinogenesis. The aim of this study was to investigate the expression of EMT-related transcription factor ZEB1 in mammary phyllodes tumours.
Method: ZEB1 expression was evaluated immunohistochemically in 86 FFPE human phyllodes breast tumours (47/86 benign, 26/86 bordeline and 13/86 malignant). We investigated correlations with tumour histopathology (benign, borderline, malignant), as well as with previously reported immunohistochemical results for EMT markers E-cadherin and integrin-linked kinase (ILK) in a subset (n = 71) of these tumours.
Results: Nuclear immunoreactivity for ZEB1 was detected in both epithelial and stromal tumour cells (83/86 and 77/86 respectively). ZEB1 expression was significantly higher in borderline/malignant tumours (p = 0.003 for epithelial and p < 0.001 for stromal cells). ZEB1 immunoreactivity was correlated to significantly higher loss of epithelial membranous E-cadherin (p = 0.003 for epithelial and p < 0.001 for stromal cells) and to significantly higher nuclear/cytoplasmic expression of ILK (p = 0.005/p = 0.001 respectively for epithelial cells and p = 0.001/p = 0.007 for stromal cells).
Conclusion: ZEB1 is overexpressed in borderline/malignant tumours and is correlated to loss of epithelial marker E-cadherin and to expression of EMT-inducer ILK. Our results suggest that an EMT-like process may be implicated in the pathogenesis of phyllodes breast tumours.

OFP-04-002
Breast cancer stromal elastosis is inversely associated with tumour cells invading blood vessels in a population-based study
Y. Chen*, T. A. Klingen, H. Aas, E. Wik, L. Akslen
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Objective: Screen-detected breast cancers with higher content of stromal elastosis have a better prognosis than predicted from established prognostic markers. We here investigated the association between tumour elastosis and vascular invasion.
Method: We performed a population-based retrospective study of invasive breast cancers (50–69 years) from Vestfold County (2004–2009), including 197 screen-detected and 75 interval cancers. Tumour elastosis was graded as 0–3. Lymphatic vessel involvement (LVI) and blood vessel invasion (BVI) were recorded separately based on immunohistochemical staining (D2-40 and CD31 antibodies).
Results: High content of elastosis was inversely associated with LVI (OR 2.5; p = 0,028) and BVI (OR 3.6; p = 0,038). In univariate survival analyses, low or absent elastosis with BVI positive cases demonstrated significantly reduced recurrence free survival compared to BVI negative cases (p = 0,002). The same trend was seen for LVI positive cases with low or absent elastosis compared to LVI negative cases (p = 0.093). Among tumours with high content of elastosis, no survival differences between positive or negative tumours for BVI or LVI were found.
Conclusion: There is an inverse association between the presence of tumour elastosis and vascular invasion in breast cancers. Absent or low content of elastosis with positive BVI is associated with poor prognosis.

OFP-04-003
Luminal-A breast carcinomas' phenotype is a strong indicator for negative axillary nodes: A cohort study
D. Koumondourou*, E. Nikolatou, K. Kekempanou, P. Ravazoula
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Objective: Lymph node status is one of the most important predictive factors in breast carcinomas. Axillary lymph node dissection has been replaced by sentinel lymph node biopsy for clinically node-negative patients. However recently, luminal-A breast carcinoma subtype is suggested as a potential predictor for negative axillary nodes status.The purpose of our study was to correlate ER, PR, Ki67 and HER-2 expression and tumour subtype with grade and lymph node status.
Method: 846 breast carcinomas (collected during the last 6 years at our pathology lab) were studied and the molecules' expression was evaluated

using immunohistochemistry. All carcinomas were classified as Luminal-A, Luminal-B, Her-2 enriched and triple negative (StGallen 2013).
Results: Presence of positive axillary lymph nodes was strongly correlated with increased Ki67 ($p < 0{,}001$), Grade III tumours ($p < 0{,}001$), as well as with HER-2 enriched and luminal-B phenotype ($p = 0{,}030$ and 0,028 respectively). Luminal-A carcinomas were significantly associated with negative axillary nodes ($p < 0{,}001$). No significant correlation emerged between lymph nodes status and triple-negative phenotype.
Conclusion: Luminal-A carcinomas show dinstinct biological characteristics being the least aggressive subtype not only in their prognosis but also in the rate of nodes' metastases and possibly consist a group of carcinomas in which axillary nodes resection can be omitted.

OFP-04-004
The MCF-7 breast cancer cell line and the chick chorioallantoic membrane. How does bevacizumab modulate this interaction?
S. Comsa*, S. Avram, A. R. Balica, A. M. Cimpean, M. Raica
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Objective: We aimed to evaluate the interraction between the MCF-7 breast cancer cells (MCF-7) and the chick chorioallantoic membrane (CAM) and the ability of bevacizumab to modulate this process.
Method: We implanted MCF-7 onto CAM and added repeatedly bevacizumab into a subset of eggs. We, then, evaluated the morphology of CAMs and the immunohistochemical expression of ER (estrogen receptor), PR (progesterone receptor), VEGF (vascular endothelial growth factor), p53, Ki67, α - smooth muscle actin, E-cadherin, HER2 and Bcl-2.
Results: MCF-7 adhered to the chorion, entered the mesodermal layer and its vessels and stimulated the mesenchymal cells to generate a vasculogenic reaction in the peritumoral zones and to aquire myofibroblastoid features. Onto CAM, MCF-7 developed an ER, PR, p53 and Ki67 negative status. Bevacizumab also inactivated Bcl-2, down-regulated the expression of VEGF and E-cadherin and inhibited vasculogenesis.
Conclusion: MCF-7 recruit the mesenchymal cells for the miofibroblastoid reaction, turning the mesodermal layer of CAM into a proper tumour stroma. The CAM environment changes the MCF-7 molecular profile and sets them into a non-proliferative, but still antiapoptotic state. Although antiangiogenic, bevacizumab might stimulate the epithelial-mesenchymal transition in MCF-7, with the loss of Bcl-2 expression, suggesting the acquisition of a more aggressive status.

OFP-04-005
Breast cancer in the neoadjuvant setting: Histopathologic features that predict treatment response
J. Lobo*, A. Luís, L. Antunes, N. Afonso, A. T. Aguiar, P. Antunes, P. Reis, M. J. Bento, C. Leal
*Porto, Portugal

Objective: To assess pathologic variables that influence breast cancer (BC) response to neoadjuvant treatment (NT).
Method: 127 women with BC submitted to NT (2012–2014) were included. Variables analyzed included molecular subtype (MS) assessed by immunohistochemistry, tumour grade (TG), histologic subtype (HS) and tumour response (TR). Chi-square tests and logistic regression were performed.
Results: Pathologic complete response was achieved in 24 patients (19 %). A significant association between both MS and TG on biopsy and TR was observed ($p < 0{,}001$ and $p = 0{,}006$, respectively). Of the patients with good/complete pathologic response (GPR), 77,4 % were ductal and 63,3 % were grade 3, but only 4,3 % were Luminal A. 91,7, 54,5 and 55,0 % of HER2, Luminal B-HER and Basal-like tumours achieved GPR, respectively. The odds of grade 3 tumours achieving GPR is 11,2 times higher than for grade 1 tumours ($p = 0{,}027$). When joining HER2 and Luminal B-HER tumours in a single group, the odds of these MS achieving GPR is 10,5 times higher than for Luminal A carcinomas ($p = 0{,}006$). On multivariate analysis only MS was found to be statistically significant.
Conclusion: Patients with grade 3, ductal and non-Luminal A carcinomas achieved better TR, highlighting the importance of a good BC pathologic characterization prior to NT to select patients who will benefit the most from it.

OFP-04-006
Breast cancer response to neoadjuvant treatment: Adding information with an intermediate biopsy
J. Lobo*, A. Luís, L. Antunes, N. Afonso, A. T. Aguiar, P. Antunes, P. Reis, M. J. Bento, C. Leal
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Objective: To assess if residual tumour cellularity (RC) evaluated in a biopsy performed halfway through the neoadjuvant treatment (NT) period (4th cycle) is associated with the final tumour response (TR) on surgical specimen (SS). Chi-square test was performed.
Method: 49 women with BC submitted to NT between 2012 and 2014 and that had performed an intermediate biopsy (IB) were included. Patients were assigned into two groups based on RC on IB (high/moderate cellularity, HRC; low cellularity/no tumour, LRC) and on TR on SS (minimal/moderate response, MTR; good/total response, GTR).
Results: RC on IB was significantly associated with TR on SS ($p = 0{,}002$). 72,7 % of patients with LRC on IB had a GTR on SS. A total of 73, 9 % of patients with MTR on SS had already a IB showing HRC and 72, 7 % of patients with GTR on SS had already a IB with LRC. Fifteen women underwent conservative surgery. In this group, 10 had LRC on IB, and 8 of these (80 %) had GTR on SS.
Conclusion: In our series, the information given in advance by IB was significantly associated with the final TR in the breast. IB might be useful to adjust treatment protocols, namely surgical strategies.

OFP-04-007
Folate receptor alpha associated with receptor negative breast cancer and poor prognosis: A preliminary study
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Objective: To examine the expression of FRA and its relationship with clinical outcomes in TRIPLE (-), ER/PR (+)/HER2 (-) and ER/PR (-) / HER2 (+) breast carcinoma subgroups using historical data that lack specific information about FRA expression and clinical outcomes.
Method: Sixty-two cases of high grade infiltrating ductal carcinoma diagnosed at Tepecik Research and Training Hospital were identified and reviewed. The expression of FRA and its relationship with clinical outcomes in TRIPLE (-), ER/PR (+)/HER2 (-) and ER/PR (-) /HER2 (+) breast carcinoma subgroups were evaluated.
Results: The expression of FRA was significantly associated with tumours with ER/PR negativity and was independent of HER2 amplification. FRA expression was apparent in 50 of 62 (80.6 %) primary high grade infiltrating ductal carcinomas and 22 of 24 (91.6 %) TRIPLE (-) tumours, 16 of 18 (88.8 %) ER (-)/PR (-)/HER (+) tumours, 12 of 20 (60 %) ER (+)/PR+/HER2 (-) tumours. The expression of FRA was significantly associated with poor prognosis.
Conclusion: FRA expressing breast cancers may represent a unique and novel molecular subtype of breast cancer that may be amenable to FRA-targeted therapeutic interventions.

OFP-04-008

Digistain: A novel biomarker imaging platform for grading breast carcinoma using routinely processed paraffin sections

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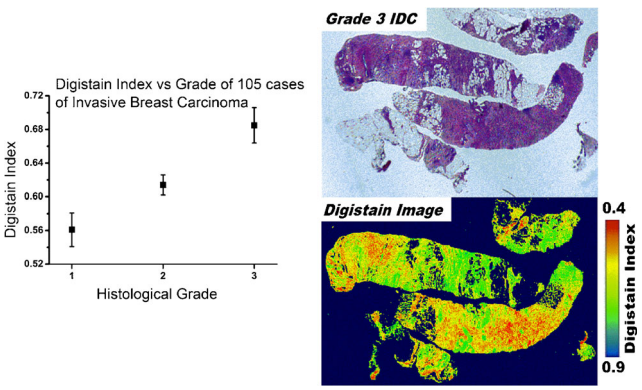
Objective: Digistain is a new technology platform that enables imaging and quantification of a newly conceived biomarker for grading breast carcinoma in routinely processed, unstained paraffin sections without the use of traditional stains or contrasting agents. By recording a unique optical signature to analyze the chemical make-up of a biopsy quantitatively, the technique is unaffected by the subjectivity of traditional grading. Within minutes of loading a slide it yields a highly reproducible and user independent numerical score reflecting the cellularity of the tumour and its nuclear: cytoplasmic ratio. We report here our findings using an objective technique to grade breast tumours using quantitative criteria.
Method: H&E stained sections from excision biopsies of 105 cases of invasive breast carcinoma were reviewed and graded using the Elston-Ellis grading system. Unstained sections from each case were loaded into the Digistain platform to yield a numerical score - the Digistain Index (DI).
Results: The cases were grouped according to histological grading. Mean DIs was calculated for each grade (1,2 and 3) to be 0.56, 0.61, and 0.68 respectively with a maximum standard error of 0.02. The DI spread within each grade was less than that across the three grades, thus validating this index as a viable grading indicator within the context of this study.
Conclusion: We believe the new Digistain approach provides for the first time a cost effective and quantitative measure of tumour grade. This can be developed to deliver an effective assessment of prognosis and recurrence risk beyond traditional qualitative measures based on H&E staining protocols.



OFP-04-009

HER2 discordance between primary Invasive Breast Carcinoma (IBC) and corresponding metastasis

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Objective: HER2 status in primary IBC guides treatment selection and reflects HER2 in corresponding metastasis. However, reported levels of discordance vary significantly. Discordance might be true i.e. biological or a result of either analytical issues or morphologic discrepancies. Aim of the study was to estimate the incidence of true HER2 discordance between primary tumour (PT) and metastasis.
Method: Institutional database was searched for metastatic breast carcinoma patients with HER2 assessed on both PT and metastasis. HER2 status in PT and metastasis was compared. In cases with discordant results HER2 and morphology were reviewed.
Results: 216 cases with HER2 status available in PT and metastasis were identified. Initially, HER2 was discordant in 13 (6 %) cases. Upon revision only 3 (1,4 %) cases were true discordant. In remaining cases discordance was due to discrepant morphology ($n = 4$; 1,9 %), false positive IHC results on either PT or metastasis ($n = 4$; 1,9 %), borderline results in both samples ($n = 1$; 0,5 %) and heterogeneous HER2 in PT while negative in metastasis ($n = 1$; 0,5 %).
Conclusion: HER2 status is highly conserved in metastasis. As majority of discordant results is associated with analytical issues or morphologic discrepancies we suggest that in all discordant cases both HER2 and morphology are reviewed in both PT and metastasis.

OFP-04-010

Comparison of immunophenotypes of primary breast carcinomas and corresponding multiple distant metastases: An autopsy study of 25 patients

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Objective: Analysis of the immunophenotype of primary breast cancers (PBC) and corresponding distant metastases (DM).
Method: Twenty-five PBCs and 91 DMs in 23 organs were collected. Histological slides were reviewed, IHC reactions were performed for ER, PR, Ki67, Her2, supplemented by HER2 FISH.
Results: Nine ER-/PR- tumours developed DMs in 10 organs, while 16 ER+ tumours in 22 organs. Tumours likely lost ER metastasizing to the abdomen ($p = 0.016$) and bones ($p = 0.018$). Loss of PR was more common: in central nervous system ($p = 0.028$), thorax ($p = 0.042$), abdomen ($p < 0.001$) and bone ($p = 0.027$). PBCs were to loose ER ($p = 0.003$) and PR ($p = 0.007$) in liver metastases, and PR in lung metastases ($p = 0.043$). Significant change in Her2 status was not observed. Seven of 25 (28 %) patients (all LuminalA) had DMs with heterogeneous immunoprofile. In their altogether 32 DMs, PR in 20 (62.5 %), ER in 9 (28.1 %) DMs was lost. The later the DM developed the more likely its immunoprofile differed from PBC. DMs in identical organs were more similar to each other differing from PBC.
Conclusion: Metastases responding differently to therapy might possess different mutational landscapes, reflected by IHC. By sampling DMs without causing harm, a better understanding and therapy of progressive BC could be achieved.

OFP-04-011

Gene signatures reflecting vascular proliferation and vascular invasion associate with immunogenic alterations and breast cancer of the basal-like phenotype

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Objective: The need for improved individualized therapy to patients with basal-like breast cancer is urgent. We here explore on genomic alterations associated with gene-signatures reflecting vascular proliferation (VP) and vascular invasion (VI).
Method: Breast cancer gene expression and clinico-pathologic data were accessed from The Cancer Genome Atlas ($n = 520$) and GEO/GSE7390 ($n = 198$). Hierarchical clustering, significance analysis of microarray and gene set enrichment analysis were performed.
Results: A cluster reflecting high VP associated with hormone receptor negativity and Her2 positivity ($P < 0.0005$). Several cancer testis antigens, in particular HORMAD1, were upregulated in the VP-high cluster. In an independent data set, high HORMAD1 was associated with reduced recurrence free survival (HR 1.9/P = 0.02). TGFß and EMT activation, VEGF, PDGF and mTOR activation as well as ER negativity associated

with the VP-high cluster. The VP and VI scores were correlated ($P < 0.0005$/rs = 0.4). Combined cluster information from the VP and VI signatures associated strongly with basal-like phenotype (OR = 8.5/ $P < 0.0005$).
Conclusion: Our findings indicate vascular invasion and increased vascular proliferation in basal-like breast cancer. Cancer testis antigens are upregulated in tumours with high vascular proliferation, and their biological role in basal-like breast cancer and VP needs to be elucidated. Our findings may suggest targets for therapy to basal-like tumours.

OFP-04-012
BRCA1 and PARP1 mRNA expression during progression from normal breast to ductal carcinoma in situ and invasive breast cancer
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Objective: The contribution of DNA damage repair mechanisms to the progression of normal breast to ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC) is largely unknown. We assessed mRNA expression of two important genes associated with DNA repair, BRCA1 and PARP1, in normal breast tissue, DCIS low (G1), intermediate (G2) and high grade (G3), and co-existing adjacent IDC.
Method: Laser microdissection and quantitative real-time PCR was performed on 13 pure DCISs, 19 IDCs with adjacent DCIS component, and 5 normal breast tissue samples.
Results: The expression of BRCA1 mRNA was significantly increased in DCIS G2 (1.6-fold) and DCIS G3 (2.2-fold) relative to normal breast tissue ($P = 0.02$, $P = 0.001$, respectively) and in DCIS G2 (1.7-fold) and G3 (2.3-fold) relative to DCIS G1 ($P = 0.02$, $P = 0.0007$, respectively). No significant differences in the expression of BRCA1 mRNA were found between normal breast tissue and DCIS G1 or between DCIS and the adjacent IDC. No significant differences in the expression of PARP1 mRNA were observed between groups.
Conclusion: Increased BRCA1 mRNA expression (but not PARP1 mRNA) occurs early in the development of breast cancer, i.e., at the noninvasive (DCIS) stage. DCIS G1 belongs to a separate family of precursor lesions with low malignant potential.

OFP-04-013
Embryonic signature in primary breast cancers and associated OSNA positive lymph nodes
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Objective: Cancer cells with stem-like properties have dysregulated self-renewal properties, the ability to develop metastases, an aggressive behavior and chemotherapy resistance. The present study is aimed to evaluate stem-associated gene expression in primary breast cancer (BC) and in the homogenized Sentinel Lymph Node (SLN) previously analyzed by biomolecular OSNA protocol, to verify their role as prognostic and predictive of response markers.
Method: Of 177 patients operated between October 2010 and June 2011, 56 ones (42 infiltrating NST and 14 infiltrating lobular carcinomas) with operable CK19 positive BC and clinically negative evaluation of the axilla were studied. The expression of CD44, SOX2, SOX9 was determined by immunohistochemistry; the gene expression of SOX2 and POU5F1 was determined by RT-PCR in the homogenized SLNs obtained as residuum of the samples analyzed by OSNA technique and stored at −80°C (41 SLN positive, SLNpos, and 15 SLN negative, SLNneg).
Results: SOX2 was expressed in 13 out of 41 primary BC from SLN positive cases and was associated with highly proliferative index (Ki67≥20, $p = 0.044$), with further metastatic axillary lymph nodes ($p = 0.008$) and showed a trend with higher tumour stages. Furthermore, SOX2 was highly expressed in 3 out of 41 SLNpos and in any of 15 SLNneg. POU5F1 was not detected neither in SLNpos nor in SLNneg. CD44 and SOX9 preliminary immunohistochemical results were uneffective for correlation analyses.
Conclusion: Our preliminary data suggest that SOX2 identifies aggressive axillary positive BC. Homogenized from SLNs, used for OSNA analysis, might represent a clinical resource to identify cancer specific genes of prognostic value.

OFP-04-014
Does surrogate molecular subtype of screen detected DCIS have any impact on the long term prognosis?
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Objective: The prognostic impact of molecular subtypes in ductal carcinoma in situ of the breast (DCIS) is yet to be clarified, especially in screen-detected DCIS (SD-DCIS). Our aims are: (i) to re-classify a series of SD-DCIS, using the St Gallen surrogate definitions of molecular subtypes; (ii) to correlate these data with prognosis.
Method: Following local ethical approval, a consecutive series of 338 SD-DCIS, operated between 1993 and 2008 was collected. Of 338, 283 cases were tested with immunohistochemistry for estrogen and progesterone receptors, Ki67 and HER2, and categorized using St Gallen 2013 classification. Clinical and follow up data were obtained. Disease free survival (DFS), disease specific survival (DSS) and overall survival (OS) were calculated.
Results: 46 % of cases were classified as Luminal A, 7 % Luminal B/HER2-, 26 % Luminal B/HER2+, 16 % HER2+ and 5 % Triple Negative (TN). Following this classification no significant differences were found in DFS nor in DSS. However HER2+ cases showed the highest rate of relapses (23.3 %, NS). Surprisingly, OS was significantly shorter in TN cases ($P = 0.003$, HR 7.95).
Conclusion: Regarding DFS and DSS, the results of our study, incorporating up to 10 years follow-up data, failed to demonstrate the prognostic value of St Gallen classification applied for SD-DCIS.

Monday, 7 September 2015, 14.30–16.30, Meeting Room 6/I
OFP-05 Oral Free Paper Session Endocrine Pathology

OFP-05-001
RET mutations in Macedonian patients with pheochromocytoma and paraganglioma: Genotype-phenotype correlations
R. Jovanovic*, S. Kostadinova-Kunovska, V. Janevska, B. Bogoeva, L. Spasevska, D. Trajkov, G. Petrusevska
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Objective: To evaluate RET mutations in pheochromocytomas and paragangliomas.
Method: We tested tumour DNA samples from 15 pheochromocytomas and five paragangliomas for RET mutations in exons 8, 10–16. Immunostainings for Ki-67 and Bcl-2 were performed, and PAS-Scoring for pheochromocytomas.
Results: We found 13 different missense changes (p.R524G, p.C528W, p.G532R, p.V648I, p.S653P, p.M674T, p.A680T, p.Q681P, p.G691S, p.R694Q, p.S696L, p.M700I, p.P720S, a single nucleotide deletion c.2000delC), and 11 synonymous (p.R525R, p.G533G, p.L633L, p.A672A, p.T675T, p.V685V, p.R694R, p.A743A, p.E768E, p.L769L, p.E713E), distributed in 4 exons. p.G691S, p.V648I, p.A680T, p.R694Q, p.E768E, p.L769L and p.E713E are previously published, but for the rest of the sequence changes we were not able to find any records in available

databases neither we could find any published papers. p.G691S (in 3 patients) and p.L769L (in 2 patients) were germline polymorphisms. The mean follow up of the patients was 89,7 months (Min. 14; Max. 158). Three of the patients died during the follow up. Ki-67 expression was significantly higher in tumours with mutations in more than 1 RET exon compared to tumours with no RET mutations and mutation in 1 exon only, as well as, in tumours with damaging RET mutations compared to reminder of the tumours.
Conclusion: RET mutations showed no correlation to the disease outcome.

OFP-05-002
Encapsulated Hürthle cells neoplasm of the thyroid with post-surgical implants in the neck: Clinical, morphological, and molecular analysis of three cases
S. Uccella*, S. La Rosa, G. Dionigi, F. Molinari, M. Frattini, F. Sessa, M. Bongiovanni
*University of Insubria, Surg. and Morphol. Sciences, Varese, Italy

Objective: Mechanical implantation of thyroid tissue can occur due to thyroid surgery and it is considered as a non-malignant lesion. We describe the clinico-pathological, and molecular analysis of three patients with an initial diagnosis of follicular adenoma, Hürthle cell variant (FA-HCT), developing thyroid implants in the neck soft tissues, followed by an aggressive clinical course.
Method: 3 FAs-HCT developing implants in the neck were retrieved in our files. Cytological and histopathological slides of both the primary lesions and of neck implants were reviewed by expert pathologists. Molecular analysis included the following: RAS, BRAF, RET/PTC1, RET/PTC3 and PAX8/PPARgamma.
Results: All lesions were encapsulated and were diagnosed as FAs-HTC at histology by thoroughly evaluation of the tumour capsule and of peritumoural vessels. Neck nodules became evident after a mean of 42 months after thyroid surgery. Nests of oncocytic cells with surrounding foreign body reaction, with no endothelium or lymphoid tissue were observed. All neck lesions relapsed after a mean of 22 months and vascular invasion, was found in only in one patient. In the other two patients vascular invasion became evident in further relapses. Two patients experienced diffuse metastatic disease 12 and 10 years after the first surgery. Molecular analysis performed on primary thyroid FA-HCT and neck lesions showed no alterations.
Conclusion: Oncocytic thyroid implants in the neck soft tissue should be considered as potentially malignant implants, also in the absence of clear-cut signs of malignancy, even in case of a bona fide diagnosis of benign encapsulated Hürthle cells neoplasm of the thyroid (FA-HCT).

OFP-05-003
Clinico-pathologic study of 63 ACTH-secreting lung carcinoids
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Objective: ACTH-secreting lung carcinoids are the most common cause of ectopic Cushing's syndrome (CS). However, the exact prevalence of ACTH expression in lung carcinoids as well as the association between ACTH production and CS onset have not been well established to date. 254 lung carcinoids have been collected with the aim of clarifying these topics.
Method: Twelve tumourlets (TLs), 205 typical (TCs) and 37 atypical carcinoids (ACs) were analyzed using a specific anti-ACTH antibody. The clinicopathological features of ACTH-expressing neoplasms were evaluated.
Results: 63/254 (24.8 %) cases were ACTH positive. Eleven of them (9 TCs and 2 ACs) showed CS with a mean percentage of ACTH-immunoreactive cells of 56 %. The 52 nonfunctioning ACTH-secreting neoplasms (6 TLs, 41 TCs, and 5 ACs) showed a mean percentage of ACTH positive cells of 12 %. Patients with functioning carcinoids were more frequently male (54 versus 27 %) and younger (mean age of 39 versus 61 years) than patients with nonfunctioning neoplasms. No different survival was observed between the two tumour categories. The mean diameters were 1.2 and 2.2 cm for functioning and nonfunctioning neoplasms, respectively. The mean mitotic counts x 10HPF were 1.43 and 0.88 and the mean Ki67 indices were 4.7 and 2 % for functioning and nonfunctioning neoplasms, respectively.
Conclusion: ACTH expression in lung carcinoids is not rare and is not always associated with the presence of CS. Patients with CS are more frequently males and younger, with smaller tumours. The survival between functioning and nonfunctioning ACTH-producing carcinoids was not statistically different.

OFP-05-004
The role of c-Met in pancreatic neuroendocrine neoplasms: Human tissue and cell line-based results
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Objective: C-Met is a membrane receptor with tyrosine kinase activity. Overexpression and activation lead to tumour cell migration and increased metastatic capability. It has been described as resistance mechanism in sunitinib treated RIP-Tag2 mice via hypoxia-related regulation mechanisms.
Method: We used a TMA comprising 173 primary human pancreatic neuroendocrine neoplasms (pNEN) to assess the clinicopathological role of c-Met expression and its relation to tumour hypoxia. Immunohistochemical stainings for c-Met, Hif-1α, CA9, GLUT1 and CD34 were correlated with established prognostic markers and outcome. C-Met and phospho-Met levels in BON1 and QGP-1 cell lines were measured by Western blot under hypoxic conditions with and without sunitinib treatment.
Results: 38 of 173 pNEN showed immunohistochemical staining for c-Met. C-Met expression correlated with Hif-1α ($p = 0.031$), MVD ($p = 0.023$), prognostic markers, relapse ($p = 0.018$) and survival ($p = 0.008$). No correlation was found with CA9 ($p = 0.072$) and GLUT1 ($p = 0.859$). Short term upregulation under hypoxic conditions was found in BON-1. Hypoxia and sunitinib treatment had no effect on phospho-Met levels in these cell lines.
Conclusion: C-Met is expressed in a subgroup of pNEN and correlates with single hypoxia markers, prognostic markers and adverse outcome. Nonetheless, a mechanistic link between c-Met expression and activation by hypoxia or sunitinib treatment could not be detected in cell lines.

OFP-05-005
Histone Deacetylase (HDAC) inhibitors as potential anticancer drugs in Neuroendocrine Carcinomas (NEC) of cervix and endometrium
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Objective: HDAC inhibitors are an emerging class of drugs whose action has been demonstrated in non-gynecologic neuroendocrine cancers and in cervical/endometrial cancer cell lines. HDAC 1, 2 and 6 immunohistochemical expression in uterine NECs, a rare type of carcinoma, was evaluated to identify patients who may benefit from this treatment. HDAC regulates PAX5 transcription, being its expression commonly found in non-gynecologic NECs and may also be a therapeutic target.

Method: Thirteen cases of previously characterized uterine NECs (1999 to 2015) were reviewed. HDAC 1, 2 and 6 and PAX5 immunohistochemistry was performed in a tissue microarray.
Results: Twenty-two samples, comprising cervical (n = 5) and endometrial NECs (n = 7), metastases (n = 7) and non-NE components of mixed carcinomas (n = 3) were analyzed. All samples were PAX5 negative. HDAC 1 and 6 were positive in all cases. HDAC 2 was positive in all but one endometrial NEC.
Conclusion: Negative PAX5 staining can be useful in the assessment of NEC origin as it is usually expressed in NECs of other organs. HDAC expression suggests the potential usefulness of HDAC inhibitors in the treatment of uterine NEC. Translational studies should clarify whether this expression is predictive of response to treatment.

OFP-05-006

Somatostatin receptor subtype 2A expression: correlation with clinicopathologic characteristics of gastric neuroendocrine neoplasms

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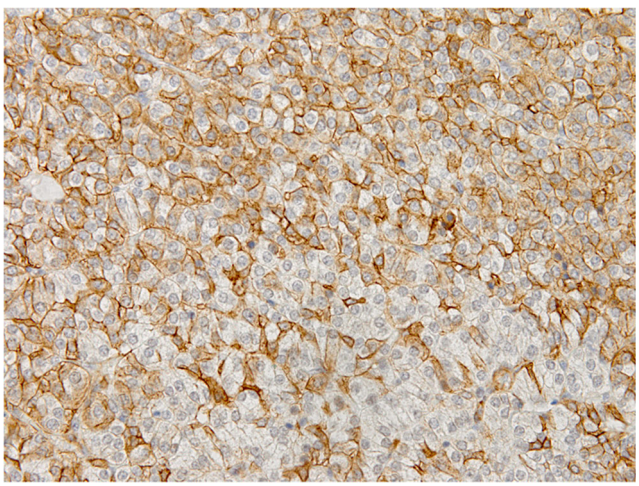
Objective: The aim of the study was to determine the immunohistochemical expression levels of the somatostatin receptor subtype 2A (SSTR 2A) in patients with gastric neuroendocrine neoplasms (NENs) and to investigate their association with clinicopathological parameters, specific type, grade, Ki67 expression, and disease outcome.
Method: Expression of SSTR2A (clones UMB-1) was retrospectively studied by immunohistochemical analysis in formalin-fixed and paraffin-embedded gastric NEN surgical specimens from 39 patients and correlated with the clinicopathological features, and outcome.
Results: High levels SSTR2A expression were observed in 53.8 % of gastric NENs (21/39) with strong membrane staining.The positive tumour cell population ranged from 15 to 90 %. The SSTR2A score was 2/3 in 64.3 % (9/14) of G1 NETs, 53.3 % (8/15) of G2 NETs, and 40.0 % (4/10) of NECs. The decreased levels of SSTR2A in gastric NENs were significantly correlated to the deep local invasion (p = 0.033), median tumour size (0.0048) and high rates of Ki67 index (0.027). SSTR2A score was not associated significantly with desease outcomes.
Conclusion: The current analysis of clinicopathologic factors in patients with gastric NENs confirms the relationship of high SSTR2A expression with reduced NET aggressiveness and provides the basis for its further study as a predictive marker for somatostatin analog therapy in a group of receptor-positive NECs.

SSTR2A-positive G1 NET:



OFP-05-007

Idiopathic pulmonary neuroendocrine cell hyperplasia and tumourlets till typical carcinoid tumour: The spectrum observed in three surgical specimens

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Objective: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) and tumourlets are proliferations of neuroendocrine cells, smaller than 5 mm and not associated with known lung disease. The former lesion is confined to the bronchial/bronchiolar epithelium while in tumourlets, the cells have broken through the basal membrane. Three cases of DIPNECH and tumourlets associated with typical peripheral carcinoid tumour, without underlying lung disease, illustrate this spectrum.
Method: Three female patients 60, 72 and 84 years old had CT-scans showing well-defined pulmonary nodule, respectively with 2.2, 1.6 and 1.4 cm. Two patients underwent surgical biopsy and one, lobectomy.
Results: Macroscopic examination showed whitish or brownish lobulated tumours, corresponding to well differentiated neuroendocrine neoplasms with less than 2 mitosis/2mm2 and without necrosis; diffuse staining for CD56, chromogranin A and CK7 was demonstrated with Ki-67 positivity under 4 %. In the remaining tissue, bronchial wall neuroendocrine cell hyperplasia and several nodules with less than 5 mm, with identical morphological and immunohistochemistry features, were observed. Remnant pulmonary parenchime had preserved morphology. The patients are well and in clinical follow-up.
Conclusion: The diagnosis of the spectrum of typical carcinoid associated with DIPNECH and tumourlets in the lung without other subjacent disease has only been demonstrated rarely, and these cases illustrate the peripheral neuroendocrine cells potentiality.

OFP-05-008

Thyroglobulin wash testing in the monitoring of patients with Thyroid Carcinoma

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Objective: 5–20 % patients treated for differentiated thyroid carcinoma (DTC) develop metastases to the neck lymph nodes. Ultrasound-guided fine needle aspiration biopsy (FNAB) is a routinely used method in the examination of suspicious lymph nodes. The measurement of thyroglobulin (Tg) levels in needle washout fluids (FNAB-Tg) has been reported to increase the diagnostic accuracy of FNAB.
Method: 132 patients who underwent DTC surgery from 1980 to May 2014 were followed-up by ultrasound-guided FNAB and FNAB-Tg measurements of cervical lymphadenopathies. Results were compared to the histology of removed lymph nodes and to clinical follow-up.
Results: 26 of 35 patients with elevated FNAB-Tg levels and positive cytology had histologic confirmation of metastasis. In one patient with negative cytology but elevated FNAB-Tg, histologic examination of lymph node disclosed cystic metastasis of papillary carcinoma. FNAB-Tg levels were not elevated in 5 patients with positive cytology; three of them presented with cervical lymphadenopathy shortly after thyroidectomy and two had cervical metastases from another malignancy.
Conclusion: Ultrasound-guided FNAB alone is not sensitive enough to detect all metastatic lymph nodes. FNAB-Tg measurement in conjunction with FNAB of suspicious neck lymph nodes, increases diagnostic accuracy of FNAB in the follow-up of patients with DTC.

OFP-05-009

Impact of Ki-67 proliferative index on survival in patients with typical and atypical pulmonary carcinoids

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Objective: Pulmonary carcinoids are separated into typical (TC) and atypical (AC) based on mitotic count and presence of necrosis, according to the WHO. Whereas for gastroenteropancreatic neuroendocrine tumours grading is applied based on mitotic counts and Ki-67 index, the use of Ki-67 for grading pulmonary carcinoids is still under debate. Our aim was to evaluate the prognostic impact of Ki-67 assessment in a multicenter cohort.
Method: Ki-67 was analyzed in 203 WHO classified carcinoids (149 TCs, 54 ACs), using digital image analysis (Leica Qwin program; ≥ 4500 cells counted) and manual analysis (500 cells counted). The frequency of Ki-67-positive cell nuclei was correlated with overall survival by univariate analysis and in comparison to clinical data by multivariate analysis.
Results: Ki-67 index was significantly higher in ACs than in TCs for both methods ($P \leq 5.6e{-}5$). Using a 2.5 % cut-off (manual counting) or a 1 % cut-off (digital analysis), a significant difference in overall survival was observed ($P \leq 0.0023$). Multivariate analysis revealed stage, age at diagnosis and digital Ki-67 index as independent predictors of outcome ($P = 0.00011$, 0.014, 0.053, respectively).
Conclusion: Our study underlines the usefulness of Ki-67 in addition to mitotic count in prediction of pulmonary carcinoid prognosis. This would be especially valuable in evaluation of small biopsy specimens.

Monday, 7 September 2015, 17.00–19.00, Blue Hall
OFP-06 Oral Free Paper Session Gynaecological Pathology

OFP-06-001

HER2-Neu, P53, MIB1 and PAX8 immunoexpression in primary serous fallopian tube carcinomas in correlation with clinicopathological prognostic parameters

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Objective: A previous review of primary serous fallopian tube carcinoma (PSFTC) from a multi-institutional study identified several poor prognosis indicators such as tumour grade, depth of invasion, presence of lymph node metastases and advanced stage disease. The aim of this study was to characterize the immunohistochemical profile of PSFTC and to correlate it with clinicopathological prognostic parameters.
Method: Immunohistochemical staining for HER2-neu, p53, MIB1 and PAX8 was performed. The results were correlated with clinical information (8 years median follow-up).
Results: Of 70 patients, 5 had low-grade and 65 high-grade PSFTC. There was a statistically significant higher expression of HER2-neu and p53 in high-grade compared with low-grade PSFTC. The expression of PAX8 was positive in 78.5 % of cases. Mean MIB1 index was 52.3 % in high-grade and 19.5 % in low-grade tumours. Overexpression of HER2-neu correlated with tumour stage (p:0.010), tumour grade (p:0.003), presence of lymph node metastasis (p:0.015) and survival (p:0.02) but not with depth of invasion (p:0.61) or patient's age (p:0.48). There was no association between p53, MIB-1 or PAX8-positivity and tumour size, patient's age, stage or survival.
Conclusion: HER-2/neu may be involved in progression of PSFTC. These data contribute to a better understanding of the molecular carcinogenesis of PSFTC and possible new therapeutic approaches.

OFP-06-002

Genomic profile analysis of uterine smooth muscle tumours by Comparative Genomic Hybridization: A useful diagnostic tool in challenging lesions

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Objective: The diagnosis and management of uterine smooth muscle tumours with uncertain malignant potential (STUMP) is often challenging. We tested the hypothesis that genomic analysis by array-CGH could split STUMP in a benign group with scarce chromosomal alterations akin to leiomyoma (LM) and a malignant group with high chromosomal instability akin to leiomyosarcoma (LMS).
Method: 29 FFPE uterine STUMP were analyzed by Array-CGH. A group of 10 uterine LM and 10 uterine LMS served as controls. The Genomic Index (GI) was calculated for each profile as follows: $GI = A^2/C$, where A is the total number of alterations (segmental gains and losses) and C is the number of involved chromosomes.
Results: The mean age was 50 years (range, 24 to 85) and the median tumour size 7.7 cm. The follow-up ranged from 12 to 156 months (average 70 months).The reference group of LM presented a flat genomic profile with no or only very few sporadic alterations [Fig.1].The group of LMS showed a rearranged chromosome profile with numerous intrachromosomal breaks. By comparing GI in LM and LMS a threshold of 10 was assessed below which non-recurring STUMPs were found and over which STUMPs with recurrences and unfavorable outcomes were recorded.
Conclusion: GI splits the STUMP category in two groups of tumours with different outcomes: a group comparable to LM and another similar to LMS, but more indolent [Fig. 2].In our STUMP series, genomic analysis by array-CGH is an innovative diagnostic tool for problematic smooth muscle uterine lesions, complementary to the morphological evaluation approach.

Figure 1.
Penetrance plots.
Genomic profiles of the LM (A) LMS (B), STUMP with GI < 10 (C) and STUMP with GI > 10 (D)

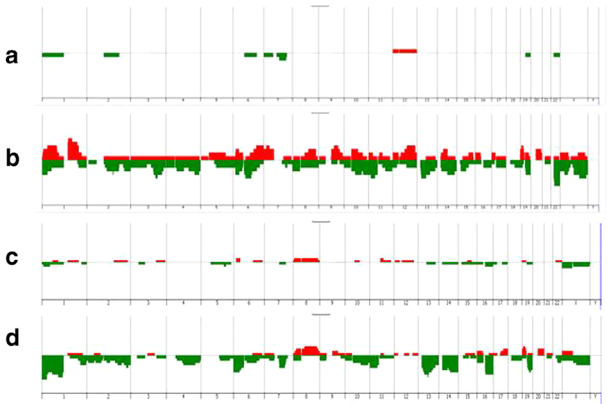
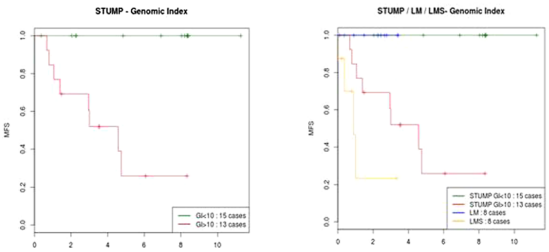


Figure 2
Kaplan-Meier analysis of metastasis-free survival for STUMP (A) and for STUMP, LM and LMS (B) according to genomic index (GI).



OFP-06-003

A selective biomarker panel increases reproducibility in endometrial biopsy diagnosis

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Objective: Grading and histologic typing of endometrial cancer in biopsy material has a direct impact on the decision to perform lymphadenectomy and/or omentectomy in many cancer centers. Endometrial biopsies are among the most common general surgical pathology specimens. Multiple studies have shown that biopsy diagnosis suffers from a lack of reproducibility. Although many biomarkers have been proposed, none have been demonstrated to improve diagnosis in the biopsy setting.
Method: In this study, 70 biopsies with endometrial carcinoma were supplemented with a biomarker panel consisting of ER, PR, P53, and DNA-ploidy. A representative H&E slide was digitally scanned and made available to 12 gynecologic pathologists in four Nordic countries: Finland, Denmark, Sweden, and Norway. Reviewers diagnosed the cases both before and after being provided with the biomarker results.
Results: Interobserver percent agreement and Cohen's kappa improved from 75.8 % (κ = 0.52, moderate) to 84 % (κ = 0.68, substantial) with inclusion of the biomarker panel. There was no statistical improvement between a reflex (84 % agreement) and a reflective testing algorithm (82.9 % agreement), suggesting selective use of biomarkers is appropriate. The difficult cases were almost exclusively high-grade tumours. Finally, a multivariable model indicated that only P53 and DNA-ploidy, in conjunction with H&E review, had an impact on the decision to up- or downgrade cases.
Conclusion: A selective biomarker panel of p53 and DNA ploidy improved interobserver agreement in endometrial biopsy classification. Reflex use of biomarkers was not necessary.

OFP-06-004

Intraoperative molecular assesment for sentinel lymph node metastasis in endometrial carcinoma using One-step Nucleic Acid Amplification (OSNA) assay

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Objective: To evaluate the efficacy of one-step nucleic acid amplification (OSNA) for intraoperative diagnosis of sentinel lymph node (SLN) metastasis compared with histopathological examination in patients with endometrial carcinoma (EC).
Method: A total of 53 SLNs from 20 patients with low- or intermediate-risk EC were enrolled. The central 1-mm portion of each node was subjected to semi-serial sectioning, sliced at 200-μm intervals and examined by H&E and cytokeratin 19 immunohistochemical staining, and the remaining tissue was analyzed by OSNA using CK19 mRNA. The accuracy of OSNA assay was evaluated based on histopathological diagnosis.
Results: Two histologically-positive SLNs were also positive by OSNA analysis. When the cut-off value was set at 250 copies/μL, eight histologically-negative cases were positive by OSNA analysis (copy number range, 270–2200 copies/μL). Among them, we detected two true false-positive cases corresponding to benign epithelial inclusions in two SLNs from the same patient. The OSNA assay had a sensitivity of 100 %, a specificity of 84.3 %, and a negative predictive value of 100 %.
Conclusion: The OSNA assay, which shows high sensitivity and specificity, suggests the possibility to be used as a novel tool for the molecular detection of SLN metastasis in EC patients. Further large scale study to validate our results is warranted.

OFP-06-005

Targeted genomic profiling reveals recurrent KRAS mutations in mesonephric carcinomas of the female genital tract

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Objective: The aim of this study is to examine the molecular alterations in mesonephric carcinoma (MCA), a rare form of gynecologic cancer, to identify driver mutations and potentially therapeutically targetable mutations.
Method: This study consisted of 16 patients with MCA. Genomic DNA was isolated from tumour samples and a targeted next generation sequencing assay was performed to detect mutations, copy number variations and structural variants by surveying exonic DNA sequences of 300 cancer genes and 113 introns across 35 genes.
Results: 81.2 % of MCA (13/16) had either a KRAS (12) or NRAS mutation (1). Mutations in chromatin remodeling genes (ARID1A, ARID1B, or SMARCA4) were present in 62.5 % of cases. Only one case harbored a mutation in TP53.
Conclusion: Unlike cervical and endometrial adenocarcinomas, which harbor KRAS/NRAS mutations in 7 and 25 % of cases respectively, this is the most common molecular aberration detected in MCA (81.2 % of patients). Targeted inhibitors of the RAS/MAPK pathway may be useful in treatment of MCA. MCA are also characterized by frequent mutations in chromatin remodeling genes while TP53 mutations are uncommon.

OFP-06-006

HLA ligandome analysis of high-grade serous ovarian carcinomas identifies potential candidates for a multipeptide vaccine

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Objective: The goal of our study was to use HLA ligandome analysis to identify tumour-associated antigens (TAA), as potential candidates for a multipeptide vaccine, and analyze their correlation with T-cell subsets and prognosis in high-grade serous ovarian carcinoma.
Method: Tumour-associated and HLA presented peptides were identified by a combined approach of immuno-affinity-chromatography of HLA bound molecules, mass spectrometry and immunogenicity analysis. Finally, the combined prognostic effect of tumour infiltrating lymphocytes (TILs) and the expression of specific antigens was evaluated with immunohistochemistry in a tissue microarray of 136 cases of high-grade serous OvCa.
Results: The most commonly presented antigens were CA-125, the CA-125 ligand Mesothelin, as well as antigens with well known immunoevasive functions like Galectin 1 and Indoleamin (IDO). High expression of CA-125, IDO and Galectin by immunohistochemistry were able to further enhance the prognostic effect of CD3 positive TILs. In contrast, high expression of Mesothelin antagonized the prognostic effect on the T-cell response.
Conclusion: The combined approach of HLA-ligandome analysis and immunohistochemical analysis not only allows analyzing the interplay of immune cell infiltrates and tumour antigens but is a valuable tool for the development of a multipeptide vaccine for ovarian cancer.

OFP-06-007

Metastatic ovarian serous carcinoma of the breast: Report of two cases and review of the literature

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Objective: Metastatic tumours of the breast account for <3 % of all breast malignancies. The differentiation of ovarian serous papillary carcinoma

metastasis, which is the most common malignancy metastasizing to the breast, from primary breast tumour may be challenging. Herein, we report two ovarian serous papillary carcinomas metastatic to the breast, both of whom with a known ovarian carcinoma diagnosis at the time of presentation.
Method: The first case is a 66 year old female with a mass in her left breast. The second case is a 47 year old female with a mass in the axillary tail of her left breast.
Results: Histologically, invasive tumour with a predominant papillary/micropapillary architectural pattern was apparent. There was no in situ carcinoma. Immunohistochemically both tumours were ER, WT1, P53, P16, PAX8 positive, PR, Cerb-B2 negative. GCDFP15 was focally weak positive in the first case and negative in the second. Both cases were diagnosed as ovarian serous papillary carcinoma metastatic to the breast.
Conclusion: The morphological and the immunohistochemical features of primary breast cancer and ovarian serous carcinoma may overlap. Although differentiation may be even harder in poorly differentiated tumours with an unknown history, correct diagnosis is crucial because the treatment modalities of these tumours are totally different.

OFP-06-008
Triage for HSIL+/CIN2+ women in type 16- or/and 18-positive primary HPV-based screening using cytology p16/Ki67 test: A pilot study

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Objective: To identify patients with risk of HSIL+/CIN2+ using double staining (DS) p16/Ki67 test among women with type 16- or/and 18-positive HPV status in cervical cancer HPV-based primary screening.
Method: 46 cases of type 16 or/and 18 HPV-positive women were involved to our study according with the ACS, ASCCP and ASCP interim clinical guidance for primary cervical cancer screening. All women were referred to colposcopy and biopsy. Random biopsy and endocervical sampling were performed in all cases. In colposcopy-positive cases the directed biopsy was performed. Simultaneously, in all patients immunocytochemistry double staining p16/Ki67 CINtec PLUS test was applicated.
Results: 16 cases with HSIL+/CIN2+ histology results were identified. Cyto-p16/Ki67 test was positive in 26 cases. All HSIL+/CIN2+ positive cases were p16/Ki67 positive. Positive predictive value/negative predictive value of p16/Ki67 DS was 62 %/100 %. The sensitivity/specificity of p16/Ki67 was 100 %/67 %. PPV type 16- or/and 18-positive HPV test was 35 % and was significantly lower than observed in p16/Ki67 DS.
Conclusion: Compared PPV in p16/Ki67-positive and type 16- or/and 18-positive HPV test were 62 and 35 %. It can indicate that p16/Ki67 DS is a good biomarker for triage HSIL+/CIN2+ and can be effective in performing less unnecessary medical procedures (colposcopy and cervical biopsy).

OFP-06-009
Clinicopathological and immunohistochemical study of Seromucinous Borderline Tumours of the ovary (SMBT)

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Objective: Seromucinous tumours (SMT) of the ovary were recently classified as a distinct entity by the World Health Organization (WHO). Mucins have been studied in normal gynecological tissues and neoplasms, being its expression correlated with cell differentiation and tumour progression. Our aim was to characterize the clinicopathological features and the mucin's immunohistochemical profile of a cohort of seromucinous borderline tumours (SMBT).
Method: Between 2000 and 2013, all cases diagnosed as ovarian borderline tumours were reviewed. From a total of 85 cases, 16 met the criteria of the 2014 WHO for SMBTs. A tissue microarray was built and stained with MUC2, MUC4, MUC5AC, MUC6, MUC16 (CA125), CDX2, SOX2 and WT1 antibodies.
Results: The clinicopathological profile and the immunohistochemical results are shown in Table 1.
Conclusion: SMBTs are predominantly diagnosed as low stage disease and associated with a benign course. Mucin expression is very close to the normal mucin profile of endocervical glands, and neither the mucins nor the transcription factors associated with intestinal differentiation were found in this tumour type.

Table 1:

	Clinicopathological summary								
	Age (years)	Serum CA125 (U/mL)	FIGO stage	Laterality	Size (cm)	Endometriosis	Microinvasive carcinoma <5mm	Implants	Follow-up (months)	Status
Patients N=16 Tumors N=19	22-61 Median: 38	Normal (<35): 5/13 (38%) High (37-1255): 8/13 (62%)	IA=6/14 (43%) IB=1/14 (7%) IC=3/14 (22%) IIA=2/14 (14%) IIB=1/14 (7%) IIC=1/14 (7%)	Bilateral 4/16 patients (25%)	3-14 Median: 6	5/19 tumors (26%)	1/19 tumors (5%)	Non-invasive 4/16 patients (25%)	6-141 Mean: 53	AWD: 13 DOC: 1 LFUP: 2

	Immunohistochemistry results							
	CA125	WT1	CDX2	MUC2	MUC4	SOX2	MUC5AC	MUC6
	18/18 (100%)	19/19 (100%)	0/19 (0%)	0/19 (0%)	18/18 (100%)	2/19 (10%)	3/18 (17%)	13/18 (72%)

AWD: alive without disease; DOC: death of other cause; LFUP: lost for follow up

OFP-06-010
Forkhead Box M1 (FOXM1) and Forkhead Box O3a (FOXO3a) expression in cervical carcinoma

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Objective: Inactivation of FOXO or overexpression of FOXM1 has been associated with tumourigenesis, cancer progression and metastasis. Our aim was to evaluate the FOXM1 and FOXO3a in a series of cervical carcinomas and to correlate its expression with the clinico-pathological data.
Method: Nuclear and cytoplasmic immunoexpression of FOXM1 and FOXO3a were assessed in tissue microarrays from 122 cervical carcinomas. The clinical data was reviewed and statistically analyzed (chi-square test).
Results: We evaluated 81 squamous cell carcinomas (SCC) and 41 adenocarcinomas (ADC), of which 12,3 % were in situ, and at the end of follow up period (mean = 42 months) recurrence and death by the disease occurred in 11,6 and 21,4 %, respectively. The clinico-pathological data and immunostainings results are shown in Table1. Combined expression of FOXM1/FOXO3a was associated with histological type (p = 0,046). Nuclear expression of FOXO3a and cytoplasmic FOXM1 in ADC are associated with poor prognosis (p = 0.025 and p = 0.020, respectively). Loss of nuclear FOXM1 was significant associated with lymph-node metastasis in SCC (p = 0,042) and cytoplasmic FOXM1 was associated with distant metastasis in ADC (p = 0,041).
Conclusion: In cervical carcinomas, transcription factors FOXM1 and FOXO3a are overexpressed and correlated with cancer progression, metastatic behavior and disease survival.

Table1:

Tumor types	FIGO STAGE	Lymph node metastasis	Status	Nº of cases evaluated	FOXM1 nuclear (+)	FOXM1 cytoplasmic (+)	FOXO3a nuclear (+)	FOXO3a cytoplasmic (+)
SCC	≤IB1 - 35 (43,2%) >IB1 - 46 (56,8%)	13 (18,6%)	AWoD 47 (68,1%) DOD -15 (21,7%) AWD - 2 (2,9%) DOC - 3 (4,3%)	Invasive (n=70)	48 (69,6%)**	52 (75,4%)##	33 (49,3%)	30 (44,8%)
				Total (n=81)	55 (69,6%)*	58 (73,4%)#	34 (45,9%)	31 (41,9%)
ADC	≤IB1 - 22 (53,7%) >IB1 - 19 (46,3%)	6 (16,2%)	AWoD -19 (55,9%) DOD - 10 (29,4%) AWD - 4 (11,8%) DOC - 1 (2,9%)	Invasive (n=37)	32 (86,5%)**	15 (40,5%)##	21 (56,7%)	17 (45,9%)
				Total (n=41)	35 (87,5%)*	16 (40%)#	22 (55%)	18 (45%)

SCC – Squamous cell carcinoma; ADC – adenocarcinoma; *p=0.032; **p=0.004; #p=0.0004; ##p=0.049.

LyNM (lymph node metastasis); AWD (alive with disease); AWoD (alive and without disease); DOC (died of other cause); DOD (died of disease).

OFP-06-011

Inter-observer agreement in assessment of response to neo-adjuvant chemotherapy in tubo-ovarian high-grade serous carcinoma

N. Singh*, I. Said, A. Faruqi, S. Leen, W. G. McCluggage, L. Hirschowitz, R. Ganesan, C. B. Gilks, G. Trevisan, S. Boehm, J. Vella
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Objective: To assess inter-observer agreement in assigning a chemotherapy response score (CRS) in tubo-ovarian high-grade serous carcinoma (HGSC). This recently described scoring system, based on omental histology in interval debulking surgery (IDS) specimens after neo-adjuvant chemotherapy (NACT) for HGSC, stratifies patients into different prognostic groups based on progression-free and overall survival, providing opportunities for early treatment modulation.
Method: After online training (http://www.gpecimage.ubc.ca/aperio/images/crs), all omental sections (4-10 slides) from 40 cases were scored independently by each study pathologist, including trainees and consultants, according to published criteria. CRS1: Mainly viable tumour with minimal regression limited to a few foci. CRS2: Multifocal or diffuse regression ranging from viable tumour in sheets, streaks or nodules, to extensive regression with multifocal residual tumour which is easily identifiable. CRS3: Complete or near-complete response with no residual tumour OR minimal irregularly scattered tumour foci seen as individual cells, cell groups or nodules up to 2 mm in maximum size.
Results: There was good agreement in CRS assignment as follows: absolute agreement in 82.5 % cases, kappa score 0.86 and Kendall's coefficient of agreement 0.968.
Conclusion: CRS assignment is highly reproducible among pathologists, irrespective of experience. This allows uniform treatment response evaluation applicable in routine clinical and trial settings.

OFP-06-012

Morphological features associated with POLE mutations: Implications for risk assessment in endometrial carcinoma

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Objective: We sought to identify histomorphological parameters of endometrial carcinomas (EC) harboring Polymerase Epsilon (POLE) mutations.
Method: 47 POLE mutated cases were identified by sequencing 500 ECs. H&E slides were reviewed for 43/47 cases and evaluated for a range of histomorphologic criteria. Risk assessment variables for decisions about adjuvant therapy were recorded. p53 mutation and Mismatch Repair status were assessed by immunohistochemistry. The nuclear grade and mitotic count were compared to an unselected cohort of EC cases.
Results: These tumours exhibited high grade nuclear features even though architectural features were typically low-grade. Similar to MSI-H ECs these tumours were associated with peritumoral lymphocytes (~79 %), intratumoral lymphocytes, and tumour giant cells. The mitotic count and nuclear grade was statistically higher than in the unselected cohort. Adjuvant radiotherapy would be offered in ~ 79 % of patients and adjuvant chemotherapy in 41 %, based on stage, grade, lymphovascular invasion and histotype.
Conclusion: POLE mutated tumours have some morphologic differences but overlap with other EC subtypes, therefore, diagnosis by routine H&E is not feasible. Decision making for adjuvant treatment, when applied to POLE-mutated tumours, results in significant numbers of patients receiving adjuvant therapy, even though these tumours are associated with an excellent prognosis.

Monday, 7 September 2015, 17.00 – 19.00, Hall 1
OFP-07 Oral Free Paper Session Uropathology

OFP-07-001

Utility of ERG in prostate cancer and high-grade prostatic intraepithelial neoplasia

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Objective: The usefulness of ERG expression in the concept of differential diagnosis of prostate neoplasms.
Method: The radical prostatectomy specimens from 100 patients (2011–2012) were investigated using immunohistochemical staining of ERG. The presence of high-grade prostatic intraepithelial neoplasia (HGPIN) and prostate cancer in the specimens was confirmed by a moderate to strong expression of P504S and presence (in HGPIN) or absence (in prostate carcinoma) of 34βE12.
Results: Expression of ERG was observed in 46 % of all carcinomas and only 21 % of HGPIN. 8 patients (8 %) presented heterogeneous ERG expression: both a high expression and no expression at all. All 6 cases with cribriform lesions, highly suspicious for intraductal carcinoma (the extension of malignant cells through the pre-existing lumina of the prostate), were found to be ERG-positive.
Conclusion: Low incidence of ERG-positive HGPIN indicates that this marker has a limited role for differential diagnosis of intraepithelial neoplasia and benign lesions that can be misinterpreted as HGPIN. However, ERG can potentially be used for distinguishing between HGPIN and intraductal carcinoma. The reported study was supported by RFBR, research project No. 15-04-03629 a.

OFP-07-002

Evaluating the capacity of novel image analysis algorithms in estimating prostate cancer patient outcomes

P. Jackman*, W. Watson
*University College Dublin, Ireland

Objective: Image analysis offers a mechanism for objective, reproducible and repeatable biopsy interpretation and also the extraction of novel features imperceptible to the human eye. These new features could add further information to stratify patients into appropriate treatments and thus reduce overtreatment of indolent patients.
Method: Digital images of prostate tissue sections from the Irish Prostate Cancer Research Consortium cohort were analyzed using novel image tissue features of entropy and symmetric wavelets. Similarly cell nuclei size and distributions were calculated along with luminal and stromal distributions. The patient outcomes of this cohort are known as is clinical information (PSA, family history, DRE, needle biopsy Gleason Score, Age).
Results: Average correct classification rates of three way patient outcomes (Indolent, Significant, Aggressive) were computed using k-Nearest Neighbors and Neural Network models. Results were calculated based on clinical datasets (53 %), novel image datasets (49 %) and combined datasets (56 %). Classification modeling was repeated for two way patient outcomes (Indolent, non-Indolent) with results calculated again based on clinical datasets (79 %), novel image datasets (77 %) and combined datasets (84 %).
Conclusion: These image features add value to the clinical features and could be used to reduce the over treatment of prostate cancer and increase the quality of life of these patients.

OFP-07-003

Cribriform growth is highly predictive for post-operative metastasis and disease-specific death in Gleason score 7 prostate cancer

C. Kweldam*, M. Wildhagen, E. Steyerberg, C. Bangma, T. van der Kwast, G. van Leenders

*Erasmus Medisch Centrum, Dept. of Pathology, Rotterdam, The Netherlands

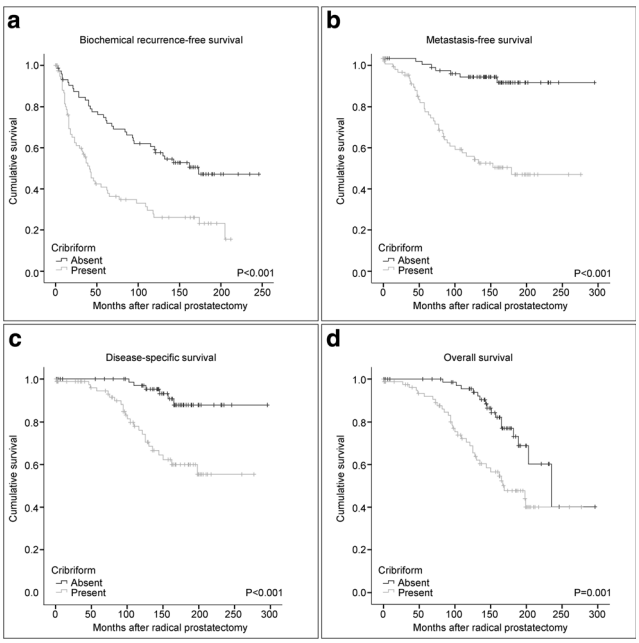
Objective: Patients with Gleason score 7 (3+4 or 4+3) prostate cancer have a wide range in clinical outcome. Gleason grade 4 prostate cancer is a mixed bag of various growth patterns including fused, ill-defined, cribriform and glomeruloid. Our objective was to determine the prognostic value of distinct Gleason grade 4 growth patterns in men with Gleason score 7.

Method: We performed a nested case-control study among 535 patients with Gleason score 7 prostate cancer at radical prostatectomy, treated between March 1985 and July 2013. We analyzed 52 cases (with metastasis, disease-specific mortality or both) and 109 controls, matched for age, PSA level and pT stage. Presence of the following Gleason grade 4 patterns was recorded: fused, ill-defined, cribriform and glomeruloid. Outcomes were metastasis-free survival and disease-specific survival.

Results: The overall prevalence of Gleason grade 4 patterns was as follows: fused 75 % (n = 121), ill-defined 64 % (n = 102), cribriform 48 % (n = 83) and glomeruloid 25 % (n = 40). Cribriform pattern was the only pattern with an unequal distribution between cases and controls. Forty-two out of 52 cases (81 %) had cribriform growth pattern versus 41/109 controls (38 %). In multivariate cox regression analysis, presence of cribriform growth was an independent predictor for distant metastasis-free survival (HR 8.0, 95 % CI 3.0–21; $P < 0.001$) and disease-specific survival (HR 5.4, 95 %CI 2.0–15, $P = 0.001$).

Conclusion: Cribriform growth in Gleason grade 4 is a strong prognostic marker for distant metastasis and disease-specific death in patients with Gleason score 7 prostate cancer at radical prostatectomy.

Kaplan-Meier estimates on impact of cribriform growth pattern in men with Gleason score 7 prostate cancer. A, biochemical recurrence-free survival. B, distant metastasis-free survival. C, disease-specific survival. D, overall survival:



OFP-07-004

Immunohistochemical expression of VEGFR in prostatic adenocarcinoma

M. Nikolic*

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Objective: The aim of the present study was to analyze the immunohistochemical expression of VEGFR in prostatic adenocarcinoma (PA) and it′s correlation with clinico-morphological prognostic factors.

Method: The study included the operative material from 20 cases of PA received by radical prostatectomy. The stage of the tumour was determined by using TNM classification from 2002, and the grade was determined by Gleason score sistem from 2009. The expression of VEGFR was semi-quantitatively evaluated based on the percentage of positive staining cells. For the analysis of statistical significance was used Fisher's test (R v.3.0.2 program), a value of $p < 0.05$ were considered statistically significant.

Results: The expression of VEGFR was present in all analyzed cases of PA: 75 % (15 cases) showed diffuse expression, while 25 % (5 cases) showed moderate expression. A statistically significant correlation was noted between higher expression of VEGFR and higher Gleason score ($p < 0.01$). Frequency of diffuse expression of VEGFR-a was higher in casses with presence of lymphatic node metastasis and higher TNM grade, but it wasn′t statistically significant ($p>0.05$).

Conclusion: Diffuse expression of VEGFR is more often observed in PA with higher Gleason score, higher TNM stage and lymph node invasion, suggesting that VEGFR is significant prognostic factor for PA.

OFP-07-005

Expression of protein arginine methyltransferase 1 in renal cell tumours

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Objective: Protein arginine methyltransferase 1 (PRMT1) regulates function of several proteins involved in transcription, telomere stability and DNA repair. It is normally expressed in nuclei of tubular epithelial cells in kidney. However, PRMT1 is dysregulated in several human cancers.

Method: Immunohistochemical analysis on tissue microarrays of 134 adult renal cell tumours was performed. We analyzed 87 clear cell renal cell carcinomas (cRCC), 19 papillary RCC (pRCC), 10 chromophobe RCC (chRCC), 6 multilocular cystic RCC (mlRCC), 4 collecting duct carcinomas (CDC) and 8 oncocytomas. Number of PRMT1 positive cells and intensity of immunostaining were evaluated semi-quantitatively, and correlated to histopathological type of tumour and its nuclear grade.

Results: PRMT1 expression was present in all mlRCC (6/6), all CDCs (4/4) and in 62,5 % oncocytomas (5/8), which was statistically significant, comparing with other analyzed tumour types (p = 0,001). Intensity of immunostaining was higher in oncocytomas, CDCs and mlRCCs (p = 0,002). High intensity of PRMT1 staining was also characteristic of RCCs with nuclear grade 1 (p = 0,001).

Conclusion: Detected differences in distribution and intensity of PRMT1 expression among different renal cell tumours types of different nuclear grades, could suggest down-regulation of PRMT1 in more malignant and advanced carcinomas.

OFP-07-006

The expression of MUC2 and MUC6 predicts survival in urothelial bladder cancer

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Objective: Overexpression and aberrant glycosylation of mucins are frequent traits of human cancers derived from epithelial cells. The aim of this research was to investigate the significance of secretory mucins MUC2 and MUC6 in urothelial bladder cancer (UBC).
Method: We investigated the relationship between mucin expression and clinicopathological characteristics in 539 cases of UBC. Immu¬nohistochemical analysis of MUC2 and MUC6 expression was performed on tissue microarrays containing representative cancer tissue samples.
Results: MUC2 expression was observed in 40.1 %, while MUC6 stained 21.9 % of the tumours. The expression of MUC2 and MUC6 was associated with low tumour grade ($P < 0.000$ and $P < 0.022$, respectively), and low pathologic stage ($P < 0.001$ and $P = 0.001$, respectively). MUC2 and MUC6 showed inverse correlation to cancer-specific death ($P < 0.001$ and $P = 0.005$, respectively). Kaplan-Meier analyses showed that expression of MUC2 and MUC6 in UBC was significantly associated with better overall survival of the patients ($P < 0.001$, respectively). In Cox regression model, the absence of MUC6 expression emerged as independent predictor of death outcome.
Conclusion: The expression of MUC2 and MUC6 indicates less aggressive behavior of UBC. These markers may serve as useful predictors of better survival in UBC.

OFP-07-007
Effusion cytology of hereditary leiomyomatosis renal cell carcinoma
S. Smith*, R. Mehra, M. Divatia, A. Udager, J. McHugh, Y.-B. Chen, S. Tomlins, M. Amin
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Objective: The features of cytologic preparations of hereditary leiomyomatosis-renal cell carcinoma-associated renal cell carcinoma (HLRCC) have not been reported, while contemporary protocols increasingly sample RCC by biopsy and aspiration for diagnosis.
Method: We retrospectively reviewed effusion cytologic findings of a confirmed HLRCC.
Results: A 42 year old female presenting with outside diagnosis of pneumonia showed a persistent pleural effusion. On transfer, CT scan demonstrated effusion, pleural nodules, adrenal mass, and kidney mass. Thoracentesis yielded sanguinous, hypocellular fluid with scattered clusters, small papillae, and individual cells with high nucleocytoplasmic ratio and variably eosinophilic to vacuolated cytoplasm. Some cells showed large vacuoles with lateral nuclear displacement. Nucleomegaly with prominent macronucleoli was more prominent in the cell block, while pap-stained liquid-based preparations showed perinucleolar clearing. HLRCC was subsequently established with next-gen sequencing showing biallelic loss of fumarate hydratase (FH). Immunohistohemistry showed lack of FH expression and induction of aberrant succination (2SC).
Conclusion: Effusion cytology of HLRCC recapitulates rudimentary aspects of its characteristic cytomorphologic nucleolar findings. These are similar to cytologic features described for collecting duct carcinoma, reinforcing the importance of additional workup to distinguish these entities.

OFP-07-008
High incidence of TP53 mutations in HPV-negative penile carcinomas revealed by NGS analysis
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Objective: Penile squamous cell carcinoma (SCC) is a rare disease which is caused by HPV infection in 50 % of cases worldwide. The etiology of the remaining cases is unclear. The objective of this study was to elucidate a possible role of TP53 mutations in the formation of HPV-negative penile carcinomas.
Method: 100 archival formalin-fixed invasive carcinomas were analyzed for presence of HPV DNA, immunohistochemical p16 ink4a overexpression and TP53 mutation by Ion Torrent Ampliseq analysis.
Results: 40/68 (59 %, average age 65 years) SCC were positive for HPV DNA (mainly HPV16-genotype) and overexpressed p16 ink4a. TP53 mutations were identified in only 4 of these HPV induced SCC. Two of these TP53 mutations were annotated as rare single nucleotide polymorphisms and the remaining 2 SCC were induced by non HPV16/18 genotypes (31/73 and 45 respectively). 28/68 SCCs were HPV-negative with TP53 mutations being present in 18 SCC (64 %; average age 63 years) while 10 SCC (36 %; average age 71 years) showed TP53 wild type. 32/100 cases were excluded from the study due to technical reasons. Immunohistochemical p53 staining correlated with presence of TP53 mutations. Statistical analysis showed correlation of TP53 mutation with early onset of SCC and with decreased survival (37 versus 48 months), but no differences in tumour stage at diagnosis or tumour-related deaths in this heterogenously treated patient group.
Conclusion: TP53 mutations are present in 64 % of HPV-negative penile carcinomas. TP53 mutation screening should be performed routinely in penile carcinomas to further clarify the role of TP53 mutations in this tumour entity.

OFP-07-009
Caspase independent factors of apoptosis expression in germ cell tumours of testis
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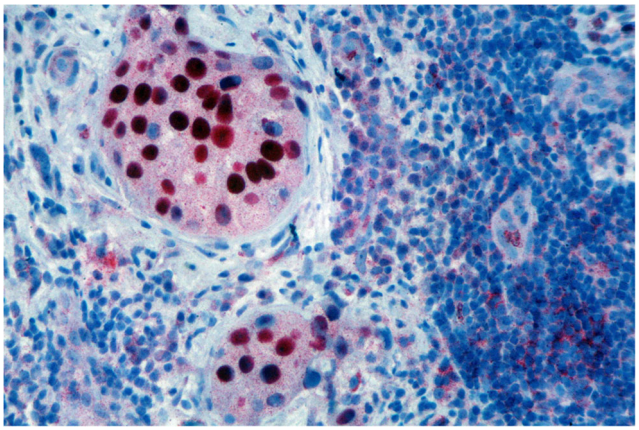
Objective: Testicular tumours are relatively frequent tumours in adolescents and men in productive age. Despite their quite good therapeutic outcome, some of them are resistant to the chemotherapy. Detection of processes participating in the development and progression of tumours can lead to development of more effective and targeted therapy. The molecules PARP-1 and AIF play a key role in regulation of cell response to cellular damage by activating apoptosis (programmed cell death) or reparation processes.
Method: We evaluated the expression of these markers in samples collected from 105 patients with different diagnoses of testicular tumours including cases of seminoma, embryonal carcinoma, yolk sac tumour, teratoma and choriocarcinoma, and samples from non-tumourous testicle and cases with intratubular germ cell neoplasia. The samples were processed to tissue microarrays and stained immunohistochemically. The results were evaluated quantitatively by morphometry.
Results: Our results confirmed higher expression of the marker PARP-1 in testicular tumours in comparison with the normal testicle tissue. It was significantly higher in cases of intratubular germ cell neoplasia, seminoma and embryonal carcinoma and was accompanied by significant decrease of AIF expression in seminoma and by an increase of AIF in areas with intratubular germ cell neoplasia.
Conclusion: The increase of PARP-1 positivity could be connected with the resistance of the tumour cells to their damage and to the activation of apoptosis. The exact mechanism will be a matter of further scientific investigation with respect to perspective application of PARP-1 inhibitors in the therapy of tumours. Supported by APVV-0016-11.

OFP-07-010
Prognosticators in Urothelial Carcinomas: The role of p40, N-Cadherin and ß-catenin in low and high risk tumours. An immunohistochemical study in invasive and noninvasive tumour
P. Stoemmer*, P. Torres- Galea
*Forschungslabor Pathologie, Augsburg, Germany

Objective: p40 (DeltaNp63) is the most common isoform, found in basal cells of urothelium and is -in contrast to p53- constitutively expressed and

only rarely mutated. It may be involved in the ERK- pathway regulating cell-adhesion-mechanisms. IHC-protein-level study on p40 and cell adhesion molecules in relation to the morphological behavior of tumourcells.
Method: FFPE archival invasive and non-invasive urothelial tumours, semiquantitatively analyzed by IHC. Antibodies: p40 (Delta-Np63):Polyclonal 1:200 ON RT Nuclear staining EDTA pH9 DCS, Germany ß-Catenin: 1/250 Thermo Scientific, Freemont CA, USA. N-Cadherin1/200Lab Vision, Ltd, UK
Results: Basal and near-basal cells in normal urothelium display high intranuclear expression of p40; umbrella cells are negative. Dysplasia and low grade papillary non-invasive carcinomas show a diminuation of its expression. Invasive pT1 and pT2 high grade tumours are subtotally or completely deprived of intranuclear p40. Loss of p40 induces epithelial-mesenchymal transition shift, resulting in N-cadherin and ß-catenin formation induced via ERK-signaling and may be the basis of the aggressivity in these tumours.
Conclusion: The loss of p40 in urothelia is correlated to dedifferentiation and invasivity of urothelial carcinoma. In contrast to p53, being reactive-and-stress induced, the loss of the constitutively expressed p40 (Delta-Np63) is a consistent marker of agressivity (and bad prognosis) in urothelial carcinomas.



OFP-07-011
Is molecular analysis the key for translocation renal cell carcinoma?: An extensive study of 23 cases
M. Classe*, G. Malouf, V. Grégoire, A. Villers, X. Leroy
*Lariboisière Hospital APHP, Dept. de Pathologie, Paris, France

Objective: Translocation Renal Cell Carcinoma (tRCC) is a rare and recently highlighted entity. Gene rearrangement involves TFE3 with 5 different described partners. Some authors suggest a prognostic role of the partner. Our goal was first to highlight fusion partners in a molecularly confirmed series of tRCC, second to compare efficiency of morphology, immunohistochemistry and FISH as diagnostic tools, finally to determine whether the rearrangement partner could play a prognostic role.
Method: 23 cases were retrieved from Lille University Pathology Department. For 13 cases cryopreserved material was used for molecular study by RNA Sequencing. Immunohistochemistry with TFE3 antibody and FISH assay were studied for all the cases.
Results: 20 cases displayed a TFE3 and one a TFEB rearrangement. Fusions partners were found for 11 cases highlighting 2 new partners: MED 15 and GRIPAP1. Fusion partner was not proved to be correlated with prognosis but lymph node involvement was associated with a pejorative evolution.
Conclusion: Fusion transcripts can be varied in Xp11.2 tRCC. RNASequencing can help in highlighting new transcripts but FISH is efficient to confirm diagnosis. Prognosis seems to be linked to lymph involvement rather than to the fusion partner.

Monday, 7 September 2015, 17.00–19.00, Hall 3
OFP-08 Oral Free Paper Session - Residents

(abstracts not assigned by printing deadline)

Monday, 7 September 2015, 17.00–19.00, Meeting Room 5/I
OFP-09 Oral Free Paper Session Head and Neck Pathology

OFP-09-001
Olfactory neuroblastoma: Morphological and immunohistochemical characterization
M. Classe*, B. Verillaud, G. Mortuaire, P. Herman, X. Leroy, G. Malouf, M. Wassef
*Lariboisière Hospital APHP, Dept. de Pathologie, Paris, France

Objective: The goal the present study is to determine an immunohistochemical profil of Olfactory Neuroblastoma that would give more objective and reproducible elements than pure morphology in their grading.
Method: 35 patients were included. All slides were reevaluated with determination of Hyams grade. The most representative bloc was selected for an immunohistochemical analysis using antibodies against S100 protein, CKAE1/AE3, vimentin, la E-cadherin, P53, Ki67, VEGF, HER2, EGFR and CD34.
Results: The most interesting morphological criteria were necrosis and mitotic count. Ki67 evaluation was well correlated to the mitotic count. P53 protein overexpression was not significantly associated with a pejorative evolution but a tendency was found. Most aggressive cases displayed a loss of E-Cadherin expression. Mean vascular density was not associated to the grade, the evolution or to VEGF expression.
Conclusion: Grading most effective morphological criteria are necrosis and mitotic count. Evaluation of Ki67 and loss of expression of E-Cadherin could be useful to determine a new grading system. A molecular analysis will maybe draw a more objective line between low and high grade tumours.

OFP-09-002
Is formaldeyde a reasonable risk for Pathologists to assume?
A. Hernández Gallego*, M. Martin, E. Fornàs, X. Sáenz, G. Puig, M. Fernández Figueras, A. Ariza
*Barcelona, Spain

Objective: Formaldehyde is the most used fixative. Due to its risks as irritant and carcinogen, occupational hazards units recommend exposure reduction or elimination. Our objective was to evaluate the efficacy of alternative fixatives.
Method: Three contiguous fragments from 20 specimens were fixed for the same length of time using three different fixatives: formaldehyde, Glyo-Fixx, and FineFIX. Sixty containers were identified with a number (from 1 to 20) and the letters A, B, or C (which identified the fixative). The choice of fixative was decided by using a die (1 or 6, formaldehyde; 2 or 5, Glyo-Fixx; 3 or 4, FineFIX). All samples were stained and processed using the same methodology. The results were evaluated using descriptive statistics.
Results: Twenty pathologists evaluated both morphology preservation and staining quality. Upon comparison of the three fixatives in relation to the various stainings, formaldehyde proved to be the best by showing statistically significant superior results. The differences between GLYO-Fixx and FineFIX were not significant.
Conclusion: Formaldehyde provides the best results in regard to both staining quality and morphology preservation. Alternative fixatives do not achieve the same quality standards. Therefore, formaldehyde fixation seems to be a reasonable risk to assume.

OFP-09-003

p16INK4a overexpression and prognosis in HPV-negative laryngeal Squamous Cell Carcinomas (SCC)

A. Nadal*, A. B. Larqué, L. Conde, S. Hakim, L. Alos, P. Jares, I. Vilaseca, A. Cardesa
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Objective: To study the expression of p16INK4a in a series of HPV-negative laryngeal squamous cell carcinomas and its prognostic value.
Method: Forty-five patients with laryngeal carcinoma were included in the study. Clinicopathological features and prognosis were reviewed. p16INK4a protein expression was analyzed through immunohistochemistry. mRNA was analyzed in 25 cases through quantitative reverse transcription polymerase chain reaction. HPV negativity was assessed by PCR using three different protocols based on MY09/11 and GP5/6 primers.
Results: Four out of 45 (9 %) cases overexpressed p16INK4a protein and showed a tendency to worse survival that was significant for stages I-III (log-rank p-value = 0.001). p16INK4a mRNA expression was 0.7 ± 0.42 (mean ± SD) and 12 out of 25 (48 %) had mRNA overexpression with an arbitrary cut off at 0.5. All tumours were HPV-negative with all three detection methods. The results were correlated to CDKN2A mutations. Two cases positive for p16INK4a immunostaining harbored CDKN2A mutations (one missense and one frameshift). Six out of seven (86 %) mutated cases presented p16INK4a mRNA overexpression whereas it was found only in 6 out of 18 (33 %) non mutated cases (p = 0.03).
Conclusion: Our findings suggest that p16INK4a overexpression, both at protein and mRNA levels may reflect CDKN2A genetic alterations in HPV-negative laryngeal squamous cell carcinomas.

OFP-09-004

Anaplastic lymphoma kinase rearrangement detected in a salivary duct carcinoma of the parotid gland - association with a consecutive non small cell lung carcinoma

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Objective: Reflex-testing of anaplastic lymphoma kinase (ALK) rearrangements is recommended for pulmonary adenocarcinomas and non small cell lung cancer (NSCLC) to predict the efficacy of ALK-inhibitor therapy.
Method: A 56 years old male patient underwent left sided parotidectomy because of a salivary duct carcinoma with lymph node metastasis. Postoperative CT staging after 3 and 6 months was negative. After 1 year the patient presented with a pulmonary infiltration in the right lower lobe by non small cell lung cancer, favor adenocarcinoma. Reflex-testing for EGFR mutation and ALK-rearrangement as routine diagnostic workup of the pulmonary adenocarcinoma was performed, immunohistochemical markers in both tumours compared.
Results: Two carcinomas of the patient were detected consecutively after 16 months. Metastases of the primary salivary duct carcinoma had been found in ipsilateral left cervical lymph-nodes. After 14 months a PET/CT showed a segmental infiltration in the right lower lobe of the lung and enlarged lymphnodes bilaterally in the mediastinum and right sided cervical. Both carcinomas had cytological and histological similarities, the infiltration in the endobronchial biopsy was partly lymphangitic, without clear correlation to the surface epithelium, there were dysplastic changes in the bronchial glands. After detection of ALK rearrangement in the lung adenocarcinoma, comparative ALK immunohistochemistry, was positive in both tumours, ALK rearrangement by FISH was seen in a similar quantity of 50 and 40 % of tumour cells respectively in lung and salivary gland.
Conclusion: ALK rearrangement in salivary duct carcinomas could be a targetable somatic alteration in comparison to TTF1 negative ALK positive lung cancer.

Table1: Comparison of tumours and figures 1 and 2:

Parameter	Clone	NSCLC	Salivary Duct Carcinoma	Comment
TTF1	SP141 rabbit, Ventana	neg	nd	
CK5/6	D5&16B4 Ventana	single cells faintly membranous pos		
CK7	OV-TL 12/30	membranous pos, in dysplastic and normal basal cells strongly, tumour moderately to strong	similar to lung	
CK20	Ks 20.8	neg	neg	
EGFR	3C6	tumour membranous pos (+++) dysplastic epithelia pos (++)	similar to lung	
PAS		cytoplasma sometimes apical faintly pos	nd	
Alcian blue		single tumour cells positive	nd	
ALK D5F3	D5F3 Ventana OptiView	pos	pos	granular, part of cells strongly, some single distinct cytoplasmic granules
Alk Protein	ALK01 Ventana	neg	nd	
ALK-FISH	ALK Dual Color Break Apart Rearrangement Probe (Vysis)	50% ALK rearranged	40% ALK rearranged	

table 1: comparison: lung- and parotid-gland tumour; pos = positive, neg =negative, nd = not done

Fig 1 tumor in bronchus

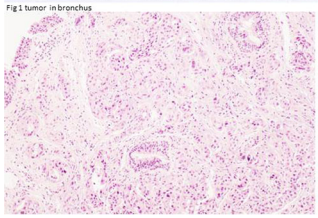
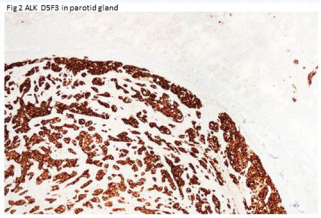


Fig 2 ALK D5F3 in parotid gland



OFP-09-005

Identification of High-risk Human Papillomavirus (HR-HPV) in oropharyngeal cancer with a single test in routine clinical practice

O. Casiraghi*, A. Ben Lakhdar, X.-J. Ma, P. Saulnier, L. Lacroix, P. Vielh, H. Mirghani
*Institut Gustave Roussy, Dept. de Biopathologie, Villejuif, France

Objective: Accurate screening of HR-HPV oropharyngeal squamous cell carcinoma (OPSCC) is a critical issue. Recently, a novel RNA in situ hybridisation test (the RNAscope HPV-test®) has been developed to detect HR-HPV E6/E7 mRNA in Formalin fixed tissue. The aim of this study is to validate this assay against the "gold standard", namely the quantitative Real-time Polymerase Chain Reaction (qRT-PCR) for HR-HPV16-18, performed on fresh frozen (FF) tissue.
Method: 50 Formalin fixed samples of OPSCC were tested with RNAscope HPV-test®, p16 immunohistochemistry (IHC) and Chromogenic In Situ-Hybridisation (CISH) for HPV-DNA. The results were compared with those of qRT-PCR on matched FF samples.
Results: Against qRT-PCR test, the sensitivity, specificity, positive and negative predictive value (PPV, NPP) of the RNAscope HPV-test® and of p16-IHC were 93, 94, 96, 88 and 96, 93, 96 and 93 %, respectively. Six cases were discrepant between the qRT-PCR test and CISH.
Conclusion: The RNAscope HPV-test® is very performant and easier to interpret than CISH. P16 performance is also very good, but it is only an indirect marker of the presence of HPV16. This study suggests that the RNAscope HPV-test® is a promising test that could be developed as a "clinical standard" for precise identification of HPV-related OPSCC.

OFP-09-006

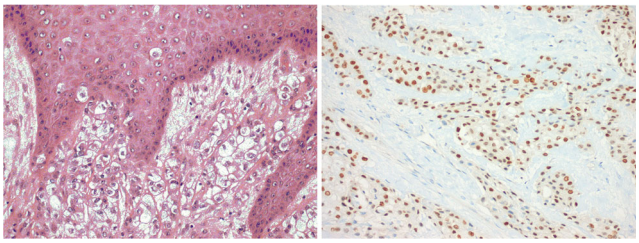
Head and Neck Clear Cell Carcinoma: The role of molecular pathology

S. Carvalho*, M. Caldas, J. Vieira, M. Teixeira, R. Henrique, M. Jácome
*Porto, Portugal

Objective: Hyalinizing clear cell carcinoma (HCCC) was first described in 1994. It is considered a diagnosis of exclusion by the World Health Organization (WHO). EWSR1-ATF1 fusion has been consistently found in HCCC and similar rearrangements are present in 63 % of clear cell odontogenic carcinoma (CCOC).
Method: We report two cases: one of HCCC (case 1) and one of CCOC (case 2). Case1: a 51-year old female with a palatal mass with local recurrence after 10 years. Case2: a 61-year old male with a mass of the maxilla that had several recurrences within 6 years of follow-up.
Results: Histologically, both cases were composed of an admixture of clear and eosinophilic cells, with rare mitotic figures, that connected to the surface epithelium. In case 2 the cells at the periphery of the nests occasionally demonstrated nuclear palisading. Immunoprofile: Cytokeratin +, p63 +,

myoepithelial markers -. Examination by FISH for the EWSR1 rearrangement was positive in case 1 and negative in case 2.
Conclusion: Molecular pathology offers new insights in the distinction of clear cell tumours. HCCC is a translocation-driven tumour that can no longer be considered a diagnosis of exclusion. CCOC probably represents a central variant of HCCC.

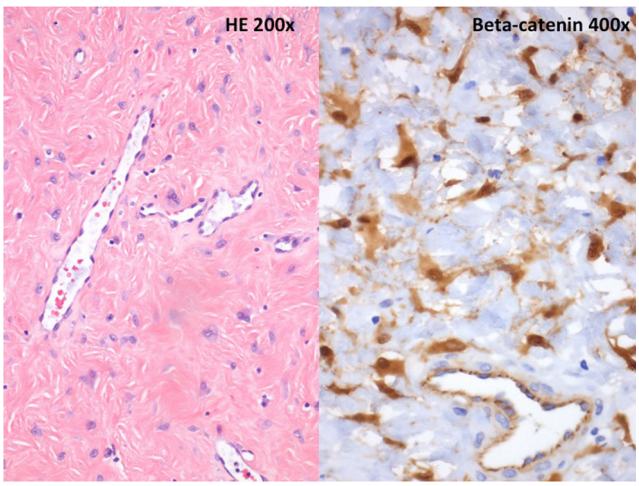
Tumour cells connected to the surface epithelium (HE 200x). Strong and diffuse p63 nuclear staining (p63, 200X):



OFP-09-007
Nasopharyngeal angiofibromas, a benign but locally aggressive neoplasm: A series of 24 cases
A. Galaghar*, C. Meireles, L. Santos, S. Carvalho, M. Jácome
*IPO Porto, Dept. of Pathology, Portugal

Objective: Nasopharyngeal angiofibroma accounts for less than 1 % of all nasopharyngeal tumours, almost exclusively occurs in adolescent males and is characterized by a local destructive growth (from Stage I-IV) with recurrences in about 20 % of patients. It consists in a variably sized and distribution of vascular proliferation in a cellular fibroblastic/myofibroblastic stroma (Beta-catenin+) with some variations depending on the time of evolution and presence/absence of treatment.
Method: All nasopharyngeal anfiobromas diagnosed in our institution were re-evaluated, including demographic, clinical, imagiological, surgical and follow-up data until April 2015.
Results: There are 24 cases. All the patients had local symptoms and were males; mean age at diagnosis is 16 (range 7–46). Preferred treatment was surgery followed by active surveillance; when recurrence occurred radiotherapy was used in 3 cases, tumour embolization in 1 case and 1 case with both treatments. Recurrence occurred in 12 cases, between 12 and 43 months after the first diagnosis. Five patients are alive without disease; 19 are alive with disease of which two had disease progression.
Conclusion: Our series is according with literature data, including the exceptional case of 45 years old patient. Imagiology plays an important role in the diagnosis, management and staging, based on local structures involved.

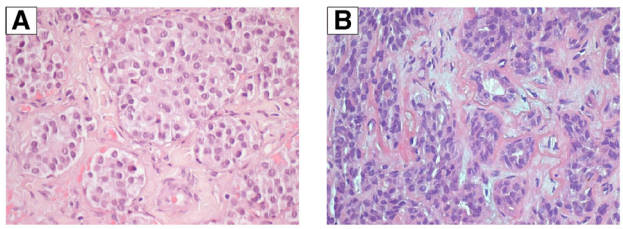
Only stromal cells express beta-catenin, suggesting that they may be the neoplastic component of nasopharyngeal angiofibroma:



OFP-09-008
Neuroendocrine neoplasms of the head and neck: A clinicopathologic series of 6 cases in a cancer institute
C. Meireles*, A. S. Pires-Luís, A. Galaghar, M. Jácome
*IPO Porto, Dept. de Patologica, Oporto, Portugal

Objective: Neuroendocrine neoplasms of the head and neck (NE-HN) are a rare and heterogeneous group of neoplasms. Despite the remaining controversies regarding terminology, NE-HN may be divided into two groups owning to its epithelial differentiation, comprising small cell neuroendocrine carcinoma (SCNC), typical and atypical carcinoid, or neural features as paragangliomas. Moreover, there is adenoma of the middle ear (AME), a benign neoplasm with variable mixed endocrine and exocrine differentiation. We aim to review NE-HN in our department and present two illustrative cases of the diagnostic challenges.
Method: We reviewed all NE-HN with epithelial differentiation from the Department of Pathology archive of IPO-Porto (2005–2015). Relevant clinicopathological information was collected from clinical files and pathology reports. We also selected two paradigmatic cases, 1AME and 1SCNC of the nasopharynx (Figure1).
Results: Five SCNC and one AME were identified. SCNC group: age (median, range): 59 (45–80), 3 (60 %) male, treated with surgery (n = 1, 20 %), chemotherapy (n = 1,20 %), chemotherapy+radiotherapy (n = 2, 40 %) and surgery+radiotherapy (n = 1,20 %); four (80 %) dead of disease. AME was treated only by surgery, without evidence of recurrence. Clinicopathological features summarized in Fig.1.
Conclusion: NE-HN are rare and there are diverse treatment options. An accurate NE-HN diagnosis and classification is essential to treatment planning. Further studies are warranted to uncover prognostic factors and to define optimal treatment.

Figure 1:



C PT	AGE (years)	SEX	DIAGNOSTIC	TUMOR SITE	TREATMENT	FOLLOW-UP (months)
1	62	F	SCNC	Larynx	S+R	DOD 6,5
2	59	M	SCNC	Paranasal sinuses	Q+R	DOD 1,5
3	80	M	SCNC	Salivary glands	S	DOD 2
4	47	M	SCNC	Hypopharynx	Q	DOD 16
5	45	F	SCNC	Nasopharynx	Q+R	AWD 16
6	58	M	AME	Middle ear	S	AND 23

S– Surgery, R– Radiotherapy, C- Chemotherapy; DOD – Dead of disease, AND – Alive no disease, AWD – Alive with disease

Figure 1. A - Middle ear adenoma. **B** - Small cell neuroendocrine carcinoma of the nasopharynx. **C** - Clinicopathological features.

OFP-09-009
Chromosome instability in tumour resection margins of oral cancers is a predictor of local recurrence
E.-J. Speel*, D. Pierssens, M. Borgemeester, S. van der Heijden, V. Bergshoeff, C. Peutz-Kootstra, A. Ruland, A. Haesevoets, P. Kessler, B. Kremer
*Maastricht Univers. Medisch Centrum, Dept. of Pathology, The Netherlands

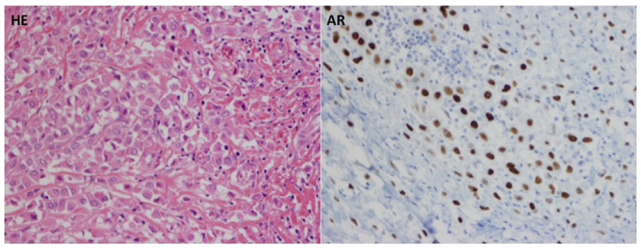
Objective: The local recurrence rate in oral squamous cell cancer (OSCC) hardly decreases. This is partly due to the presence of (pre)malignant cells in remaining tissue after resection, that may lead to development of a new tumour in time. Because histolopathological identification of (pre)malignant cells in tumour resection margins may be difficult in routine practice, we examined if detection of chromosomal instability (CIN) by FISH in histopathologically tumour-free margins could predict recurrence.
Method: Formalin-fixed paraffin-embedded tissue sections of 40 OSCC, 233 resection margins, and 11 recurrences of 40 patients (radically resected primary tumour, treated between 1994 and 2003 with curative intent without postoperative treatment, ≥ 5 years-follow-up) were subjected to FISH to examine chromosome 1 and 7 copy number variations, and to p53 immunohistochemistry. Results were statistically correlated with each other and clinical data.
Results: 11 out of 40 patients developed local recurrence within 5 years. FISH analysis showed that nine of 11 OSCC that recurred exhibited in at least one resection margin CIN (p 0.018), defined as imbalances and/or polyploidization for chromosomes 1 and 7. P53 overexpression and WHO classification did not correlate with recurrent disease.
Conclusion: CIN in OSCC resection margins can reliably identify patients at risk for developing a local recurrence.

OFP-09-010
Interplay between Epidermal Growth Factor Receptor (EGFR), Keratin 5 (K5) and TNM staging parameters in Head and Neck Squamous Cell Carcinomas (SCC)
A. M. Cimpean*, N. C. Balica, C. I. Doros, M. Raica
*'Victor Babes' University of Medicine, Timisoara, Romania

Objective: To evaluate keratin 5 in head and neck squamous cell carcinomas (HNSCC) with emphasis to EGFR expression and TNM staging parameters.
Method: K5 and EGFR were immunohistochemically highlighted for 42 cases of HNSCC (25 cases of laryngeal SCC and 17 cases of pharyngeal SCC). K5 and EGFR microscopic evaluation was completed with a statistic analysis between their expression, tumour grade and TNM staging parameters.
Results: HNSCC evaluation showed K5 positivity for 59.5 % of total cases and EGFR expression in 85.7 % of cases. Coexpression of K5/EGFR characterized 59.5 % of total cases ($p = 0.05$) and their assessement based on origin, showed that 60 % of laryngeal SCC had K5+/EGFR+ tumour cells while only 40 % of pharyngeal SCC were positive for both markers. K5 expression was correlated with T parameter ($p = 0.009$) and the same significant correlation was found between tumour grade and EGFR. For laryngeal SCC a significant correlation was observed between EGFR expression in tumour cells and vascular invasion ($p = 0.05$). Pharyngeal SCC showed K5 expression correlated with vascular invasion ($p = 0.02$).
Conclusion: Our data suggest the existence of a K5+/EGFR+ cell subpopulation with a high invasiveness potential.

OFP-09-011
Salivary duct carcinoma with rhabdoid features is an extremely rare subtype of salivary duct carcinoma: Down-regulation of E-cadherin expression
K. Kusafuka*, T. Kawasaki, M. Maeda, K. Yamanegi, S. Baba, T. Nakajima
*Shizuoka Cancer Center, Dept. of Pathology, Nagaizumi, Japan

Objective: Although salivary duct carcinoma (SDC) is a relatively common malignancy of the salivary glands, the tumour cells showing rhabdoid features are extremely rare. Recently, we reported such two cases of SDC as "salivary duct carcinoma with rhabdoid features (SDCRF)". We aim to elucidate clinico-pathologic features of SDCRF.
Method: We extracted SDCRF cases from the pathology files of our hospitals during 1995–2014. We examined them clinico-pathologically and immunohistochemically. Immunostains were performed for CKs, GCDFP-15, AR, Her-2, vimentin, p63, ASMA, CK14, E-cadherin, p53, INI1, and Ki-67.
Results: Eight cases of SDCRF (0.4 %) were selected. Seven cases were male with a mean of 62 years (range: 36–85 years), which included six parotid gland cases and two submandibular gland cases. Three cases are alive with disease, whereas other four cases are dead. Histologically, six of eight cases showed carcinoma ex pleomorphic adenoma. The carcinoma components showed diffuse proliferation of non-coherent large ovoid atypical cells showing eosinophilic cytoplasm and eccentric nuclei. Immunohistochemically, such cells were positive for pan-CK, GCDFP-15, AR and INI1 in all cases, whereas they were negative for vimentin. Seven cases showed Her-2 overexpression. Such rhabdoid cells were negative for myoepithelial markers. Decreased or no expression of E-cadherin was seen in seven cases. Carcinoma cells showed high labeling index of Ki-67. Finally, we diagnosed these cases to be "SDCRF".
Conclusion: SDCRF is an extremely rare subtype of SDC, and such a subtype indicates an aggressive clinical behavior. The morphogenesis of "the rhabdoid cells" in SDCRF is related to down-regulation of E-cadherin.



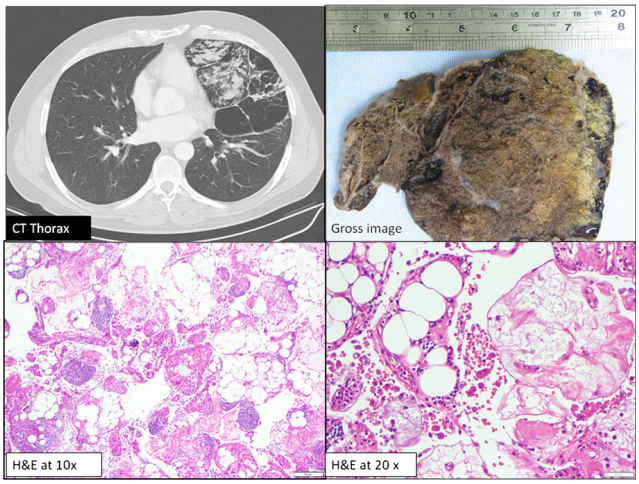
Monday, 7 September 2015, 17.00–19.00, Meeting Room 6/I
OFP-10 Oral Free Paper Session Paediatric and Perinatal Pathology

OFP-10-001
Placental transmogrification of the lung
L. Aalto*, B. Tietz, M. B. Casey, R. Rutherford, M. da Costa
*University Hospital Galway, Dept. of Histopathology, Ireland

Objective: Case presentation: A 37 year old male, non smoking farmer presented with a 4 month history of feeling unwell with lethargy, chills, night sweats and loss of appetite.
Method: Physical examination and peripheral blood profile were normal. Autoantibody screen, serology for viral, fungal and bacterial pathogens and Mantoux skin test were negative. CT thorax showed complex consolidation of the left upper lobe with associated emphysema. The other lobes appeared normal. Bronchoscopy was unremarkable. Cultures for AFB, TB and Fungi were negative.
Results: Post multidisciplinary team meeting he proceeded to upper lobectomy. Replacement of the upper lobe of lung by a spongy, haemorrhagic encapsulated lesion was seen. Histology showed bullous emphysematous change with immature placental structures. Epithelium expressed TTF-1, CK,AE/AE3. The stromal component was negative for TTF-1. A diagnosis of placental pulmonary placental transmogrification was made.
Conclusion: Pulmonary placental transmogrification is rare, first described by Chesney in 1978. It presents as a cystic, locally destructive lesion in the young or middle-aged. It is thought to be a reactive lesion secondary to emphysema. The clinical presentations range from an incidental finding in an asymptomatic patient to severe respiratory symptoms.

Though considered a benign lesion, it is locally destructive and warrant surgical resection. Prognosis post-resection is excellent.

Placental transmogrification images:



OFP-10-002

Postmortem MRI to determine the time of intrauterine fetal death

U. Tumanova*, V. Lyapin, S. Voevodin, A. Shchegolev, G. Sukhikh
*RCOGP, Dept. of Pathology, Moscow, Russia

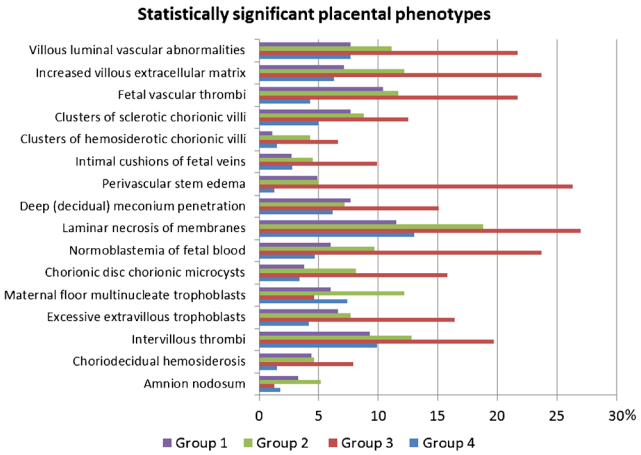
Objective: Explore possibilities of postmortem MRI for evaluation of the severity of the maceration and time of fetal death.
Method: At postmortem MRI bodies of 8 fetuses (gestational age: 18–21 weeks) and 18 stillbirths (15 antenatal, 3 intranatal, gestational age 22–40 weeks) was calculated MR maceration indicator of the brain, liver, kidney, lung, and thigh muscle. At autopsy, were evaluated macroscopic (area of desquamation, edema of the subcutaneous tissue, the mobility of the joints and bones) and histological (disappearance of basophilia of the nuclei of cells of the internal organs) signs and the time of death.
Results: Based on the results of morphological research of stillbirths degree of maceration (0–4). Prescription of death coming ranged from 0 h to 14 days in cases of antenatal death. Correlation analysis showed a direct positive correlation of MR-maceration indicator and data of autopsy: for lung tissue ($r = 0{,}99$, $p = 0{,}004$), femoral muscles ($r = 0{,}95$, $p = 0{,}003$), brain ($r = 0{,}94$, $p = 0{,}015$).
Conclusion: At fetal death the degree of maceration is characterized by changes of the T1WI and T2WI signal during postmortem MRI. Definition of MR maceration indicator with a high degree credibility allows us to estimate the severity of the time of occurrence of fetal death.

OFP-10-003

Morphological abnormalities of umbilical cord but not clinical umbilical cord compromise feature villous pathology

J. Stanek*
*Children's Hospital Cincinnati, Dept. of Pathology, USA

Objective: To assess the usefulness and limitations of placental villous associations of clinical umbilical cord (UC) compromise and morphological UC abnormalities.
Method: 5634 consecutive placentas divided into four groups were statistically compared: Group 1: 182 cases from pregnancies with clinical features of UC compromise (variable decelerations, UC entanglement, prolapse or true knot at delivery); Group 2: 1355 placentas with morphological UC abnormalities (UC itself or its abnormal insertion); Group 3: 152 cases with at least one phenotype from Group 1 and one from Group 2, Group 4: 3945 cases with no umbilical cord-related phenotypes. Frequencies of phenotypes were analyzed by ANOVA or $\chi 2$ with 3 df with 0.0007353 Bonferroni adjustment for 68 clinical and placental phenotypes analyzed.
Results: 30 phenotypes featured statistically significant differences: 13 clinical and 17 placental. 2 clinical phenotypes (oligohydramnios and abnormal fetal heart rate tracing) were most common in Group 1, 6 in Group 2: 4 clinical (abnormal umbilical artery Dopplers, nonmacerated stillbirth, multiple pregnancy, fetal growth restriction) and 2 placental, and 22 in Group 3: 7 clinical (gestational hypertension, polyhydramnios, induction of labor, cesarean section, macerated stillbirth, congenital malformations, abnormal 3rd stage of labor), and the remaining placental (Figure).
Conclusion: Clinical signs of UC compromise were associated with no pathomorphological placental abnormalities, while the coexistence of clinical and abnormal morphological placental phenotypes was statistically significantly associated with placental histological signs of decreased fetal blood flow, hypoxia (acute and chronic postuterine), shallow placental implantation, and/or amnion nodosum. One should not expect confirmation of clinical umbilical cord compromise on placental examination if no morphological abnormalities of the umbilical cord itself or its abnormal implantation have been found.



OFP-10-004

Examination of placenta: Nr. 1 tool in investigation of stillbirth

J. Stanek*
*Children's Hospital Cincinnati, Dept. of Pathology, USA

Objective: To assess the usefulness and limitations of placental examination in evaluation of stillbirth.
Method: Placentas from 520 consecutive stillbirths were extracted from the clinicoplacental database of several thousand placentas from high risk pregnancies. Frequencies of clinical and placental phenotypes were analyzed by ANOVA or Chi-square where appropriate, with Bonferroni correction for multiple comparisons.
Results: With subclassifications according to gestational age and fetal maceration status, statistically significant differences in abnormal clinical and placental phenotypes are presented in Figure which shows that placental diagnosis in stillbirth is gestational age- and fetal maceration-dependent. Notably absent are lack of differences in frequencies of hypertensive diseases of pregnancy by either subclassification. Abnormal placental phenotypes are more common than clinical phenotypes.
Conclusion: The cause of non-macerated stillbirth is frequently ascending infection, typically complicated by placental abruption, particularly in the 2nd trimester of pregnancy. This is also true of second trimester stillbirth, independently of maceration status. Even in totally fibrotic placenta of macerated stillbirth, villous hemosiderosis in lobular distribution highlighted with Prussian blue stain is diagnostic of fetal thrombotic

vasculopathy. In preterm 3rd trimester, the most common cause of fetal demise is uteroplacental insufficiency, characteristically with malperfusion histotopathology. At term, the cause of stillbirth is usually either placental dysmaturity or acute in-utero hypoxia. However, many cases of stillbirth are of still unknown cause either clinical or placental.

Statistically significant variations in clinical and placental phenotypes in stillbirth:

Clinical and **placental** statistically significantly different phenotypes in GESTATIONAL AGE AT DELIVERY subclassification (p-Bonferroni < 0.00069 for 72 dependent variables)

2nd trimester	Preterm 3rd trimester	Term
Premature rupture of membranes	**Uterine hypoxic pattern**	*Thick meconium*
Hydropic placenta	**Chorangiosis**	**Meconium penetration**
Acute chorioamnionitis, fetal inflammatory reaction	**Intimal cushions of fetal veins**	**Preuterine hypoxic pattern**
Retroplacental hematoma		**Normoblastemia of fetal blood**
		Fetal vascular thrombi
		Stem obliterative endarteritis
		Chronic villitis of unknown etiology

Clinical and **placental** statistically significantly different phenotypes in MACERATED vs. NONMACERATED fetuses (p-Bonferroni < 0.00066 for 76 dependent variables)

Macerated fetus	Nonmacerated fetus
Maternal diabetes mellitus	*Premature rupture of membranes*
Fetal growth restriction	**Acute chorioamnionitis, fetal inflammatory reaction**
Induction of labor	**Retroplacental hematoma**
Luminal vascular abnormalities of chorionic villi	
Increased extracellular matrix of chorionic villi	
Clusters of avascular chorionic villi	
Clusters of hemosiderotic chorionic villi	
Hypocoiled umbilical cord	
Other umbilical cord abnormalities	

OFP-10-005

Cadherins expression during mesenchymal-epithelial transformation on CD56 and beta-catenin positive nephron progenitors

S. Cirovic*, C. Müller, J. Tadic, J. Vjestica, M. Zivotic, M. Bosic, S. Tatic, D. Dundjerovic, D. Opric, J. Markovic-Lipkovski
*University of Belgrade, Faculty of Medicine, Institute of Pathology, Serbia

Objective: Neural cell adhesion molecule (NCAM/CD56) and β-catenin are required for self-renewal and differentiation of nephron progenitors (NPs), during mesenchymal-epithelial transformation (MET) stages in kidney development. In embryogenesis differential expression of cadherins (CDHs), calcium-dependent adhesion molecules, runs morphogenesis by stimulating cell aggregation, placing boundaries between groups of cells and promoting cell migration. Thus, expression of several different CDHs in relation to NCAM+/β-catenin+ NPs was investigated.
Method: Double immunofluorescent labeling was performed on cryostat human fetal samples from 15th till 36th week of gestation. Five different CDHs antibodies: CDH1, CDH2, CDH6, CDH11 and CDH16, as well as NCAM and β-catenin were analyzed.
Results: CDH11 expression was found only at pre-MET stage (uninduced and condensed mesenchyme) on NCAM+/β-catenin+ NPs. Nevertheless, NCAM+/β-catenin+ NPs in post-MET stage (renal vesicle, comma and S-shaped body) showed expression of CDH1, CDH6 and CDH16. Interestingly, during MET, at pre-tubular aggregate stage, NCAM+/β-catenin+ NPs expressed exclusively CDH6, while CDH2 was detected only on S-shaped body.
Conclusion: Our data indicated that CDH6 is required for early aggregation of condensed cells, while CDH2 is necessary for further elongation of newly formed epithelium. Specific CDHs expressions at each stage of MET illustrates capacity of NCAM+/β-catenin+ NPs to undertake cadherin switching, potential driving force of nephrogenesis.

OFP-10-006

Evaluation of the effect of propranolol on the rate of apoptosis in the infantile haemangioma

J. Kobos*, A. Wnek, P. Przewratil
*Medical University Lodz, Dept. of Pediatric Pathology, Poland

Objective: The aim of this study was to assess of the effect of propranolol on the rate of apoptosis in the Infantile Haemangioma through the examination of the expression of selected proteins Bax, Bcl2 and Caspase3.
Method: For the purpose of the study a histopathological diagnosis of IH was performed in 57 paraffin-embedded blocks. A total of 27 patients were treated with propranolol. The remaining 30 constituted the control group. The expression of Bcl-2, Bax and Caspase3 was determined by immunohistochemistry by means of a panel of monoclonal antibodies and peroxidase detection system. In each case, 1000 cells were evaluated in the vascular endothelial tissue. The expression of cell nucleus was assumed to be positive upon brown discoloration in a clinical study of Bax and brown cytoplasmic staining in Bcl-2 and Caspase3. Immunochemical interpretation and method were also used to analyze the control group. Nikon optical microscope and computer image analysis system (Multi Base v 808 Computer Scanning System) were applied in the study. In cases of controversy concerning the results, mean results were recorded and consulted with an experienced pathologist.
Results: The number of positive cells in Caspase3 showed a significant increase in the treatment group in comparison with the control ($P < 0.05$). This outcome confirms the assumed hypothesis. The expression of Bcl-2 and Bax did not differ significantly across the group of treated versus untreated children. The calculations were performed by means of Statistica v10.0 software.
Conclusion: The application of propranolol seems to be a factor that has an impact on the apoptosis process in the treatment of Infantile Haemangioma.

OFP-10-007

Congenital pulmonary airway malformation Type 4: Case report

I. H. Ozbudak*, H. S. Toru, G. Karaguzel
*Akdeniz Uni. School of Medicine, Dept. of Pathology, Antalya, Turkey

Objective: Congenital pulmonary airway malformation (CPAM) is a rare abnormality characterized by disorganized overgrowth of respiratory bronchioles and intercommunicating cysts. In the classification by Stocker of CPAM, five types were described. Herein, we report a CPAM Type 4 in a symptomatic 1-month-old child.
Method: The baby presented to hospital with dyspnea, cough and poor feeding. During examination, diminished breath sounds were detected at right hemithorax. Radiologically, the chest radiograph and the high resolution computerized tomography (HRCT) revealed solid mass, 4 × 3 cm in diameter with cystic component in the posterior segment of right lower lobe. The patient underwent surgery.
Results: Microscopically, the lesion consisted of a multicystic spaces which had relatively thin and uniform connective tissue walls lined by type 2 alveolar lining cells positive with TTF-1. Other parts of the lesion was composed of thin alveolar wall-like structures. The differential diagnosis was made from pleuropulmonary blastoma (PPB) by confirming the absence of a cambian layer of rhabdomyosarcoma in the wall of the cysts along with negative staining for desmin and the patient diagnosed as CPAM Type 4.
Conclusion: CPAM Type 4 is the acinar malformation lesion that consists of varying sized cysts; all lined by type 1 and 2 alveolar lining cells in benign fashion. Due to the similarity in microscopy, distinguishing the Type 4 lesion from (PPB) is critical for treatment modalities.

OFP-10-008

Extracranial germ cell tumours of childhood: The thirty-eight-year experience of the largest Serbian center

S. Djuricic*, G. Samardzija, D. Bozic, V. Dedic
*Mother and Child Institute, Dept. of Clinical Pathology, Belgrade, Serbia

Objective: A review of the occurrence of extracranial germ cell tumours (GCT) of childhood in a large national pediatric institution in a very long period and comparison with the related world studies.

Method: The distribution of GCT in relation to anatomic localization, sex, age, and histological category (mature, immature, malignant) was analyzed in children aged 0–18 years diagnosed and treated in Mother and Child Health Institute of Serbia during 38-year period (1977–2014).
Results: Frequency distribution of primary GCT in 259 patients was: ovary 44.4 % (median age 159 months), sacrococcygeal 27.4 % (1 mo), testis 12.7 % (35 mos), mediastinal 5.4 % (40.6 mos), head/neck 3.5 % (1 mo), retroperitoneal 3.0 % (12.5 mos), other localizations 3.5 % (11 mos). Age distribution curve shows increasing pattern for ovarian and bimodal pattern for testicular GCT. 49.6 % of sacrococcygeal GCT were diagnosed in newborns (it was the most frequent perinatal GCT), the youngest patients with the malignant form being four 11-month-old babies. Malignant category was dominant in testicular and retroperitoneal localizations.
Conclusion: The distribution of GCT in our series was in accordance with relevant summary data from the literature. Along with progress in the understanding of the GCT pathobiology, recap based on the long-time experience still may have general significance.

OFP-10-009

A comprehensive analysis of placental insufficiency in late-onset small for gestational age births

A. Nadal*, M. Parra Saavedra, F. Crovetto, S. Triunfo, S. Savchev, A. Peguero, A. Saco, F. Botet, E. Gratacos, F. Figueras
*Barcelona, Spain

Objective: Identify lesions of placental insuficiency in late-onset small for gestational age (LOSGA) fetuses with normal doppler ultrasound.
Method: A series of placentas from 142 singleton pregnancies of SGA births (birth weight < p10) delivered after 34 weeks with normal umbilical artery Doppler (pulsatility index < p95), were matched by gestational age with 142 adequate-for-gestational age (AGA) controls. Middle cerebral and uterine arteries, umbilical vein blood flow and Placental Growth Factor (PlGF) in maternal blood were evaluated. Placental lesions were classified according to Redline's as placental underperfusion (PUP) maternal or fetal, or inflammation. Perinatal morbidity and neurodevelopmental outcomes at 24 months were evaluated.
Results: Placentas were smaller and had more lesions reflecting PUP in the SGA group. Among LOSGA babies, those with PUP had higher perinatal morbidity, more alterations in prenatal ultrasound parameters (high uterine and low middle cerebral arteries pulsatility indexes and low umbilical vein blood flow normalized for expected fetal weight) and lower PlGF. Neurodevelopmental outcomes were also significantly poorer.
Conclusion: LOSGA babies without Doppler evidence of placental insufficiency have PUP changes that can be prenatally predicted by a combination of parameters. These infants are at greater risk of perinatal morbidity and abnormal neurodevelopmental outcomes.

Tuesday, 8 September 2015, 14.30–16.30, Meeting Room 6/I
OFP-11 Joint Oral Free Paper Session Cardiovascular / Soft Tissue and Bone Pathology

OFP-11-001

Does the type of mechanical circulatory support system have a predictive value for the outcome of the cardiac allograft with regard to antibody-mediated rejection?

K. Wassilew*, E. Potapov, D. Kemper, T. Krabatsch, R. Hetzer
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Objective: As the use of mechanical circulatory support (MCS) is constantly increasing due to the shortage of donor organs, its possible immunomodulatory effects are of growing importance in the routine diagnostic workup for antibody-mediated rejection (AMR) in cardiac allografts. We investigated the hypothesis that the type of MCS device used may influence the outcome of the cardiac allograft in terms of intramyocardial capillary C4d depositions.
Method: We evaluated right ventricular endomyocardial biopsies of two consecutive years (2011–2012) taken from 82 patients with MCS prior to heart transplantation (MCS group) and 138 patients without MCS (non-MCS group). The MCS group was subdivided (HeartMate II, HeartWare, Novacor, Incor I, Excor). Conventional histology and immunohistochemistry (C4d) were performed on formalin-fixed paraffin-embedded tissue sections.
Results: While there was a significant difference in C4d deposition between the MCS group ($n = 82$) and the non-MCS group ($p = 0.021$, odds ratio = 0.524), the Excor patients (39/82) did not show an increase in C4d depositions ($p = 0.838$, odds ratio = 1.11). Patients with the remaining MCS types (43/82) showed signs of AMR in more cases than the non-MCS group ($p = 0.003$, odds ratio = 2.97).
Conclusion: Our results suggest that the type of device used may influence the outcome of cardiac allografts with regard to AMR.

OFP-11-002

Myocardial remodeling of cardiac allografts in the late posttransplant course - the role of acute cellular rejection with special emphasis on macrophages

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Objective: Acute cellular rejection (ACR) and an increase of interstitial fibrosis (IF) often correlate with impaired ventricular function. The innate immune system, in particular macrophages, plays an important role in the resorptive process of ACR and is known to promote IF. We analyzed the effect of ACR and the level of macrophages on the degree of IF in endomyocardial biopsies (EMBs) of cardiac allografts.
Method: During two consecutive years (2011–2012) we investigated EMBs from 254 patients [mean age 37 years, mean time after heart transplantation (HTx) 8.9 years]. Tissue sections of formalin-fixed paraffin-embedded EMBs were evaluated histologically using immunohistochemical stains (CD3, CD68). The amount of macrophages was assessed by eyeballing. The EMBs were evaluated for level of IF on a Sirius red stain and further quantified using NIKON software (NIS elements AR 4.10.02). Statistical analysis was done in R using Fisher's exact tests, bootstrapped Cochran-Mantel-Haenszel tests, GLM methods and tree analysis.
Results: The density of macrophages correlated with ACR ($p = 0.000$) and with both pure IF ($p = 0.017$) and overall IF ($p = 0.001$). Interestingly, ACR appeared to have no direct impact on pure or overall IF ($p = 0.749$, $p = 0.760$).
Conclusion: Our results suggest that the density of macrophages is an important predictive factor for the remodeling in cardiac allografts.

OFP-11-003

Next generation sequencing is highly sensitive for the detection of beta-catenin mutations in desmoid-type fibromatoses

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Objective: Desmoid-type fibromatoses (DTFs) are locally aggressive and frequently recurrent tumours, the majority of which harbor beta-catenin (CTNNB1) mutations; accurate diagnosis is essential for patient management. We used next generation sequencing (NGS) to detect CTNNB1 mutations, and compared the sensitivity and specificity of NGS with our standard mutation detection technique: mutation-specific restriction enzyme digestion (MSRED).

Method: DNA was extracted from formalin-fixed paraffin-embedded needle biopsy or resection tissue sections from sporadic DTFs (n = 144), syndrome-related DTFs (n = 4), and morphological mimics (n = 11). Two primer pairs were designed for CTNNB1 mutation hotspots. Using ≥10ng of DNA, libraries were generated by Fluidigm and sequenced on the Ion Torrent Personal Genome Machine.
Results: NGS had a sensitivity of 92.36 % (133/144, 95 % CIs: 86.74 to 96.12 %) and a specificity of 100 % for the detection of CTNNB1 mutations in DTF-like spindle cell lesions. All mutations detected by MSRED were identified by NGS. NGS identified additional mutations in 11 tumours that were not detected by MSRED, two of which have not been previously described.
Conclusion: NGS is highly sensitive for the detection of CTNNB1 mutations. This multiplex assay has the advantage of detecting additional mutations compared to those detected by MSRED (sensitivity 82.41 %). The technology requires minimal DNA and is time- and cost-efficient.

OFP-11-004
Alpha Methylacyl-CoA Racemase (AMACR) expression in chordomas differentiates them from chondrosarcomas
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Objective: Chordomas and chondrosarcomas are malignant mesenchymal tumours with overlapping morphological and immunohistochemical (IHC) characteristics. Our objective was to compare the expression of α-methylacyl-CoA racemase (AMACR / P504S), β-catenin and E-cadherin in chordomas relative to chondrosarcomas by IHC stains.
Method: Archival sections of 18 chordomas, 9 chondrosarcomas and 10 mature cartilage samples were immunostained and scored for AMACR β-catenin and E-cadherin. The relative differential capacity of each marker was calculated from the scoring results. In addition, AMACR mRNA level was assessed in 5 chordomas by RT-PCR and evaluated by comparative CT method. Results were analyzed by the appropriate statistical methods.
Results: AMACR and β-catenin stained 88.9 % of the chordomas, 22.2 and 11.1 % of chondrosarcomas respectively and none of the mature cartilage samples. E-cadherin stained positively 77.8 % of the chordomas, 77.8 % of the chondrosarcomas and 30 % of the mature cartilage cases. Both AMACR and β-catenin showed statistically significant difference between chordomas and chondrosarcomas ($p < 0.01$ for both), unlike E-cadherin. AMACR was detected at the mRNA level.
Conclusion: AMACR is expressed in most of the chordomas but only in a minority of chondrosarcomas. AMACR may serve as IHC marker of chordoma with differentiating ability comparable to that of β-catenin.

OFP-11-005
Is histology of embolectomy specimens a useful endeavor?
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Objective: To determine whether there is any value in the routine histological examination of embolectomy specimens.
Method: Cases were identified by interrogating the departmental reporting software to identify all embolectomy specimens over the course of 5 years (31.12.2009 to 31.12.2014) using a SNOMED code search. A retrospective review of histology reports was then undertaken.
Results: 118 cases were identified; mean age 68 years (23–96 years). The most common indication for embolectomy was acute limb ischaemia (48 %) and the most common site of embolism was the leg (73 %). The principle indications for sending histology were to identify the source of the embolism, or to determine if the source was neoplastic or infective. One hundred percent of the cases were diagnosed as 'thrombus'; no neoplasia were identified.
Conclusion: Histological examination confirmed the presence of thrombus, with no significant pathology in all cases. In the absence of a specific clinical question or abnormal macroscopic appearance it would save time and resources if embolectomy specimens were not routinely sent for histology.

OFP-11-006
Sudden unexplained death in alcohol misuse: A comparison of characteristics and post-mortem findings with non-alcohol drinkers
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Objective: To identify differences in patient characteristics and post-mortem findings in people who died from Sudden Unexplained Death in Alcohol Misuse (SUDAM) and those of individuals who did not drink alcohol and died from sudden adult/arrhythmic death syndrome (SADS).
Method: Cases of SUDAM and SADS (using alcohol consumption history) in people aged 16–64 years old were identified from a database of cases referred to our cardiovascular tertiary referral centre since its inception (spanning approximately 40 years). A retrospective analysis of cases, including demographics and post-mortem results, was conducted.
Results: 41 cases of SADS and 62 cases of SUDAM were identified. The SUDAM group were older at death than the SADS group (P = 0.0002). There was also higher incidence of significant psychiatric illness in SUDAM cases. Post mortem examination of the liver in the SUDAM groups was more likely to be enlarged (P = 0.0033) or demonstrate fatty change.
Conclusion: Heavy alcohol use does not preclude the possibility of a heritable channelopathies. It may therefore be advisable to recommend genetic screening of relatives in cases thought to be SUDAM when the person who died was young or had a normal liver to avoid misattributing a case of SADS.

OFP-11-007
CD34, CD31 and D2-40 co-expression on early endothelial cells present in aspirated coronary thrombi from patients with ST-elevation myocardial infarction
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Objective: During angiogenesis blood endothelial cells (BECs) and lymphatic endothelial cells (LECs) express specific markers, which help their discrimination and easier identification. Since coronary thrombi material aspirated from ST-elevation myocardial infarction (STEMI) patients proved as good angiogenesis model, we investigated expression of CD34 and CD31 as BECs markers, and D2-40 as LECs marker in this material.
Method: Aspirated thrombi were stained immunohistochemically for CD34, CD31 and D2-40. Immunopositive cells were organized as single, clusters or microvessels. Immunohistochemically positive material was stained with double immunofluorescence for CD31, CD34 and D2-40. Thrombi were also graded as fresh (<1 day old), lytic (1–5 days old) and organized (>5 days old).
Results: Serial sections of aspirated thrombi showed concordant CD31, CD34 and D2-40 immunopositivity. Double immunoflorescence proved co-expression of CD34 and CD31, and CD31 and D2-40. Clusters and microvessels of D2-40+ cells were mainly present in lytic and organized thrombi.
Conclusion: Co-expression of CD34, CD31 and D2-40 on the same non-tumourous cell during thrombus neovascularization indicates existing in vivo plasticity of BECs and LECs. It also points that CD34 and CD31 on one hand, and D2-40 immunostaining on the other hand, cannot solely be a reliable indicator whether vessel is lymphatic or not.

OFP-11-008

The prevalence of quilty effect in endomyocardial biopsy of patients after heart transplantation - its relation to antibody-mediated rejection

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Objective: The significance of Quilty effect (QE), lymphocytic infiltrate bulging in the endocardium of cardiac allograft with or without involvement of myocardium, is still not completely understood. It was proposed to be related to Acute Cellular Rejection (ACR). The aim of this study was to assess the relation between QE prevalence and Antibody-Mediated Rejection (AMR).
Method: 1350 EMBs from 212 patients who underwent heart transplantation in years 2001–2013 were initially diagnosed in The Department of Pathology, The Children's Memorial Health Institute, as AMR1 and AMR0, according to ISHLT 2004 criteria (based on C4d positive stain). Presence of QE with distinguishing subtypes A (without involvement of myocardium) and B (lymphocytic infiltrate bulging in the endocardium and infiltrating myocardium) were assessed.
Results: 121 EMBs from 16 patients with AMR1 (group 1), and 1229 EMBs from 196 patients with AMR0 (group 2), were analised. QE type A was found in 16 (13,22 %) EMBs in group 1; in 96 (7,81 %) EMBs in group 2, $p < 0.001$. QE type B was diagnosed in 562 (42,97 %) EMBs in group 1; in 245 (19,93 %) EMBs in group 2, $p < 0.001$. QE was not present in 53 (43, 80 %) EMBs in group 1; in 888 (72,25 %) EMBs in group 2, $p < 0.001$. There was no difference in the frequency of each QE subtype between groups in AMR positive biopsies.
Conclusion: The relation between Quilty effect prevalence and AMR is possible as QE is present statistically more often in EMBs with C4d positive stain.

OFP-11-009

Interventional anatomy of the tricuspid valve and histopathologic findings after transcatheter atrioventricular junction ablation

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Objective: Catheter ablation of atrioventricular junction (AVJ) combined with pacemaker implantation is used for atrial fibrillation therapy. Aim of the study was to assess the anatomic variability of the tricuspid valve (TV) and the histologic features after catheter ablation.
Method: A total of 100 human hearts were examined for the anatomic variability of the continuity between the anterior and septal TV leaflets. In four patients with previous AVJ catheter, serial section conduction system investigation was performed.
Results: A continuity between anterior and septal TV leaflets was found in 98 % of hearts (3.8 ± 2.9 mm) and in 3 of the 4 cases with AVJ ablation, one of whom requiring a left side approach. Conduction system investigation revealed fibrosis of AV node and/or distal His bundle in all three with a right side approach and of branching bundle/proximal bundle branches in three cases. In the setting of a left side approach, fibrosis the ventricular septum crest was noted with intact compact AV node.
Conclusion: Our data suggest a crucial role of the anatomic variability of antero-septal TV leaflets commissure on the efficacy of AVJ ablation. The continuity protects the AV node from ablation with a right side approach, as to require multiple shocks and a left approach.

OFP-11-010

TGF-beta1 pathway activation and adherens junction molecular pattern in non-syndromic mitral valve prolapse

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Objective: Dysregulation of the TGF-β pathway has been associated with mitral valve (MV) prolapse due to myxoid degeneration (floppy MV). The activation of TGF-β pathway and its effect on differentiation of valvular interstitial cells (VICs) in myofibroblasts and on adherens junction (AJ) in MV prolapse are investigated.
Method: Floppy MV leaflets were obtained from 30 patients (24M, mean age 55.5 ± 12.7 year) underwent surgical repair. Ten age and sex-matched Homograft Tissue Bank samples served as controls. MV leaflet cellular and extracellular matrix composition was evaluated by histology and trasmission electron microscopy. Phosphorylated Smad2 (p-Smad2), α-smooth muscle actin (α-SMA) and junctional proteins in VICs were assessed by immuno-histochemistry and immunoblotting. Quantitative real-time PCR was carried out for components of TGF-β pathway cascade.
Results: Floppy MV leaflets were thicker ($p < 0.001$) and had higher α-SMA+ cell density ($p = 0.002$) and collagen III ($p < 0.001$) than controls. Enhanced p-Smad2 nuclear immune-reactivity ($p < 0.001$) and TGF-β1 gene ($p = 0.045$), TIMP1 ($p = 0.020$) and CTGF ($p = 0.047$) expression but no differences in FLN-A and total Smad2 gene expression levels were found between floppy MV and controls. Higher expression of cadherin-11, either exclusively or in colocalization with N-cadherin, and aberrant presence of plakophilin-2 at the AJ was found in floppy MV vs. controls.
Conclusion: TGF-β1 activation in MV prolapse induces VICs differentiation into contractile myofibroblasts and changes in the AJ, with increased cadherin-11 and aberrant plakophilin-2 expression. AJ reinforcement might promotes latent-TGF-β1 activation eventually leading to extracellular matrix remodeling in floppy MV.

OFP-11-011

Reduced connexin43 expression and gap junction coupling of neoplastic stromal cells in giant cell tumour of bone affect prognosis

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Objective: Missense mutations of the GJA1 gene encoding the gap junction channel protein connexin43 (Cx43) cause bone malformations, while GJA1 mutant mice develop osteopenia. In this study we investigated Cx43 expression and channel functions in giant cell tumour of bone (GCTB), a locally aggressive osteolytic lesion with uncertain progression.
Method: Cx43 protein levels were correlated with GCTB cell types, clinico-radiological stages and progression free survival in 89 primary and 34 recurrent GCTB cases. Subcellular localization of Cx43 and gap junction coupling was also tested in neoplastic GCTB stromal cells.
Results: In GCTB tissues, Cx43 protein was mainly produced by neoplastic stromal cells. Significantly less Cx43 was detected in osteoclast-rich tumour nests than in the adjacent reactive stroma. Progressively reduced Cx43 production in GCTB was significantly linked to advanced clinico-radiological stages and worse progression free survival. In GCTB stromal cell cultures most Cx43 protein was stuck in the paranuclear-Golgi region compared to fibroblast or bone marrow stromal cells without phosphorylation at Ser369, Ser372 or Ser373. Also, GCTB stromal cells transferred significantly less fluorescing calcein dye (622 Da) between them.
Conclusion: Significant downregulation of Cx43 expression and gap junction coupling in neoplastic stromal cells are associated with the clinical progression and worse prognosis in GCTB.

Tuesday, 8 September 2015, 17.00–19.00, Hall 2
OFP-12 Oral Free Paper Session Nephropathology

OFP-12-001
Recombinant human erythropoietin treatment in a rat model of nephrectomy
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Objective: We aimed to evaluate the impact of rHuEPO on anemia, renal function and structure in chronic renal failure (CRF), using a rat model of nephrectomy.
Method: Male Wistar rats, 12 weeks old, were divided in 3 groups: CRF (induced by a two-stage 5/6 nephrectomy); rHuEPO-CRF (treated with 100 IU/kg/week during 3 weeks) and Sham (surgery without mass reduction). Hematological and biochemical studies were performed. Kidney tissue sections were stained with Periodic acid-Schiff for histological studies. Statistical analysis were performed using the Mann-Whitney test.
Results: At the end of protocol, CRF group presented anemia ($p < 0.05$) and reduced glomerular filtration rate (GFR), whereas rHuEPO-CRF group showed an improvement in hematological parameters ($p < 0.05$) and a slight improvement in GFR. The histopathological analysis of kidney tissue showed that CRF group presented global glomerulosclerosis, tubular necrosis, IFTA and arteriolosclerosis. Due to surgery, we also found some inflammatory cell infiltration. The rHuEPO-CRF group presented mesangial expansion and a reduction in tubulointerstitial and vascular lesions, as compared to CRF rats.
Conclusion: The introduction of rHuEPO corrects the anemia associated with renal failure and improved the degree of renal lesions, slowing the progress of renal failure.

OFP-12-002
Role of macrophage differentiation in the pathogenesis of Lupus nephritis
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Objective: The role of macrophages in particular their differentiation (e.g. M1 or M2) in lupus nephritis is unknown. We investigated if macrophage differentiation is associated with stage of lupus nephritis and clinical parameters.
Method: 69 renal biopsies with lupus nephritis (ISN/RPS classes II-V) were assessed for M1(iNOS/CD68), M2a(CD206/CD68) and M2c(CD163/CD68). Blood pressure, proteinuria and serum urea were correlated using Spearman-test. Cluster analysis was used to define Lupus nephritis subtypes by macrophage activation markers.
Results: The mean number of CD68+macrophages was related to ISN/RPS class with the highest macrophage infiltration in diffuse proliferative class IV and the lowest number in class V. In all ISN/RPS classes more CD163+/CD68+ M2c-like than CD206+/CD68+ M2a-like cells were seen. We predominantly detected M2-macrophages independent of ISN/RPS classification. The majority of M2a- and M2c-macrophages were localized in the tubulointerstitium. Using data for macrophage activation markers, 3 different clusters were described. Interestingly, some beeing dominated by one ISN/RPS-class; e.g. >75 % of patients from cluster 1 were allocated to ISN/RPS class IV. Serum creatinine correlated positively with the number of CD68+ ($r = 0.411$; $p < 0.002$) and CD206+/CD68+ M2a-like macrophages in the tubulointerstitium ($r = 0.441$; $p = 0.001$). The number of tubular CD163+/CD68+ M2c-like cells was related to serum urea ($r = 0.611$;$p = 0.001$). Mean number of CD206+/CD68+macrophages was sig. higher in hypertensive compared to normotensive patients ($p < 0.007$).
Conclusion: M2-type macrophages are key players in lupus nephritis and macrophage subpopulations seem to be involved in the development of disease progressing hypertension.

OFP-12-003
Effect of chronic therapy with chaethomellic acid A on renal fibrosis in 5/6 nephrectomized rats: A preliminary study
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Objective: The high prevalence of chronic kidney disease underscores the failure to provide therapies to effectively halt, prevent, and/or reverse renal fibrosis. Thus, the aim of this study was to evaluate the effect of chronic treatment with chaethomellic acid A (CA) on renal fibrosis associated to 5/6 nephrectomy.
Method: Male Wistar rats were subjected to 5/6 nephrectomy (RMR) or sham-operated (SO). One week after surgery, rats were placed in four experimental groups: RMR: rats without treatment ($n = 13$); RMR+CA: rats treated with CA ($n = 13$); SO: rats without treatment ($n = 13$); SO+AC: rats treated with CA ($n = 13$). CA was intraperitoneally administered in a dose of 0.23 μg/Kg three times a week for 6 months. Renal samples were scored for the following lesions: glomerulosclerosis, interstitial fibrosis, arteriolosclerosis and interstitial inflammation.
Results: Animals from the SO and SO+AC groups presented no kidney histological changes. Glomerulosclerosis, interstitial fibrosis and arteriolosclerosis scores were significantly lower ($p < 0.001$) in RMR+AC group when compared with RMR group. There were no significantly differences in interstitial inflammation score between RMR+AC and RMR groups.
Conclusion: This preliminary data suggests that pharmacological inhibition of Ras (small GTPase proteins) activation may be a future strategy in the prevention of renal fibrosis.

OFP-12-004
Polyvinylpyrrolidone storage disease in opioid addicted patients
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Objective: Opioid addicted patients may inject oral substitution drugs such as methadone or buprenorphine. Some of these drugs contain high molecular polyvinylpyrrolidone (PVP) as an excipient, which is not excreted from the body when given intravenously. PVP deposition is diagnosed histologically by characteristic macrophages with bluish, vacuolated cytoplasm in various tissues. We present a biopsy series from opioid addicted patients showing renal insufficiency as a main clinical sign of PVP deposition disease.
Method: Biopsies ($n = 28$) and one autopsy with characteristic PVP deposition were collected between 2009 and 2013, from 13 opioid addicted patients (mean age 38 years, 12 males, 1 female).
Results: Renal biopsies ($n = 8$) showed interstitial PVP storing macrophages accompanied by various degrees of tubular atrophy and signs of glomerular hypoperfusion. Other main biopsy sites showing the characteristic macrophages were bone/bone marrow ($n = 11$) and the gastrointestinal tract ($n = 5$). Main clinical signs were reduced kidney function (mean serum creatinine 219 micromol/L) and anemia (mean hemoglobin 9.9 g/dL). Abdominal discomfort and fractures were found sporadically. Two patients died. One autopsy confirmed PVP deposition as underlying cause of death.

Conclusion: PVP storage is important to recognize histologically in kidney biopsies because it might explain multiorgan affection in opioid addicted patients.

OFP-12-005

Fibroblast markers in the fetal, normal adult and glomerulonephritic kidneys

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Objective: Fibroblasts are normally present in the kidney interstitium and myofibroblasts play the main role in the process of interstitial fibrosis. We compared the expression of (myo)fibroblast markers in fetal, normal adult and glomerulonephritic kidneys.
Method: We performed immunostainings with Vimentin, alpha-SMA, S100A4, Cadherin 9 and CD34 on formalin fixed, paraffin embedded tissue samples of 20 fetal, 40 normal adult and 40 glomerulonephritic kidneys with interstitial fibrosis of at least 10 %.
Results: The common mesenchymal marker Vimentin was widely expressed in the interstitium of all three groups. All of the fibroblast markers were present in the interstitium of the fetal kidneys and also some tubules showed weak signal for Vimentin and S100A4. In the normal adult kidneys, single interstitial cells were positive for S100A4 and Cadherin 9, while alpha-SMA and CD34 were absent. The tubules were negative for all markers. The glomerulonephritic kidneys hosted numerous interstitial cells positive for all markers with emphasized expression of alpha-SMA, but also atrophic tubules expressing Vimentin, S100A4 and alpha-SMA.
Conclusion: After fibrogenic stimulation, the fibroblasts and atrophic tubules in the glomerulonephritic kidneys re-express their fetal phenotype, while the atrophic tubules express de-novo alpha-SMA, thus gaining myofibroblast phenotype.

OFP-12-006

Up-regulation of calreticulin and 14-3-3 proteins in renal biopsies from IgA and membranous nephropathy patients

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Objective: Renal fibrosis is the common anatomical feature of most renal pathologies. Novel markers are need for better understanding of mechanisms and more accurate diagnosis. Our previous work in rodent models of renal fibrosis has established that calreticulin is up-regulated in tubular epithelial cells. In addition, proteomic analysis of cultured renal tubular epithelial cells over-expressing calreticulin identified up-regulation of the family of 14-3-3 proteins. Based on these findings, we opted to evaluate these proteins in renal biopsies from patients suffering from IgA and membranous nephropathy.
Method: Human kidney biopsies were obtained from patients suffering from IgA nephropathy ($N = 33$) and membranous nephropathy ($N = 13$). Healthy areas adjacent to renal carcinoma were used as controls ($N = 6$). Biopsies were evaluated using immunohistochemistry, immunofluorescence. and the Image J software.
Results: All biopsies from IgA nephropathy patients and membranous nephropathy patients showed intense up-regulation of calreticulin and 14-3-3 proteins specifically in distal tubular epithelial cells, but not in any other renal compartment.
Conclusion: Biopsy material findings raise the possibility that calreticulin and 14-3-3 proteins may be novel markers of renal tubular epithelial cells alterations, suggesting an important cross-talk between the glomerular and the tubular compartment. Supported by ARISTEIA grant 2681 to AC.

OFP-12-007

Comparative expression of Pax2 and Oct4 in fetal, normal adult and glomerulonephritic kidneys

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Objective: We aimed to compare the expression of Pax2 and Oct4, two genes responsible for the development and the differentiation of the embryonic stem cells in fetal, normal adult and glomerulonephritic kidneys.
Method: We performed immunohistochemical analysis with commercial antibodies against Pax2 and Oct4 on formaline-fixed, paraffin embedded tissue samples from 20 fetal kidneys with different gestational age, 40 adult and 40 glomerulonephritic kidneys.
Results: The analyses showed nuclear presence of both markers in fetal kidneys, in immature blastemic mesenchyme and early glomerular and tubular precursors. The signal persisted in parietal cells with the process of maturation. Weak Pax2 signal was present also in the parietal cells and in some distal tubules of the adult normal kidneys, while Oct4 was negative. Increased signal of both markers in parietal glomerular cells incuding cellular crescents as well in atrophic tubules was observed in the glomerulonephritic kidneys. The interstitial cells in the three groups were negative.
Conclusion: The presence of both markers in the immature fetal kidney structures points to the pluripotency of the mesenchymal blastemic cells that precede the mature cells of all types. The presence of Pax2 and Oct4 in parietal epithelial cells and cellular crescents indicates they might be responsible for origin of stem cells in glomerulonephritic kidneys.

OFP-12-008

Standardization of measurement and determination of normal glomerular basement membrane thickness at department of Pathology and Cytology, Dubrava University Hospital, Zagreb

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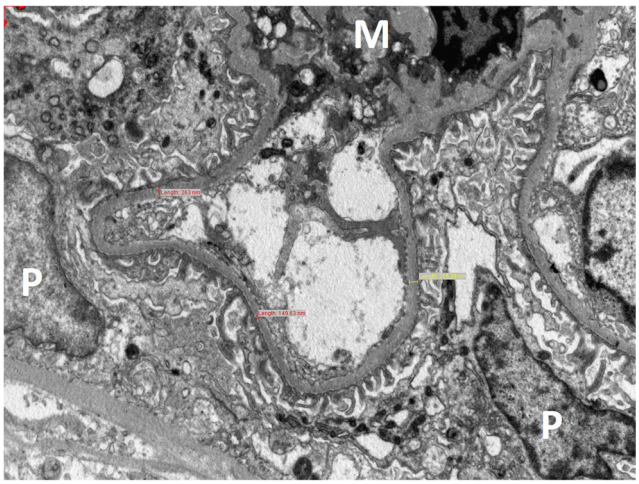
Objective: Glomerular basement membrane (GBM) thickness depends on multiple factors and many authors emphasize need for referential span of normal GBM thickness for each laboratory.
Method: We have applied modification of the direct measurement/arithmetic mean method to measure GBM thickness on digital EM photographies (30 measurements for each biopsy) using iTEM software (Olympus Soft Imaging Solutions GmbH). Position of measurements in capillary loops was determined similarly as described by Haas (Arch Pathol Lab Med, 2009).
Results: We obtained mean ± SD values for the normal GBM thickness of adult males and females of 340 ± 36 and 301 ± 44 nm. These values were based on average GBM thickness for each of 23 males and 22 females, aged 19 to 84 years, with minimal change disease, acute interstitial nephritis, normal renal parenchyma or acute tubular injury. Exclusion criteria were hematuria and diabetes mellitus. We defined normal ranges for each gender (268–412 nm for males, 213–389 for females), as being within 2 SD of these means.
Conclusion: With this research we have standardized method for GBM thickness measurement and defined referential span of normal GBM thickness for our laboratory. These results are crucial for accurate diagnosis of disorders characterized with structural changes of GBM.

Full glomerular capillary loop with mesangium (M), 3 measurements of GBM thickness, and podocytes (P). Magnification x8000:



OFP-12-009

Quantitative changes of kidney microvasculature in transplant glomerulopathy

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Objective: Chronic antibody mediated rejection with transplant glomerulopathy (TxG) is one of the major causes of late renal allograft loss. However, renal survival of TxG is variable and morphologic correlates of poor outcome are not well defined. The aim of this study was to identify ultrastructural markers predictive of less favorable renal prognosis in TxG.
Method: Forty-eight patients with TxG but no additional significant comorbidities biopsied at UCSF between 2007 and 2012 were enrolled into the study. Fifteen management biopsies, 6 month post-transplant, served as controls. Ultrastructural quantitative morphometric data, laboratory and serological variables were correlated with renal survival.
Results: The glomerular and peritubular capillaries were markedly thickened in TxG (938 ± 368 and 350 ± 121 nm, respectively) relative to controls (346 ± 27 and 140 ± 12 nm, respectively). Mean estimated glomerular filtration rate (eGFR) in the TxG group was 36,13 ± 17, 86 ml/min/1,73m2. With a median follow-up of 50.35 months, multivariable Cox-regression analysis of patients with TxG revealed the significant negative prognostic value of decreased eGFR (hazard ratio = 0, 328{0,128–0,841}, p = 0,020; per 1 SD increase) and increased mean harmonic glomerular basement membrane (GBM) width (HR = 1,558{1, 021–2,378}, p = 0,040; per 1 SD increase).
Conclusion: Our data suggest that measurement of GBM thickness in kidney allograft biopsies with TxG can improve prognostication for renal survival.

OFP-12-010

A 15 year review of renal tumours in native kidneys of patients with end-stage renal disease

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Objective: The aim of this study was to investigate the clinical and histopathological features of the renal tumours in native kidney of patients with end-stage renal disease (ESRD).
Method: Twenty-one patients with ESRD were identified in the files of the Department of Pathology in our Hospital. A histological review and immunohistochemestry was performed in all patients and tumour staging and grading was done.
Results: Data on 21 cases diagnosed between 2000 and 2015 were identified in 16 men (76.2 %) and 5 women (23.8 %). Transplanted patients accounted for 9 cases. The mean age at diagnosis was 64 years (33–74). pT1 disease was found in 19 patients with a mean tumour size of 2.5 cm. Twenty patients were treated successfully with radical nephrectomy, and 1 with tumourectomy. Three cases had multiple tumours and 1 patient had bilateral disease. Among the 21 cases the majority were papillary carcinomas (low grade), other diagnosis were conventional clear cell carcinomas, chromophobe carcinomas, and 2 unclassified renal cell carcinomas.
Conclusion: Most carcinomas in patients with ESRD are incidental low-stage, low-grade tumours with a good prognosis, and our results are similar to those described in the literature.

OFP-12-011

Ten reasons why I prefer digital slides in renal biopsy diagnostics

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Objective: In 2012 digitization of all non-neoplastic native renal biopsies was started at our department. In collaboration with the Norwegian Kidney Biopsy Registry a digital archive of non-neoplastic renal biopsies was built, now comprising 3256 biopsies covering 5 years.
Method: As a feasibility study 375 diagnoses were made solely on digital slides by one nephropathologist.
Results: Positive experiences can be summarized as follows: 1. Every digital slide is just "one" mouse click away no matter where you are, if only internet is accessible. 2. This applies even for previous biopsies. 3. Microscopic findings can be followed effortlessly through series of sections. 4. Comparison of immunohistochemical stains by viewing the slides simultaneously side by side allows for superior interpretation. 5. Measurements, e.g. of glomerular size, are easily performed. 6. Annotations allow documentation of important findings. 7. Biopsies can easily be demonstrated in clinicopathological conferences, even with remote participants. 8. Annotations hugely facilitate demonstration of renal biopsy findings. 9. Clinicians may have access to renal biopsies from their patients. 10. Collaboration between researchers is facilitated. There is a limitation for diagnoses requiring polarization, such as amyloidosis or oxalate nephropathy.
Conclusion: Digital slides from renal biopsies provide superior functionality compared to conventional microscopic glass slides.

Tuesday, 8 September 2015, 17.00 – 19.00, Annex B
OFP-13 Joint Oral Free Paper Session IT / Other Topics / Infectious Diseases / History of Pathology

OFP-13-001

Borrel or csokor bodies. Who has a priority in description of viral elementary bodies in fowl pox?

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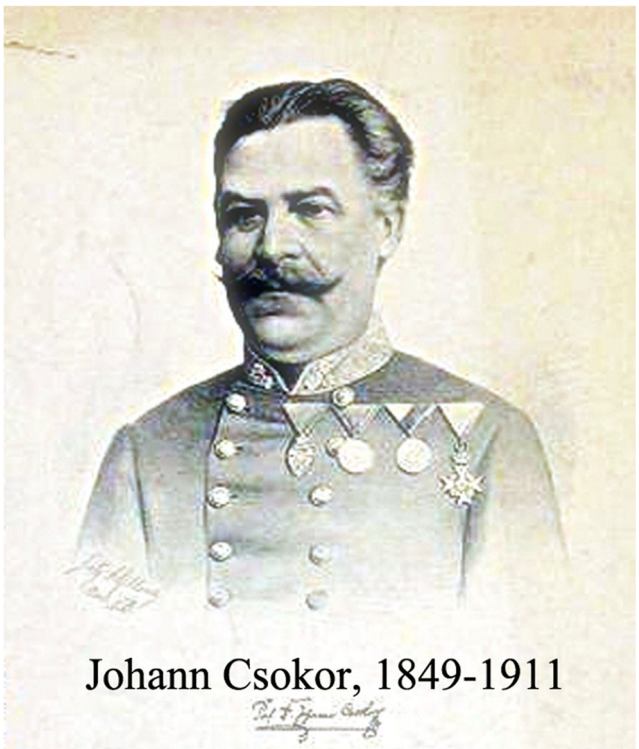
Objective: Johann Csokor (Jovan Čokor, 1849–1911) was medical doctor, professor of pathology at the Veterinary faculty in Vienna. Csokor published papers about fowl pox, rabies, few parasites, especially about tuberculosis, and the first was documented that animal tuberculosis maybe transmitted on humans.
Method: Historical investigation.
Results: Fowl pox extensively investigated by famous pathologist Ernest W. Goodpasteure (1886–1960) about 1920–30′. In his paper in 1955

Goodpasteure cited Amedee Borrel (1867–1936) as author whose described minute inclusions in cytoplasm of infected epithelial cells in 1904. Borrel bodies are now recognized as elementary bodies or virions of this Pox viruses. Twenty years before Borrel, Csokor published paper about fine structure of Fowl pox with detailed line-drawings. In comparison of Csokor's drawings and photographs in Goodpasteure's paper, the structure of fowl pox cytopathic effect is identically described. Csokor's paper about fine structure of fowl pox - "Ueber den feineren Bau der Geflügelpocke (Epithelioma Contagiosum B)", was published 1884 in Mittheilungen des Ornithologischen Vereines in Wien, in three consecutive issues, on pages 13, 21–25, and 39–42. Although was published 20 years before Borrel's paper "Sur les Inclusions de L'Epithelioma Contagieux des Oiseaux (molluscum contagiosum)" Comptes Rendus de la Soc. de Biologie 1904, pp. 642–3, Csokor's paper not been mentioned by others, maybe that Ornithology journal was not been read by pathologist or microbiologist.

Conclusion: We propose that elementary bodies in fowl pox must be renamed as Csokor's bodies, especially that Borrel paper is very short and without illustrations.



OFP-13-002

New data concerning the etiology of lung and lymph node granulomas

V. Zinserling*, T. Novitskaya, F. Mazitova, N. Semenova, A. Kozak, A. Avetisyan, A. Starshinova, P. Yablonskii, V. Karev

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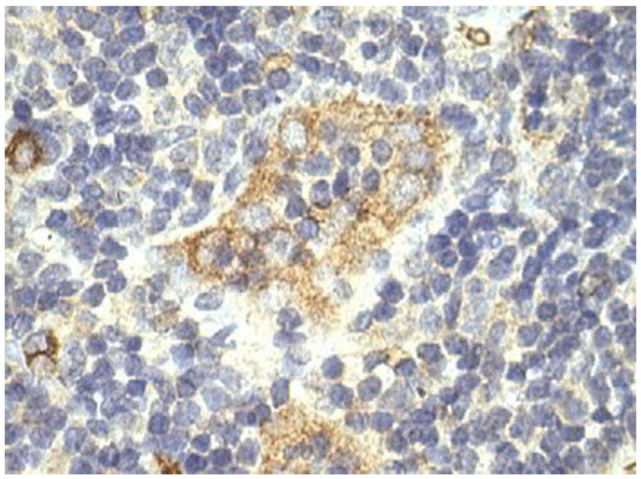
Objective: Lung granulomas play an important role in pulmonology, but their etiology frequently stay unclear. In routine practice the differential diagnostics is usually reduced to tuberculosis and sarcoidosis in spite of probable role of other pathogens.

Method: We analyzed seven cases (patients in age 15–55 ys) with history of focal lung lesions in which clinical and immunological data could not allow to diagnose firmly either tuberculosis, nor sarcoidosis. Operational and/or bioptic material of lungs and/ or lymph nodes was investigated histologically. In all cases Ziehl-Neelsen and PAS - stainings were provided. Immunehistochemistry included sera against CD68, M.tuberculosis complex, Toxoplasma gondii, Chlamydia trachomatis, Mycoplasma pneumonia.

Results: In all cases histologically were revealed non necrotic macrophageous granulomas (CD68+), cytoplasm of many cells contained small vacuoles and small PAS-positive dots. No acid fast bacteria or antigen of Mycobacteria were present in investigated slices. In 4 cases we have found strong expression of M. pneumonia, and in 3 - C. trachomatis antigens.

Conclusion: The comparison of clinical, immunological, histological and immunohistochemical data allows to diagnose practically not known before Mycoplasma and Chlamydia etiology of macrophageous granulomas in lungs and lymph node, which seem to be not rear.

Antigen of Chlamydia trachomatis in Lymph node granuloma:



OFP-13-003

The ratio of CD8+ and GranzymeB+ cells in the peritumoural stroma is associated with tumour regression grade in rectal cancer after neoadjuvant radiotherapy

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Objective: It has long been known, that the immunological tumour microenvironment is of utmost importance for the prognosis of a tumour disease. CD8+GranzymeB+ (CD8+GrB+) as cytotoxic effector T-cells are major players in tumour immunity and increased numbers of them in the tumour are associated with improved survival. We analyzed the immune cell infiltrate after neoadjuvant radiation of rectal cancer specimens and the association of CD8+GrB+ cells to tumour regression.

Method: 120 patients with advanced rectal cancer underwent neoadjuvant radiotherapy and a consecutive radical resection. Formalin fixed and paraffin embedded tissue was immunostained in a double reaction for CD8/GrB. Slides were digitized and evaluated for the number of immune cells.

Results: The number of CD8 +cells in the peritumoral stroma in samples with Dvorak tumour regression grade (TRG) 2 is generally higher than in lower TRG (3–4) (163 vs. 112/HPF). The proportion of GrB+ relative to CD8+ cells in patients with better treatment response was significantly higher than in those patients with worse tumour regression (p = 0 .008).

Conclusion: Not only the number but the ratio of CD8+GrB+ cells is associated with tumour regression grade in rectal cancer after neoadjuvant radiotherapy and could be a marker for favorable response to radiation and good clinical outcome.

OFP-13-004

Paleopathological analysis on the skulls of 19th century Padua University professors

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Objective: In Padua there is the oldest permanent anatomical theater in the world, dated 1595. Near there is the Hall of Medicine, where the medical students have their final exam behind a somber display of 8 skulls of prominent University professors. Among them there are five Padua University Rectors: Mabil (1752–1836), Gallini (1756–1836), Meneghelli (1765–1844), Dal Negro (1768–1839), and Caldani (1772–1836). The remaining were famous physicians, such as Santorio (1561–1636), who invented instruments to measure body temperature and pulse frequency, Giacomini (1797–1849), and Signoroni (1796–1844). The last of the series is Conti (1802–1849), mathematician. A legend tells that these professors donated their body to science. The myth originates because these skulls were placed in a Medical Museum, and served for phrenological investigations during the 1800's.
Method: Anthropological, paleopathological and historical analysis have been recently performed on these skulls to acquire new information about their natural history.
Results: Four of them, for instance, died during a cholera epidemic in 1836.
Conclusion: The research has allowed us to understand what is behind this myth: even if nobody of these professors explicitly donated their body to science, they mostly derived from exhumation and we can say that nowadays this implicit donation serves the purpose of scientific investigation.

OFP-13-005

"Monsters" in a World Heritage Museum

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Objective: Human deformities and monstrosities have always attracted mankind. They have been a source of scientific and cultural interest and investigation.
Method: The XIIIth century Coimbra University was classified World Heritage by UNESCO in 2013 and within it, the Medical School Pathology Museum.
Results: FMUC's Pathology Museum dates from the XIXth century; occupies a 500 m2 area and gathers 3000 pieces (fixed and dehydrated pathological specimens, wax models, ancient books and pictures); among which are human "monster" specimens, namely conjoint twins.
Conclusion: The authors will travel through the medical and cultural History of "Siamese Twins" by presenting examples of their various types, which have been preserved as a heritage for future generations.

OFP-13-006

CHLO's Cardiovascular Museum: A legacy for the future...

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Objective: Museums, despite their content, have the major duty of contributing to the general or specific populations' enrichment through "knowledge". The authors present the cardiovascular anatomopathological collection of a Portuguese Hospital.
Method: The collection comprises specimens received, for anatomopathological examination, from Cardiothoracic and General Surgery Departments and from Cardiology / Pediatric Cardiology Hemodynamics Units; as well as material harvested during autopsies. They have been prepared and kept, first, in alcohol-glicerin and lately in formalin; and adequately cataloged in an anonymous way.
Results: At present, the Museum contains hundreds of specimens of Congenital Cardiopathies, of Cardiac and Vascular Acquiered Diseases, of Post-surgical Material and of Transplanted-related Hearts (both native and explanted); whose examples will be showed.
Conclusion: Following the footsteps of other international Institutions, CHLO began collecting cardiovascular specimens in 1983. It is an ensemble of both very typical cases and of rare specimens, mainly used for teaching purposes during courses and residencies. It is an active / dynamic Museum, that contributes to the scientific formation of younger generations of Medical Doctors belonging to different specialties.

OFP-13-007

Proliferation index evaluation in breast cancer using a new image segmentation algorithm: A preliminary report

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Objective: Breast cancer is divided into luminal, Her2-positive and triple negative types accordingly to St Gallen 2013 recommendations. Luminal type is further divided into luminal A, B and B Her2-positive subtypes. Both proliferation index (PI) and progesterone receptor (PgR) expression may be used to distinguish between luminal A and B subtypes. The cutoff point 20 % of PI has been accepted by the most of experts.The commonly applied method of determining PI is its rough assessment by pathologist's eye. The only precise method is one-by-one nuclei counting throughout microscopic field. However it is rarely encountered in routine diagnostics, because this method is laborious and time-consuming.
Method: We developed a new image segmentation algorithm, which combines both Pawlak's data mining concept and fuzzy reasoning. The proposed approach was implemented and tested over histopathology images. The archival slides stained with MIB-1 antibody derived from 21 female invasive breast cancer patients. The results were compared with reference values which were obtained by precise nuclei counting (cell counter plugin for ImageJ application).
Results: The study showed strong correlation ($r = 0{,}84$, $p < 0{,}05$) between PI assessed by our method and reference values.
Conclusion: The results revealed usefulness of our method in proliferation index evaluation. The system needs further improvements which are currently under development.

OFP-13-008

A comparative study of colon and rectal tumour specimens: Gross examination by biomedical scientists, residents and pathologists

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*Hosp. Prof. Dr. Fernando Fonseca, Serviço de Anatomia Patológica, Amadora, Portugal

Objective: Nowadays, gross examination (GE) of surgical specimens in Portugal is performed by pathology assistants/ biomedical scientists (BMS), residents and pathologists. Our aim is to compare the GE of colon and rectal tumour specimens performed by these three professional groups.
Method: The GE of 179 specimens (61 BMS; 58 residents; 60 pathologists) was compared according to: number of blocks

submitted, number of lymph nodes (LN) harvested, smallest LN and smallest metastatic LN. Statistical analysis was performed (t-Student; $\alpha = 0{,}05$).

Results: Statistical significance was observed between: BMS/residents and pathologists in the number of blocks without LN ($p = 0{,}36/p < 0{,}0001$) and number of LN harvested ($p = 0{,}37/p < 0{,}0001$); BMS and residents/pathologists in the size of the smallest LN ($p < 0{,}002/p = 0{,}07$); BMS, residents and pathologists in the number of tumour blocks ($p < 0{,}02$). No statistical significance was observed between BMS, residents and pathologists in the size of the smallest metastatic LN ($p = 0{,}81/p = 0{,}72/p = 0{,}52$).

Conclusion: In colon and rectal tumour specimens, BMS/residents show a better LN retrieval and BMS harvest the smallest LN. However, BMS/residents submit more blocks without LN compared to pathologists. These results suggest a promising BMS performance in the GE of the studied specimens.

Table 1:

	Parameters (average)				
	Number of blocks without LN	Number of tumour blocks	Number of LN	Smallest LN (mm)	Smallest metastatic LN (mm)
BMS	15,07	7,08	24,44	1,34	1,34
Residents	16,10	8,93	22,40	1,75	1,75
Pathologists	10,23	5,65	14,67	2,03	2,03

OFP-13-009

Digital image-analysis processes to determine Ki-67 proliferation index in ER positive breast cancer: A comparative study

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Objective: The semiquantitative method utilized in routine pathology to determine Ki-67 proliferation index (KIPI) might be associated with remarkable intra-/interobsever variability. Thus, we aimed to compare the conventional semiquantitative method (SQ) and digital pathological image-analysis processes (full automation = FA, semi-automation = SA) for the detection of KIPI.

Method: In our study, 188 estrogen receptor positive breast cancer patients' samples (diagnosed through 1999–2002) and follow-up data were included with a median follow-up of 8.6 years. Tissue microarrays were prepared from the representative paraffin-embedded tumour blocks. After performing Ki-67 (MIB1) immunoreaction, SQ, SA and FA were applied to digital slides.

Results: Dichotomizing Ki-67 index value, according to the 2013 St. Gallen guideline, significant difference was detected between the FA, SA and SQ ($p < 0.001$, for all comparisons). For prognostic prediction, none of the three was able to perform statistically significant splitting the cohort at 14 %, although the SQ proved to be slightly superior to the digital analysis at 20 % cut-point ($p = 0.033$).

Conclusion: Despite digital image-analysis processes are more objective methods, and they might be able to reduce intra-/interobserver variability, further refinement and validation are needed to verify applicability of tumour pattern recognition software in pathological routine before further utilization in the routine setting.

OFP-13-010

Life-threatening antibiotic-associated enterocolitis and severe dysbiosis in critically ill intensive care unit patients

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Objective: We report on a novel form of antibiotic-associated colitis presenting with intractable watery high volume diarrhea in intensive care unit (ICU) patients following concomitant therapy with steroids. All patients presented with severe enterocolitis and showed histologic patterns resembling gastro-intestinal (GI) graft-versus-host disease (GvHD), with dramatically increased epithelial cell apoptosis and cytotoxic CD8+ T-cell infiltration as well as highly reduced CD4+ T-cell counts in the GI mucosa.

Method: Microbiota analysis of biopsy and stool samples including short-chain fatty acid measurements as well as immunophenotyping of biopsy specimens were used to discern the pathogenesis of this novel form of apoptotic enterocolitis.

Results: Microbiota analyses performed during the course of disease revealed a severe dysbiotic intestinal microbiota with severe overgrowth of Proteobacteria, including the presence of opportunistic pathogens like Haemophilus parainfluencae, and the loss of the physiological Firmicutes/Bacteroidetes colonization. Fecal microbiota transplantation (FMT) performed in one patient with this potentially fatal disease lead to rapid improvement of symptoms, mucosal healing and restored intestinal dysbiosis.

Conclusion: The eradication of the phsiological GI microbiota seems to be the main driver of this disease. The efficacy of fecal microbiota transplantation indicates a possible therapeutic option for this often fatal condition.

Tuesday, 8 September 2015, 17.00–19.00, Meeting Room 5/I
OFP-14 Oral Free Paper Session Neuropathology

OFP-14-001

Central 'ganglioneurocytoma': A rare variant of central neurocytoma

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Objective: Central neurocytoma (CN) is tumour consisting of round cells with neuronal differentiation, located at the foramen of Monro. Rarely, ganglion cell differentiation is reported; such tumours have been designated central 'ganglioneurocytoma'. Since the term was introduced in 1990 however, this variant of CN has remained poorly recognized. We report a case of central 'ganglioneurocytoma'.

Method: A 40 year old female presented with right hemiparesis. Neuroimaging showed a 63 mm solid-cystic tumour in the lateral ventricles, suggestive of CN. The tumour showed uniform round cells typical of CN. There was also widespread ganglion cell differentiation and tumour cells with transitional features between typical neurocytoma cells and ganglion cells. Abundant fibrillary matrix, a delicate vascular network and calcifications were seen. There was no mitotic activity, necrosis or microvascular proliferation. NeuN showed strong nuclear labeling of the tumour cells including the neurocytoma cells, ganglion cells and cells with transitional morphology. Synaptophysin was positive.

Results: A variant of CN (WHO grade II) was diagnosed. There was no tumour recurrence 46 months post-excision.

Conclusion: Central 'ganglioneurocytoma' is rare. It must be distinguished from extraventricular neurocytoma and ganglioglioma with an oligodendroglial component, and from more aggressive entities including oligodendroglial neoplasms with ganglioglioma-like maturation, and cerebral ganglioneuroblastoma.

OFP-14-002

Differential diagnostic problems in a case of lumbar hemorrhagic synovial cyst

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Objective: Lumbar synovial cysts are rare. We present a case of hemorrhagic synovial cyst that reinforces the opinion that synovial and ganglion cysts are stages in a cycle of cyst formation and degeneration.
Method: A 64 year-old female patient with a 3-month history of lumbar pain and right S1 radiculopathy was presented. She had also a 4-year history of right-sided lumbosciatalgia and neurogenic intermittent claudication for which she underwent L4-L5 fusion 2 years ago. MRI revealed a partially cystic lesion (1,9 cm) at the right L5-S1 foramen, which was removed surgically.
Results: Sections from the lesion revealed a cyst, the wall of which consisted of bundles of collagen fibers. There were many slit or star-shaped vessels, as demonstrated by CD34 stain, hemorrhagic areas and deposits of hemosiderin, giving the impression of vascular lesion. Despite multiple sections only focally the cystic wall was coated by synovium.
Conclusion: Synovial lining may be found only focally and in such cases multiple sections are needed in order to differentiate them from ganglion cysts. The cyst wall may be highly and/or abnormally vascularized, due to angiogenic factors produced by synovium. Clinicopathological correlation is recommended in order to reach the correct diagnosis.

OFP-14-003
Clinicopathological phenotypes associated with SQSTM1 gene mutations: Description of two cases

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Objective: There is a strong genetic influence on the clinicopathological phenotypes associated with frontotemporal lobar degeneration (FTLD) and frontotemporal dementia (FTD). Intracellular deposition of TDP-43 is the hallmark of a frequent subgroup of cases with FTLD. Mutations in the sequestosome 1 (SQSTM1) gene have rarely been found in individuals with FTD.
Method: We provided a comprehensive clinicopathological description of two cases.
Results: The clinical phenotype of patient 1 was compatible with the behavioral variant (bv) of FTD. Genetic analysis revealed a nonsense mutation NP_003891.1:p.(Glu396*) in SQSTM1. TDP-43 pathology was compatible mostly with the features of type B, however, neuronal granular cytoplasmic TDP-43 immunoreactivity was numerous and abundant oligodendroglial inclusions were seen in the white matter. The clinical phenotype of patient 2 was compatible with bvFTD associated with parkinsonism and bulbar symptoms in the later stage. Genetic testing of patient 2 identified a C9orf72 repeat expansion mutation together with a missense mutation NP_003891.1:p.Arg212Cys in SQSTM1. TDP-43 pathology was characterized by neuritic profiles and oligodendroglial cytoplasmic inclusions compatible mostly with type A of FTLD-TDP pathology similar to cases with the C9orf72 mutation.
Conclusion: Our study expands the neuropathology spectrum of genes associated with FTLD-TDP.

OFP-14-004
Ependymal tumour with sarcomatous differentiation-ependymosarcoma: A case report

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Objective: To report the case of a female with an ependymal tumour with sarcomatous differentiation - ependymosarcoma. Gliosarcomas, a variant of glioblastoma, are composed of glial and sarcomatous components. In most cases the glial component is astrocytic but can also be oligodendroglial or ependymal.
Method: A 44-year-old female, with a history of intracranial hemorrhage, presented with frontotemporal headache and aggravation of the already existing motor deficits. The CT-scan revealed a left frontal, 70 × 40 mm, heterogeneous lesion. She was submitted to a craniotomy.
Results: A 10 gr specimen of multiple white fragments was received. The specimen was composed of an ependymal component of rounded or elongated cells with eosinophilic and ill defined cytoplasm and irregular, hyperchromatic nuclei, collected around blood vessels forming pseudorosettes and a spindle cell component with marked nuclear atypia intermingled with fascicles of reticulin fibers. The mitotic count was very high in both populations. The immunohistochemical study revealed positivity of the first population for EMA (focally and dot-like), GFAP and S-100 Protein and the second population, for SMA and focally for S-100 Protein.
Conclusion: The patient was submitted to adjuvant therapy (chemotherapy and radiotherapy) and she is alive for 4 months now. Ependymosarcomas are rare tumours with less than 20 cases reported so far.

OFP-14-005
Gliosarcomas: Eight years of experience of a single pathology department

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Objective: To describe the experience of a single Surgical Pathology Department on diagnosing gliosarcomas. Gliosarcoma is a biphasic tumour with glial and sarcomatous components considered to be a glioblastoma variant.
Method: To identify all cases of gliosarcoma by searching the Pathology Department's database from January 2007 to December 2014.
Results: Twenty two cases of gliosarcoma were identified. The mean age was 55.1 years and the patients were mainly males (12 males and 10 females). The lesions were predominantly located in the temporal lobe (54,5 %) but also in the frontal (31,8 %), parietal (4,5 %) and occipital lobes (4,5 %) and thalamus (4,5 %). Six patients were previously diagnosed with glioblastoma and one, with ganglioglioma. In one case the glial component demonstrated to be of ependymal nature and in two cases, oligodendroglial. Mesenchymal differentiation was observed in one case, neuronal differentiation in two, muscle differentiation in four and blood vessel differentiation in one (some cases presented with more than one differentiation).
Conclusion: Gliosarcoma has a poor prognosis. Twelve of the patients (54,5 %) have already died (mean survival: 6,5 months), eight are alive, three with evidence of disease (13,6 %) and five with no evidence of disease (22,7 %) (longest survival: 18 months).

OFP-14-006
Absence of the alternative lengthening of telomeres phenotype and low prevalence of TERT promoter mutations in ependymal tumours

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Objective: To assess whether alternative lengthening of telomeres (ALT) or telomerase reverse transcriptase (TERT) promoter mutations are involved in the pathogenesis of ependymal tumours.
Method: We analyzed a series of ependymal tumours (n = 128), including conventional ependymomas (WHO grades II and III), subependymomas and myxopapillary ependymomas (each WHO grade I), for presence of the ALT phenotype by fluorescence in situ hybridization (FISH) and expression of ATRX and DAXX by immunohistochemistry. We also performed mutation analysis for the presence of TERT promoter hotspot mutations.
Results: No tumour showed ALT phenotype by FISH or loss of nuclear ATRX/DAXX expression. 9 out of 122 tumours (7 %) were TERT mutated. These included adult WHO grade II and III ependymomas located supratentorially, infratentorially or in the spinal cord.

Conclusion: ALT is not involved in the pathogenesis of ependymal as opposed to astrocytic tumours. TERT promoter mutations occur in a minority of cases without apparent association with clinical or pathological features.

OFP-14-007

Cerebellar dysplasia in prenatal vitamin C deprived Guinea pigs: A new animal model of lissencephaly type II

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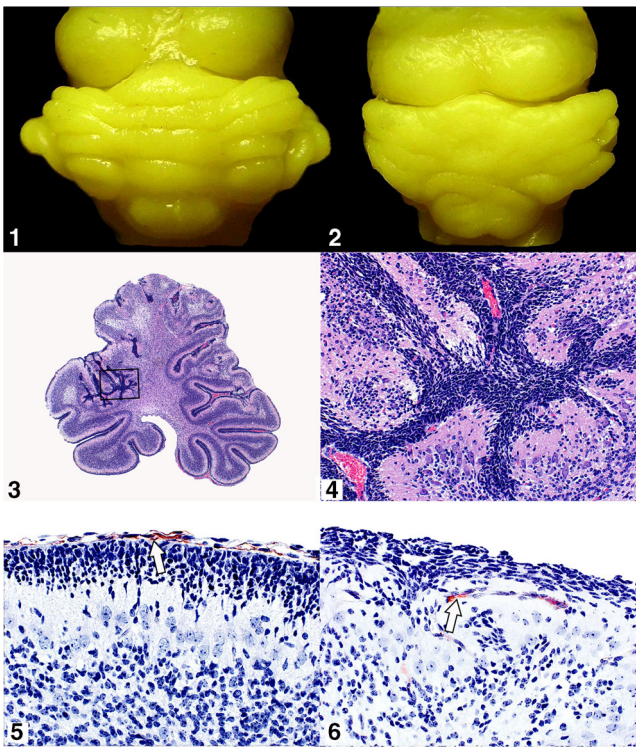
Objective: Vitamin C deficiency in humans and guinea pigs cause disturbance in collagen synthesis. We based the experiment on the fact that the integrity of pial basement membrane (PBM) is essential for the proper neuron migration.
Method: The experiment included pregnant guinea pigs divided in a control, and 2 experimental groups, E1 and E2. Vitamin C deprivation began on the 20th day of gestation for group E1 and on the 10th day for group E2 and continued until the 50th day of pregnancy, when the all groups were euthanized. Fetuses were removed, perfused with fixative and the brain was removed from the scull. Midsagittal section from the cerebellar vermis was immunohistochemicaly analyzed (with anti-collagen IV, anti-Ki-67, and anti-GFAP antibody).
Results: We found excessive overmigration of the external germinal layer cells into the subarachnoid space of the cerebellum through defects in the PBM. The changes ranged from focal rupture of PBM to their complete disintegration with severe cerebellar dysplasia. The cerebellar surface was flattered.
Conclusion: The fact that neither humans nor guinea pigs are able to synthesize vitamin C creates an opportunity for further research of the impact of prenatal deprivation of vitamin C in pathogenesis of Lissencephaly type II in humans.

Plate 1. Plate - Gross and pathohistological characteristics of experimental Lissencephaly; Dorsal view of normal cerebellum in control group (Fig. 1) and absence of folia and sulci on the cerebellar surface in E2 group (Fig. 2). Low (Fig. 3) and high mag:



OFP-14-008

Primitive neuroectodermal cell features and neural stem cell features of malignant peripheral nerve sheath tumours

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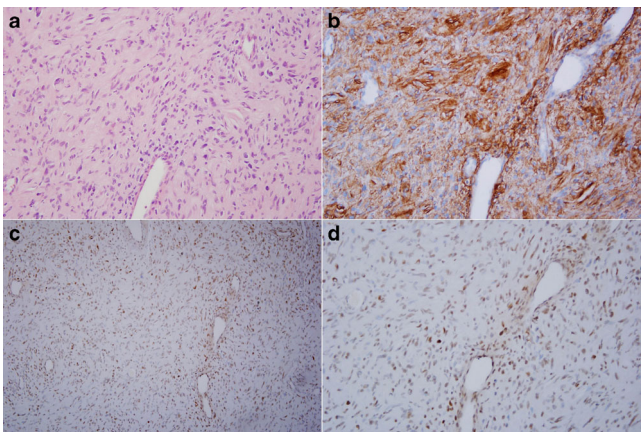
Objective: Malignant peripheral nerve sheath tumours (MPNST) are malignant neuroectodermal tumours which present diagnostic and therapeutic challenges. Morphological diversity include primitive neuroectodermal tumours (PNET)-like morphology. We explored expression of a panel of PNET-associated markers along with neuroectodermal stem cell markers.
Method: SOX-10, SOX-2, p75NTR, CD99, FLI-1, WT-1 was permormed by IHC on 96 MPNST cases (30 with known NF1).
Results: Briefly; >50 % of the cases showed positive reaction with p75NTR and SOX-10, >25 % of them were positive with CD99, Fli-1 and WT-1. SOX-2 was positive for 20 %. There was significant positive correlation between CD99 and SOX-2, WT-1 and SOX-10 immunostaining. Regarding the whole series; p75NTR immunostaining was significantly positively correlated with both WT-1 and SOX-10 immunostaining. For the NF1 cases; SOX-2 staining was significantly correlated with Fli-1 and SOX-10.
Conclusion: Some neuroectodermal stem cell markers such as P75NTR and SOX10 were frequently expressed by MPNSTs. This might be a helpful diagnostic tool and might also help to understand the etiopathogenesis. The PNET - associated markers should also be cautiously interpreted in MPNST suspicous cases. To focus on the primitive neuroectodermal cell features and neural stem cell features of these rare and aggressive tumours might also enable identification of specific targets for the development of therapies.

a) H&E, b) P75NTR, c)SOX-2, d) SOX-10 staining of MPNST:



OFP-14-009

BRAF (V600E) analysis by immunohistochemistry in 204 low-grade glial and glioneuronal tumours

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Objective: To explore the utility of immunohistochemistry (IHC) against BRAF (V600E) mutant protein in FFPE tissue from low grade CNS tumours.
Method: A cohort of 204 low-grade gliomas was successfully evaluated for BRAF (V600E) mutation using IHC on tissue microarrays (n = 198) and/or whole tissue sections (n = 10), including 101 sporadic pilocytic astrocytomas (S-PA), 12 NF1-associated PA, 12 anaplastic PA (APA), 29 diffuse astrocytomas (DA), 14 gangliogliomas (GG), 9 low-grade astrocytomas NOS (LGA), 7 pleomorphic xanthoastrocytomas (PXA), 4 DNETs, 4 angiocentric gliomas (AG), 3 low-grade glioneuronal tumours

(LGGT), 3 SEGA, and 6 pediatric oligodendrogliomas (POD). DNA sequencing data was available in a subset of cases ($n = 7$).
Results: BRAF (V600E) mutant protein was identified in 16/204 (8 %) cases across all tumours tested, including 5/101 S-PAs, 1/12 APA, 5/14 GGs, 4/7 PXAs (one with anaplastic features), and 1/29 DA. All NF1-PA, DNET, AG, LGA, LGGT and SEGA were negative. When looking at this subset of tumours with BRAF (V600E), the mean age of presentation was 21.2 years (ranging from 0.5 to 47 years). Cases were grade I ($n = 11$) or grade II ($n = 5$). There was a perfect correlation between IHC on TMA and whole sections ($n = 4$) and between IHC TMA results and sequencing (BRAF V600E present in 3 and absent in 4).
Conclusion: BRAF V600E can be detected by IHC in a subset of low-grade glial and glioneuronal tumours, especially in PXA, GG and PA. The findings support the feasibility of BRAF (V600E) IHC testing on TMAs for low grade glioma and glioneuronal tumours, which merits further investigation.

OFP-14-010
Two cases of intracranial fibrosarcoma in children
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Objective: We present two cases of intracranial fibrosarcoma in previously well children, a rare tumour in this location.
Method: Case 1: A 10-month old male child with irritability, neck hyperextension and a bulging fontanelle. MRI revealed a 68 mm predominantly solid mass, centered in the left lateral ventricle. Case 2: a 2-year old girl, with language delay admitted for seizures and fever. MRI revealed a 57 mm solid tumour in the upper part of the tentorium, with a mass effect on the left temporal lobe and hippocampus.
Results: In both cases, histological examination revealed a highly cellular spindle cell tumour, with a fascicular pattern, with elongated nuclei without prominent atypia. Mitoses were readily identified. Silver staining showed a dense reticulin network. Single cells were en-sheathed by argyrophilic fibers. The tumour cells strongly expressed vimentin, with focal and weak expression of actin. No expression of GFAP, S100, synaptophysin, desmin, EMA, cytokeratins, CD34 or beta-catenin was observed. A reverse transcription polymerase chain reaction assay to detect the gene fusion transcript ETV6-NTRK3 was negative. Neither tumour has recurred 3 months after resection.
Conclusion: Intracranial fibrosarcoma arising spontaneously is extremely rare. Although it is postulated to arise from meninges, vessel walls or choroid plexus, the origin remains controversial.

OFP-14-011
Molecular characteristics of meningeal solitary fibrous tumours/ hemangiopericytomas
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Objective: The hypothesis that hemangiopericytoma (HPC) and solitary fibrous tumour (SFT) form a spectrum of the same entity has been reinforced by the discovery of the recurrent NAB2-STAT6 fusion gene. The still used dichotomy of CNS SFT and HPC is based on different clinical behavior. We evaluated the molecular characteristics and expression of STAT6 in 58 CNS SFTs/HPCs and correlated the molecular data with histopathological parameters.
Method: Cases were reviewed and graded (WHO grade I, II, III). Immunohistochemistry for STAT6 and RT-PCR for detection of NAB2-STAT6 fusion were performed.
Results: All cases tested ($n = 31$) showed nuclear STAT6 expression. NAB2-STAT6 fusion transcripts were found in 49/58 (85 %) cases. The most common fusion variant, NAB2 exon 6 and STAT6 exon 17/18 ($n = 37$), did not show a clear predilection for one of the malignancy grades. NAB2 exon 4 and STAT6 exon 3 was detected in 12 cases; only to one of these cases WHO grade III was assigned.
Conclusion: Detection of NAB2-STAT6 fusion and the resulting nuclear expression of STAT6 protein are robust tools for the diagnosis of CNS SFTs/HPCs and underscore that they belong to the same entity. NAB2 exon 4 and STAT6 exon 3 fusion was associated with morphologically "lower grade".

OFP-14-012
Eukaryotic initiation factors and their contribution to gliomas might be relevant for the development of new therapies
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Objective: Glioblastoma multiforme (GBM) is one of the most devastating neoplastic tumours and current therapies can only marginally improve overall survival. One rate limiting step of protein synthesis is translation initiation monitored by eukaryotic initiation factors (eIFs). Deregulation of these proteins might lead to uncontrolled cell growth and malignant transformation. The mechanism of action of eIFs is associated with the mammalian target of rapamycin (mTOR) signaling.
Method: Expression of eIFs and mTOR related proteins was analyzed in human astrocytoma samples (grade I-IV) by immunohistochemistry and immunoblotting. For mRNA, qRT-PCR results and expression microarray data sets were evaluated. Mouse xenograft models of astrocytomas were treated with various chemotherapeutics and screened for their effects on eIFs.
Results: A protein expression profile of all eIF subunits revealed a significant deregulation for most eIFs in all tumour grades compared to controls. Interestingly, different expression patterns could be observed between low and high grade gliomas. Moreover, xenografts displayed unexpected profile changes upon treatment. Temozolomide drastically down-regulated eIF expression, whereas other established drugs even exhibited inverse effects.
Conclusion: Deregulation of eIFs in gliomagenesis may provide the fundament for the development of novel therapeutic strategies to prolong the survival of high grade glioma patients, in particular GBM.

Wednesday, 9 September 2015, 08.30–12.00, Meeting Room 6/I
OFP-15 Oral Free Paper Session Pulmonary Pathology

OFP-15-001
ROS-1 protein status in non-small cell lung cancer
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Objective: Chromosomal rearrangements of ROS1 gene has been identified in 1–2 % of lung adenocarcinomas and define a distinct molecular subgroup of non-small-cell lung cancers (NSCLC) that may benefit from therapies with ROS1 thyrosine kinase inhibitors. Fluorescence in situ hybridization (FISH) technique is considered to be a standard procedure for the evaluation of ROS-1 translocations, however, immunohistochemistry (IHC) could be a promising alternative mode of screening for detection of mutant fusion protein.
Method: A total of 208 NSCLC samples were tested for ROS-1 protein expression using anti-ROS-1 antibody (D4D6 clone). The case with ROS-1 translocation that had been previously confirmed by next-generation sequencing method was selected as a positive control.

Results: Four adenocarcinomas (1,9 %) were identified with ROS-1 immunoreactivity (H-score ≥ 100). Among these tumours, two showed predominantly acinar pattern and in the remaining two – one was solid, another one had papillary pattern of growth. ROS-1 FISH analysis of these tumours is pending.
Conclusion: Proportion of patients with tumours positive ROS1 IHC is consistent with published data. Genomic analysis of selected IHC positive and IHC negative tumour samples is pending to confirm potential use of ROS1 IHC for patient selection to ROS1 inhibitors.

OFP-15-002
DSG3/TTF-1: A single chromogen antibody cocktail to distinguish between Squamous Cell Carcinoma (SCC) and adenocarcinoma of the lung
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Objective: Due to advances in individualized treatment of lung cancer, pathologists are required to discriminate between squamous cell carcinoma (SCC) and adenocarcinoma (ADCA) of the lung in small specimens, while also preserving tissue for molecular studies. We have developed a simple, single chromogen antibody cocktail that takes advantage of differential localizations of SCC marker DSG3 (cell membrane staining) and lung ADCA marker TTF-1 (nuclear staining).
Method: To investigate the utility of this antibody cocktail, tissue microarrays were constracted of 101 SCCs and 113 ADCAs of the lung. The tumours were classified according to the 2011 IASLC/ATS/ERS criteria. Deparaffinized sections were stained with a mixture of DSG3 and TTF-1 antibodies. In comparison, a p63 antibody was also evaluated.
Results: Staining results for the DSG3/TTF-1 cocktail were as follows: sensitivity and specificity of DSG3 for SCC were 87 and 100 %, respectively; sensitivity and specificity of TTF-1 for ADCA were 87 and 100 %, respectively. The sensitivity and specificity of p63 single stain for SCC were 99 and 74 %, respectively.
Conclusion: DSG/TTF-1 is a simple, single chromogen antibody cocktail that can be effectively utilized in distinguishing SCC and ADCA of the lung. Although the sensitivity of DSG3 is lower, its specificity exceeds that of p63.

OFP-15-003
The impact of the epidermal growth factor receptor phosphorylation on downstream signaling in pulmonary adenocarcinomas
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Objective: Pulmonary adenocarcinomas express EGFR in variable intensities and quantities, regardless of the EGFR mutation. The internal domain of EGFR has eight phosphorylation sites at position Tyr845, Tyr992, Tyr1045, Ser1046, Ser1047, Tyr1068, Tyr1148, and Tyr1173. Each of these phosphorylation sites has different binding partners, which can issue either activation or degradation of the receptor. It is not known whether phosphorylation in pulmonary adenocarcinomas occurs randomly or specifically.
Method: Three tissue microarrays (TMA) were produced. One contained 345 cases of primary pulmonary adenocarcinomas (resection specimen), another consisted of acinar and papillary adenocarcinomas, half of which with EGFR mutations. A third TMA consisted of 74 mucinous adenocarcinomas with KRAS mutations (all EGFR mutation negative). Antibodies for phosphorylated EGFR at 845, 1045, 1068, 1148, and 1173 (Cell Signaling Technology, USA) were used.
Results: In EGFR mutated adenocarcinomas phosphorylation was commonly found on Tyr845 and Tyr1148, whereas in mucinous adenocarcinomas it was commonly seen only at Tyr1148. On the large TMA the following phosphorylations were uncommon: 1045, 1068, 1173, whereas 845 and 1148 were commonly seen. In some cases there was an additional nuclear expression, pointing to a translocation of the phosphorylated receptor into the nucleus.
Conclusion: From this initial study it seems that non-mucinous adenocarcinomas preferentially show phosphorylation at Tyr845 and 1148, which points to the activation of SRC kinases as well as MAP kinases, respectively as the downstream signaling pathways.

OFP-15-004
FGFR1 expression and amplification exist in lung pleomorphic carcinomas
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*University of Coimbra, Faculty of Medicine, Dept. of Anatomical Pathology, Portugal

Objective: Pleomorphic carcinoma (PLMC) is rare and reported with poor outcome due to aggressive biological behavior and undeterminated response to chemotherapy. FGFR1 has emerged as a potential molecular target, especially in Lung Epidermoid Carcinoma (SQC). In order to define targeted therapies and improve survival, 10 PLMC were studied.
Method: A basic IHC panel (including CK7, CK5.6, TTF1 and Vimentin) defined PLMC and FGFR1 Polyclonal AB-ThermoScientific and FISH (FGFR1(8p11)/SE8(D8Z1) Kreatech, Leica Biosystems. were applied.
Results: Patients' median age was 74, between 56 and 82 years, 7 men and 3 women. The main histological pattern was adenocarcinoma (ADC) in 8 (80 %) cases and SQC in 2(20 %) cases; all cases had 3+ FGFR1 general expression, without differences between PLMC with ADC or SQC component. FGFR1 FISH positivity was present in 3(30 %) cases: 2(100 %) with SQC and 1(12.5 %) with ADC component.
Conclusion: In this small series, FGFR1 amplification was more frequent in those PLMC with SQC epithelial component. No correlation was found between IHC and FISH results but protein overexpression seemed to be more frequent in PLMC than in ADC and SQC (unpublished data). FGFR1 amplification and protein expression should then be searched in this group of tumours in order to define score to include patients in targeted therapy, as already defined by some authors.

OFP-15-005
Bronchial biopsies: Is our rate of diagnosis of non-small cell lung cancer not otherwise specified in keeping with national expectations?
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Objective: To determine if the rate of diagnosis of 'non-small cell lung cancer not otherwise specified' (NSCLC NOS) at our institution, a large London teaching hospital, is in keeping with national expectations.
Method: All bronchial biopsies with a malignant diagnosis were identified over a 2 year period (31.12.2012–31.12.2014) using SNOMED codes. A retrospective review of histology reports was then undertaken and the rate of NSCLC NOS was compared to the national standard of <15 % (Royal College of Pathologists; Dataset for lung cancer histopathology reports, May 2014).
Results: 166 malignant bronchial biopsies were identified; mean age 69 years (range 19 to 92 years). 24 cases (14.5 %) were NSCLC without features of glandular, squamous or neuroendocrine differentiation. Of these it was possible to favor a more specific diagnosis in all but five cases (3.0 %).

Conclusion: Our rate of diagnosis of NSCLC NOS is in keeping with national expectations.

OFP-15-006

Simultaneous detection of ALK gene and protein in NSCLC biopsies using FISH break apart and ALK/EML4 fusion probe and anti-ALK D5F3 rabbit monoclononal antibody

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Objective: The ALK gene rearrangement in NSCLC represents a very complex change resulting in ALK fusion protein formation. However, identification of ALK gene status by FISH with a break-apart probe (BAP) is considered to be sufficient for purposes of therapy targeted on ALK protein.
Method: From a series of ALK gene FISH BAP tests of 649 NSCLC patients biopsies, we examined, with ALK/EML4 fusion probe and immunohistochemically (IHC) using D5F3 antibody, all 74 cases showing gene rearrangement and 44 "negative cases" selected for retesting due to disputable or interesting features.
Results: 44 "negative cases", incl. those showing 10–14 % rearranged nuclei were all negative also by other tests. From 74 "positive cases", a) in 4 cases material was insufficient for FISH retesting, b) 64 were IHC positive, while ALK gene rearrangement was confirmed in 60/64 and not confirmed in 1/64 cases, and c) 10 were IHC negative and in 1/10 the rearrangement was not confirmed by ALK/EML4 FISH examination.
Conclusion: The ALK gene status verification of NSCLC used in our study helps to confirm a negative status proved by using BAP and underscores the complexity of ALK gene rearrangement in cases considered to be positive when using single break-apart probe only.

OFP-15-007

The process of tissue collection, processing and storage in EORTC SPECTA program

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*European Organization for Research and Treatment of Cancer, Brussels, Belgium

Objective: EORTC SPECTA (Screening Patients for Efficient Clinical Trial Access) is a standardized, quality-assured molecular screening program for tumour characterization and systematic collection of human biological material in validated biobanks for biomarker discovery and optimizing access of patients to biomarker driven clinical trials.
Method: After informed consent, clinical and pathological data are captured and relevant HBM is collected centrally for quality assessment. Correlating mutational signatures via next generation sequencing with clinical/pathological data from long term patient follow-up is pivotal in SPECTA. Tumour samples are collected and stored under the guardianship of a pathologist. NGS data is reported to treating physicians under the auspices of SPECTA Molecular Advisory Board consisting of pathologists, molecular biologists and clinical oncologists.
Results: Launched in 2013, SPECTAcolor for colorectal cancer patients is initiated in 22 centers in 9 countries. As of March 2015, more than 600 patients are enrolled with 587 accepted tumour samples at the biobank in Dresden and 13 rejected samples due to insufficient quality (absence of viable tumour cells) or quantity (low number of tumour cells). Four hundred ninety seven samples were analyzed for baseline biomarkers with mean turnaround time of 17 days between sample receipt and biomarker status reporting.
Conclusion: SPECTAcolor is the first international longitudinally clinically annotated tumour tissue biobank and biomarker analysis platform. Its success proves that a logistically complex infrastructure to run innovative trials in a multinational setting is feasible. SPECTA will be extended to thoracic malignancies (SPECTAlung), melanoma (SPECTAmel) and neuro-oncology (SPECTAbrain). SPECTA for rare tumours is being developed.

OFP-15-008

Evaluation of lymph nodes in non small cell lung cancer: The role of H&E levels and routine immunohistochemistry

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Objective: To assess whether the use of immunohistochemistry and additional H&E levels is helpful in detecting lymph node metastases in non small cell lung cancer.
Method: 50 patients with a total of 568 lymph nodes were evaluated independently by two pathologists. 188 of the lymph nodes were examined in 3 levels and all 568 lymph nodes were stained using broad spectrum keratin. A positive lymph node was defined as a lymph node demonstrating isolated tumour cells, micro- or macrometastases in at least one H&E level or by immunohistochemistry.
Results: The two observers identified 58 and 67 positive lymph nodes respectively in, the same, 25 patients. The two observers detected 32 and 36 lymph nodes containing isolated tumour cells by immunohistochemistry but only four and 14 on H&E. Both observers identified 26 lymph nodes with micro- or macro metastases by immunohistochemistry vs. 24 on H&E. The additional micrometastases were found in two different patients. One of the patients was upstaged from N1 to N2, using the AJCC staging system. Additional levels were found to change the size and category of metastases.
Conclusion: Immunohistochemistry is helpful in detecting isolated tumour cells that would otherwise have been missed, however rarely leads to upstaging.

OFP-15-009

Expression levels of Filamin A protein predict survival outcomes in non-small cell lung cancer patients treated with Carboplatin and Navelbine

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Objective: Resistance to cytotoxic chemotherapeutic drugs represent the major impediment for the successful treatment of non-small cell lung cancer patients. Recently, it has been shown that cytoskeletal protein Filamin A is required for efficient DNA damage repair and modulates cisplatin sensitivity in vitro. We investigated the relationship between the expression levels of filamin A protein and survival outcomes in non-small cell lung cancer patients, treated with adjuvant Carboplatin and Navelbine.
Method: We analyzed filamin A protein expression in resection specimens from 135 non-small cell lung cancer patients, from which 73 patients were treated with adjuvant Carboplatin and Navelbine, and 62 patients did not receive adjuvant treatment. Archived formalin-fixed and paraffin- embedded (FFPE) tissue sections were stained immunohistochemically using EP2405Y antibody against C-terminus of filamin A.
Results: Cox regression analysis of survival showed that increased expression of filamin A protein (histoscore > 90) is significantly related with shorter overall survival (HR = 1.005, 95 %CI[1.000;1.010], p = 0.037) and disease free survival (HR = 1.004, 95 %CI [1.001:1.008], p = 0,017) in patients with adjuvant platinum-based chemotherapy. Such relationship was not seen in patients without adjuvant treatment.
Conclusion: Filamin A expression might represent a novel potential predictive marker of platinum-based treatment outcome in patients with non-small-cell lung cancer.

OFP-15-010

Detection of EGFR mutations in tissue and plasma from Slovenian patients with NSCLC prior to and during treatment

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Objective: Non-small cell lung cancer (NSCLC) patients with tumours that harbor EGFR sensitizing mutations are eligible for tyrosine kinase inhibitors (TKIs) due to a high likelihood of response. The majority of EGFR mutations are exon 19 deletions or exon 21 L858R point mutations. However, most patients will eventually develop resistance and show disease progression. We followed NSCLC patients with EGFR sensitizing mutations by measuring EGFR mutations in plasma during TKI treatment.
Method: We collected baseline tumour tissue and plasma samples from patients prior to TKI therapy and at approximately 8 week intervals after initiation of therapy (plasma only). We used the cobas® EGFR Mutation Test for tissue (CE-IVD) and plasma (under development, Roche, Pleasanton, CA).
Results: Thirteen patients with EGFR sensitizing mutations in tumour tissue have been enrolled in the study (9 exon 19 deletions, 2 exon 21 L858R mutations, 2 exon 18 G719X mutations). All but one baseline plasma samples were mutation positive. After initiation of TKI treatment, subsequent plasma testing showed no EGFR mutation in three patients and a decrease in two patients. No EGFR resistance mutations have been detected.
Conclusion: These early data support the value of plasma testing to monitor the patient response to EGFR TKIs.

OFP-15-011

Reproducibility of plasma based detection of EGFR mutations

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Objective: EGFR sensitizing mutations in patients with advanced non-small cell lung cancer predict clinical response to TKI therapy. EGFR mutations can be detected in patient's plasma with different technologies and varying performance. The aim of this study was to analyze the reproducibility of an allele-specific PCR assay to detect EGFR mutations in plasma.
Method: Plasma samples were collected from patients with tumour tissue confirmed EGFR sensitizing mutations. Paired blood samples were collected before and/or during targeted treatment and centrifuged to collect plasma. DNA was extracted from plasma using a modified cobas® DNA Sample Preparation kit (under development by Roche Molecular Systems).
Results: We collected 35 paired samples where 30 were identical for mutation status in duplicate samples. For 14 cases with EGFR mutations (7 exon 19 deletions, 4 exon 21 L858R mutations, 2 exon 18 G719X mutations, 1 T790M resistance mutation), we assessed the difference of a semi-quantitative index between replicates. There were 5 discordant cases between paired samples (three for exon 19 deletions, one for exon 21 point mutation L858R, and one for resistance mutation T790M). The overall concordance rate was 85.7 %.
Conclusion: We report a high rate of concordance for EGFR mutation status in paired plasma samples.

OFP-15-012

Immunohistochemical analysis of stromal changes in preinvasive and invasive adenomatous lung proliferations: Preliminary observations

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Objective: The new WHO histological classification of lung tumours describes such proliferations as atypical adenomatous hyperplasia (AAH), adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA) and invasive adenocarcinomas (InvADC). Differentiation all these entities based only on histological criteria often is difficult. Aim: To observe the usefulness of immunohistochemical reactions in differentiation of AAH, AIS, MIA and InvADC.
Method: Twelve AAH cases, 7 AIS, 3 MIA and 12 InvADC were stained with anti-calponin-1, SMA and podoplanin antibody. The presence and intensity of the reactions in the stroma was assessed.
Results: Calponin was negative in AAH cases (6/12), short fibers were observed in AAH (6/12), AIS (3/7) and InvADC (1/12), short and long distinct fibers was in AIS (3/7) and MIA (1/3), numerous long fibers were seen in InvADC (11/12), MIA (2/12) and AIS (1/12). SMA: positive reaction direct under the epithelial cells was seen in all preinvasive lesions. Dense reaction in the stroma concerned InvADC (11/12) and MIA (2/3). Podoplanin expressed by stromal cells was detected only in InvADC (8/12). Small lymphatic vessels proliferation was observed in all lesions except AAH.
Conclusion: Immunohistochemical reactions with calponin, SMA or podoplanin can be useful in differentiation AAH, AIS, MIA and InvADC. Intense stromal reaction with SMA and calponin seems to be the most diagnostic for invasion and lymphatic vessels proliferation for distinction neoplastic proliferations from AAH.

OFP-15-013

Large airway inflammation carries high risk for developing chronic lung allograft dysfunction

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Objective: We hypothesized that large airway inflammation (lymphocytic bronchitis) may be predictor of developing chronic lung allograft rejection (CLAD). CLAD includes bronchiolitis obliterans (BOS) and restrictive allograft syndrome (RAS). Current grading system grades only small airway inflammation from B0 to B2R. Large airway inflammation is not included in the grading system. Any grade of small airway rejection, without accompanying acute vascular rejection is associated with an increased risk of BOS.
Method: We evaluated 311 biopsies from 71 patients and graded large airway inflammation following grading system for small airway inflammation. Clinical follow-up was obtained regarding presence or absence of CLAD.
Results: 10 biopsies from 9 patients met criteria for large airway rejection. 8 of the patients had a B1R and 1 had B2R. 5 of 9 patients (56 %) were subsequently diagnosed with CLAD. Three of nine patients (33 %) developed BOS and 2 of 9 patients (22 %) developed RAS. Two of the patients had donor specific antibodies (DSA). Eight of nine patients had concurrent vascular rejection or vascular rejection in any of the previous/follow up biopsies (2 had A1 and 6 had A2).
Conclusion: Our results show that large airway inflammation may be associated with developing CLAD.

OFP-15-014

Programmed cell death 4 nuclear loss and miR-21 overexpression in malignant mesothelioma

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Objective: MiR-21 over-expression has been recently reported in malignant pleural mesothelioma (MPM) compared to normal mesothelium. Programmed cell death 4 (PDCD4) is a tumour suppressor gene whose expression is directly controlled by miR-21 in several cancers. The aim of this study is to assess the expression of miR-21 and PDCD4 in MPM in order to define a possible new oncogenic pathway.

Method: PDCD4 nuclear expression was assessed with immunohistochemistry (IHC) in 40 non-neoplastic pleura (NNP) and 40 MPM formalin-fixed and paraffin-embedded specimens. PDCD4 and miR-21 expression were analyzed by qRT-PCR in all cases. In situ hybridization (ISH) of miR-21 was performed in 5 representative cases of both groups.
Results: Immunohistochemistry showed a lower PDCD4 nuclear expression in MPMs than in NNPs. PDCD4 was down-regulated, whereas miR-21 was over-expressed in MPM cases compared to NNP ones. ISH detected miR-21 only in MPM specimens.
Conclusion: These data highlighted a substantial switch between PDCD4 and miR-21 expression in MPM carcinogenesis. Further larger studies should assess the diagnostic value of these two markers for MPM.

OFP-15-015
Updated regulatory guidelines lead to incomplete test execution in molecular diagnostics
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Objective: A drug label modification for panitumumab and cetuximab by EMA caused a shift in the molecular diagnostic testing strategy for the treatment selection of metastatic colorectal cancer patients. The ESP Colon External Quality Assessment (EQA) scheme was able to monitor how quickly laboratories expanded their testing procedures.
Method: Diagnostic reports, submitted by the participants from two consecutive EQA rounds were reviewed to determine which codons were included in the laboratory's tests.
Results: Only exon 2 (codon 12 and 13), one of the three required RAS exons, is covered routinely by all participating laboratories. In 2014, 45 and 57 % of the participating laboratories tested for codon 59 in KRAS and NRAS respectively. In 2015, this improved to 67 % for KRAS and 71 % for NRAS. Also codon 117 (78 % of laboratories) and 146 (88 %) of NRAS still show shortcomings to cover the requirements. A shift towards next generation sequencing and a decrease in the use of non-commercial methods was observed.
Conclusion: The time pressure to change routine test procedures compromises adherence to updated regulatory guidelines. Two consecutive EQA rounds demonstrated progress in the implementation of complete RAS testing, and emphasized that EQA participation is indispensable to monitor performance and quality assurance.

Wednesday, 9 September 2015, 14.00–16.00, Annex B
OFP-16 Oral Free Paper Session Molecular Pathology

OFP-16-001
VE1 (BRAF V600E) immunohistochemistry in colorectal cancer: Validation, assessment of heterogeneity and clinicopathological associations in three colorectal cancer cohorts
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Objective: BRAF is mutated in approx. Ten percent of colorectal cancers (CRC). In addition to its diagnostic role in Lynch syndrome, BRAFV600E is a prognostic factor in metastatic CRC and a potential predictive biomarker for future combined therapies. Here, we validate the VE1 antibody against BRAFV600E, assess heterogeneity and investigate clinicopathological associations of VE1 in CRC patients.
Method: VE1 immunohistochemistry was performed on cell lines, whole tissue sections and a next-generation tissue microarray (ngTMA) of 33 cases, with known mutational status. Additional ngTMAs were investigated: 1) primary/metastasis cohort of 14 patients with punches from all tumour blocks (n = 100 areas), 2) colon cancer cohort (n = 259 patients) with six punches/resection, 3) preoperative biopsies (n = 125 patients).
Results: VE1 was homogeneous in whole tissue sections and cell lines and 100 % concordant with mutation. Inter-observer agreement was 100 %; sensitivity/specificity for mutation was 100 and 93 %. Primary tumour blocks were homogeneous; two metastases showed heterogeneity. VE1-positivity correlated with older age (p = 0.0455), mucinous histology (p = 0.0277), right-sided location (p = 0.001), tumour grade (p < 0.001), MLH1-deficiency (p < 0.0001), and poor prognosis in pM1 patients (p < 0.0001).
Conclusion: VE1 is highly specific and sensitive for V600E mutation and correlates with expected clinicopathological features. Because of low/no heterogeneity within the same tumour samples, TMA studies using VE1 are feasible.

OFP-16-002
Collagen XI Alpha I: A new marker to identify infiltration in colonic tubular adenomas with in situ carcinoma
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Objective: The accurate diagnosis of malignancy of in situ carcinomas settled on adenomatous polyps is sometimes very difficult because microinfiltrative areas in endoscopic biopsies are subtle changes. Our hypothesis is that the presence of COL11A1 (described as a marker of tumour infiltration) in endoscopic biopsies of colon may be associated with microinfiltrative early changes.
Method: Immunohistochemistry for pro-COL11A1 (1E8.33, Oncomatrix) was performed in samples of colon adenocarcinoma (10), non tumoural o polypoid lesions (21) and in situ carcinomas settled on adenomatous polyps (23), 13 of which showed infiltration in the subsequent surgical biopsy. We considered as positive any lesion presenting at least one stained fibroblast.
Results: Nine out of ten adenocarcinomas presented COL11A1 immunostaining, while none of benign lesions presented COL11A1 expression (p < 0.0001). Comparison between in situ lesions that presented subsequent infiltration respect of which were pure in situ showed statistical significance (p = 0.0027) because 7 out of 13 cases that confirmed infiltration were positive, while none of the ten pure in situ showed immunolabeling.
Conclusion: To conclude, expression of COL11A1 in endoscopic biopsies from in situ carcinomas settled on adenomatous polyps is associated with a higher probability of presenting infiltration in the entire lesion.

OFP-16-003
Concomitant Immunohistochemistry (IHC) and Silver in Situ Hybridisation (SISH) in gastrooesophageal junction and gastric adenocarcinoma: Concordance or discrepancies?
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Objective: HER2 analysis in gastroesophageal junction (GEJC) and gastric adenocarcinoma (GC) is required to predict patient's responsiveness to trastuzumab therapy. The current recommendations for HER2 testing include IHC. ISH are additionally performed in equivocal cases (IHC2+). Here, we compare IHC and SISH in 221 consecutives cases of GEJC and GC.
Method: From 01/2013 to 03/2015, 221 cases of GEJC (n = 71; 6 poorly cohesive carcinoma (PCC) and 65 intestinal type (IT)) and GC (n = 150; 42 PCC and 108 IT were tested by both IHC (ventana 4B5) and SISH (Inform Her2) using benchmark Ventana. Results were interpreted according to European guidelines.

Results: Concordant HER2 positive rates in GEJC and GC using IHC and SISH are 29.2 and 17.6 % respectively. False positive results (IHC3+ SISH-) concern 13.6 % of GEJC (3/22) and 24 % of GC (6/25). Equivocal cases (IHC2+) are SISH+ in 28 % of GEJC (7/25) and 12.8 % of GC (6/47). Only one false negative (IHC-; SISH+) was observed in a GEJC case.
Conclusion: Significant discrepancies are observed when comparing IHC and SISH for HER2 testing. False positive results by IHC may be caused by misinterpretation of staining, sampling errors or technics which supports a need for more frequent utilization of SISH.

OFP-16-004
Identification of proteomic profiles associated with tumour regression grading in rectal cancer

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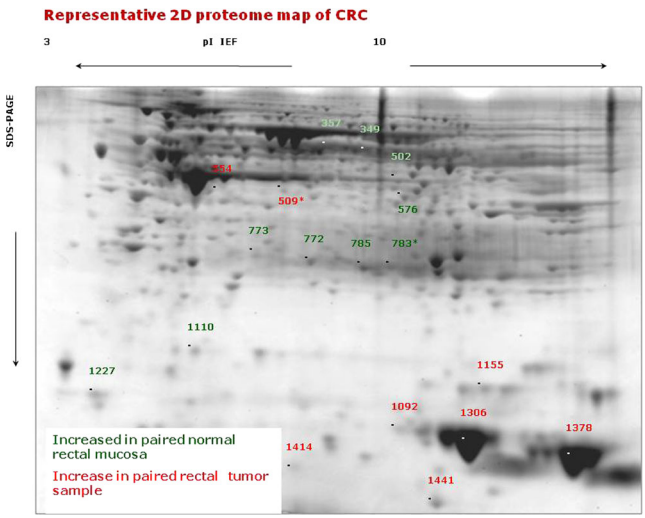
Objective: Rectal cancer response to neoadiuvant chemo-radiotherapy (CRT) is variable. Identifying markers of response will help select patients more likely to benefit from therapy. Objective of the study is to identify at diagnosis proteomic profiles associated with tumour regression grading (TRG) in rectal cancer.
Method: This study includes 40 patients with rectal cancer treated with CRT followed by surgery. Proteins from pre-treatment tumour biopsies and control from paired normal bioptic specimens were screened for comparative proteomic approach by using 2D difference gel electrophoresis (2D-DIGE). Differential spots found with Decyder were identified by MALDI-TOF and peptide fingerprinting with Mascot search engine. Interactions among identified proteins was analyzed with STRING 9.1 search tool. Pathological TRG was assessed on surgical specimens.
Results: A total of 30 proteins were identified as discriminators between tumour samples and controls by principal component analysis and hierarchical clustering ($p < 0.01$; spot map>50 %). These proteins were already described as involved in rectal metabolic cell pathways and angiogenesis. Possible correlations between these proteins and TRG are under evaluation.
Conclusion: Comparative proteomics approach based on 2D-DIGE and MALDI-TOF identification succeeded in differentiating rectal tumour samples from paired normal rectal mucosa. Further analyses will unravel possible correlations between distinct protein profiles and TRG response to CRT treatment that could be used to select optimal therapy in rectal cancer patients.



OFP-16-005
Translation initiation in endometrial carcinoma

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Objective: Eukrayotic translation initiation factors (eIFs) are important for induction of gene expression, wherefore they play a critical role in cellular activity. eIFs are involved in cancer formation, progression and thus prognosis. Endometrial carcinoma (EC) belongs to the most common gynaecologic malignancies. According to the aetiopathogenesis, type I and type II EC can be disdinguished.
Method: Tissue samples from 297 female EC patients and control samples from nine subjects with normal endometrium were included into the study. Each sample was tested for seven different eIF-subunits (eIF 2alpha, 3p110, 3h, 4e, 4g, 5, 6).
Results: High expression levels of eIF4g in tissue samples with a low expression were significantly associated with reduced overall-survival ($p < 0.05$). For eIF2alpha, 3p110, 3h, 4e, 5 and 6, however, no significant results emerged. Nevertheless, a trend towards reduced overall-survival with particular expression alterations was present.
Conclusion: According to these results, one eIF was significantly associated with short overall-survival in patients suffering from EC. Though expression levels of the remaining eIF-subunits showed a trend towards reduced overall-survival, no significant results could be archived. eIFs may constitute markers prediciting outcome in EC, though further investigations will be needed in order to strengthen the clinically useful readout.

OFP-16-006
Characterizing the effect of mutation and natural selection on KRAS mutation subtype distribution

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Objective: KRAS oncogene shows different mutation distribution in different malignancies. The purpose of this work was to determine the relative contribution of mutational biases and natural selection to the distribution of KRAS mutations in colon, lung and pancreatic adenocarcinomas.
Method: Distribution of KRAS mutation subtypes was determined using the Catalog Of Somatic Mutations In Cancer. Data of synonymous mutations from the Cancer Genome Atlas (TCGA) was used to determine mutational biases. Normalization of actual mutation subtype to expected base pair change determined the selective power of each mutation. The clinical significance of positively selected mutations was evaluated in 100 lung adenocarcinoma cases.
Results: KRAS mutation subtype distribution was significantly different between the tumour types with c.35G>A presenting 35, 17 and 51 % of KRAS mutations in colon, lung and pancreatic adenocarcinoma, respectively ($p < 0.0001$). Following normalization to the TCGA data, p.G12V and p.G12C were the most positively selected mutations in colon and lung adenocarcinomas, respectively. In our lung adenocarcinoma data set the evolutionary selected mutations were associated with higher tumour stage and grade.
Conclusion: Analysis of the expected and actual distribution of mutation subtypes can determine the relative selective strength of different mutations in each tumour type and may provide higher resolution for personalized anti-cancer therapy.

OFP-16-007

ALK gene rearrangement in Non-small Cell Lung Cancer (NSCLC) with squamous differentiation

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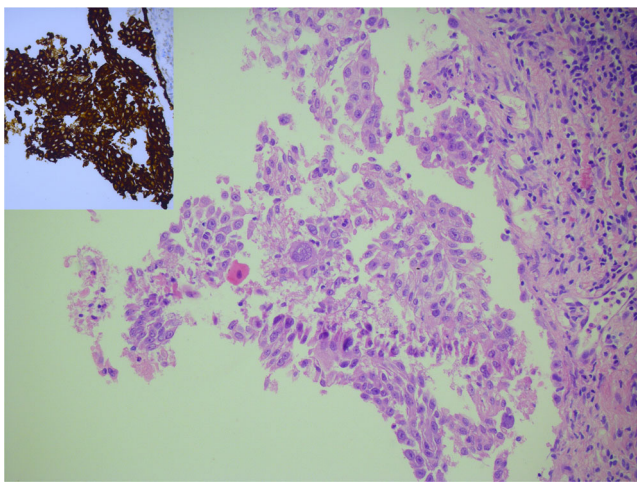
Objective: ALK testing to identify patients with adenocarcinoma of the lung likely to benefit from crizotinib therapy is now standard practice. However, the prevalence of ALK translocation in NSCLC with squamous differentiation has not been well characterized in the published literature.
Method: This series included 3317 cytology, biopsy and resection specimens referred to our service from over 20 UK hospitals for ALK testing. Parallel fluorescence in situ hybridisation (FISH; Vysis Abbott break apart probes) and immunohistochemistry (IHC; Ventana D5F3 antibodies) was performed for each case.
Results: Although the majority of cases were adenocarcinomas, 56 squamous cell and 48 adenosquamous carcinomas were successfully tested with FISH and IHC. Of these 10 were FISH+ (9.6 %), significantly higher than the overall series rate of 3.2 % ($p = 0.005$). The proportion of FISH+/IHC- squamous tumours with significantly greater than the proportion of discrepant adenocarcinomas (70 and 23 % respectively, $p = 0.004$).
Conclusion: Contrary to conventional wisdom this large series shows that ALK gene rearrangements may be seen in NSCLC with squamous differentiation. We plan to investigate the high rate of FISH+/IHC- discordance using RT-PCR. Data for response to crizotinib is being collected to determine the clinical significance of ALK translocation in this subset of patients.

A case of NSCLC with squamous differentiation which was ALK positive on FISH and IHC (inset):



OFP-16-008

Molecular testing of Gastrointestinal Stromal Tumours (GISTs): The Birmingham experience of 1249 cases

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Objective: In addition to testing for KIT and PDGFRA mutations, which are found in most GISTs, we have recently incorporated SDH and BRAF testing for wild type GISTs into our routine service.

Method: All 1249 cases (formalin-fixed paraffin-embedded) tested between 2007 and 2014 were included. Exons 9, 11, 13 and 17 of KIT and exons 12, 14 and 18 of PDGFRA were screened by direct (Sanger) sequencing. From 2013 wild type GISTs were also tested for BRAF mutation (real time PCR) and SDHB/A deficiency (immunohistochemistry).
Results: Of the 1200 successfully tested cases 73.9 % showed KIT mutations, of which exon 11 deletion was most frequent, and 11.0 % showed PDGFRA mutations, of which exon 18 D842V missense mutation was most frequent (see table for full spectrum). Wild type GISTs accounted for 15.1 % of cases. Five of the 35 cases tested for SDH showed a deficiency and these patients are now under investigation for germline testing. One codon 600 BRAF mutation has so far been detected.
Conclusion: This large series demonstrates the feasibility of multiple molecular testing and integrated reporting by a single laboratory. The relatively high proportion of SDH deficiency detected so far highlights the importance of routine SDH immunohistochemistry for wild type GISTs.

Frequency of mutations detected:

KIT mutations	**887 (73.9%)**
Exon 11 deletion	486
Exon 11 missense	242
Exon 11 duplication	62
Exon 9 duplication	75
Exon 13 mutation	18
Exon 17 mutation	4
PDGFRA mutations	**132 (11.0%)**
Exon 18 D842Vmissense mutation	81
Exon 18 other mutation	34
Exon 12	13
Exon 14	4
Wild type	**181 (15.1%)**

OFP-16-009

A complete workflow for diagnostic microbiome analysis using Ion Torrent PGM and QIIME

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Objective: Infectious diseases and the gut microbiome are the two main areas in which the assessment of microbial communities is part of pathological routine. Recently, NGS sequencing has greatly facilitated microbial community analysis in a research setting. The aim of this project was to make 16s microbiome analysis available to routine pathological diagnosis performed within a molecular pathology laboratory.
Method: DNA extraction from diverse matrices is accomplished by Roche MagnaPure and Promega Maxwell semiautomated systems. PCR is performed using 515–806 16s rRNA gene primers fused to Ion Torrent barcodes and sequencing adapters. Library processing is done by agarose gel extraction and picogreen measurement followed by sequencing on the Ion Torrent PGM using a 400bp sequencing kit. The bioinformatics pipeline is divided into sequence preparation (trimming, error correction, chimera removal) and sequence analysis using QIIME scripts.
Results: We have successfully tested and validated a generic workflow for the extraction of bacterial DNA from fresh, frozen and formalin fixed tissue and bodily fluids. The analysis of bacterial communities has been standardized and optimized to yield results even from paraffin tissue blocks with very limited bacterial load. The bioinformatics pipeline has been validated and made accessible to technical personnel through a web-interface. To date more than 100 pathological diagnostic reports have been generated with this workflow, both encompassing gut microbiome analysis as well as bacterial identification requests.

Conclusion: 16s microbiome analysis has entered the routine pathological repertoire and can be performed in a well equipped molecular pathology lab in a standardized and highly efficient semi-automated routine workflow by Ion Torrent NGS sequencing.

OFP-16-010
Impact of cytopathology samples in determining ALK gene-arrangement status in lung cancer patients

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Objective: Recently, anaplastic lymphoma kinase gene-rearrangement (EML4-ALK) particularly in adenocarcinoma occurring in younger commonly non-smoker patients is one of the new targets for personalized medicine. Cytology sampling is less invasive and preferred modality in inoperable patients. The objectives are to assess the utility and adequacy of cytology specimens to determine ALK gene-arrangement status by immunohistochemistry and FISH assay.
Method: At our institution after rapid onsite evaluation when possible at least 2 additional passes are dedicated to cell block preparation. Pathology information system search from January 2013 to March 2015 identified 574 cytology samples from 554 patients screened for ALK gene-rearrangement by immunohistochemistry using 5A4 antibody. Positive cases were tested with FISH assay for confirmation using Vysis ALK Break Apart FISH Probe Kit (ABBOTT Labs).
Results: 19 cases (age range 38–81 years, sex 11 F: 8 M) were 2+ or 3+ positive by IHC and another 5 cases were very faintly positive. The average number of tumour cells present in the cell block was 500 in these cases. Seven case samples were from metastasis and 12 were from primary lung tumours. All 2+ and 3+ IHC positive samples were confirmed positive with Break Apart FISH assay but all faintly IHC positive cases were negative by FISH assay. The overall FISH confirmed ALK positive rate was 3.4 % in screened cytology cases which is within the expected range of ALK positive cases.
Conclusion: Less invasive cytology samples are an excellent source for ALK gene-rearrangement testing when optimized fine needle protocols are used to procure and process adequate specimens.

Wednesday, 9 September 2015, 14.00 – 16.00, Meeting Room 6/I
OFP-17 Joint Oral Free Paper Session Dermatopathology / Ophthalmic Pathology

OFP-17-001
Significance of plasma cells in melanoma

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Objective: Despite the beneficial effects of humoral immunity in vivo and in vitro, several small studies have claimed that melanomas harboring sheets of plasma cells (PC) carry a poor prognosis. We aimed to investigate the significance of PC in a large series of consecutive primary melanomas (PM) and loco-regional lymph nodes (LN).
Method: We revised 710 melanomas to correlate the presence of PC with histological prognostic markers. Immunohistochemistry for CD138, heavy and light chains was done in PM and LN. In 3 PM and in 9 LN with frozen material, VDJ-rearrangement was analyzed by Gene Scan Analysis.
Results: 41 cases (5 %) showed clusters/sheets of PC. PC-rich melanomas occurred at an older age and were thicker, more often ulcerated and more mitotically active ($p < 0.05$). PC were polyclonal and often expressed IgA in addition to IgG. In LN, IgA+ PC were found both in the sinuses and subcapsular areas. The number of IgA+ PC was higher in involved than in non-involved LN. Analysis of VDJ-rearrangements showed the IgA to be oligoclonal.
Conclusion: Sheets of PC in melanoma are associated with poor prognostic features. IgA oligoclonality suggests an antigen-driven response that facilitates melanoma progression by a hitherto unknown mechanism.

OFP-17-002
Ocular adnexal lymphoma: The eyelid stands out

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Objective: The ocular adnexa (OA) include the eyelids, conjunctiva, lacrimal apparatus, and orbital soft tissue. One percent of all lymphomas and approximately 8 % of all extranodal lymphomas arise in the OA and the incidence is increasing. The different OA structures show a distinctly different disease spectrum. The objective is to gain insight into the relative frequencies of the types and location of OA lymphoid disease through a single center review.
Method: The diagnoses and location of 226 lymphoproliferative lesions from the past 27 years in the department of Pathology of the Erasmus University Medical center were evaluated.
Results: The relative frequencies of ocular adnexal lymphoma presentation are orbit, 38 %, conjunctiva, 31 %, lacrimal apparatus, 18 % and eyelid, 13 %. The most frequent primary lymphoma types of the ocular adnexa are extranodal marginal zone lymphoma, 63 %, follicular lymphoma, 16 %, diffuse large B cell lymphoma 10 %. The eyelids show the highest proportion of secondary lymphoma involvement, 47 % of all eyelid lymphoproliferative lesions, compared with 20 % in the other ocular adnexa. This probably also explains the most varied list of 12 different diagnostic entities in the eyelid, including T-cell lymphoma.
Conclusion: The eyelid lymphoid lesions are clearly distinct from the other ocular adnexa.

Table:

Diagnosis, anatomic localization and frequency of tumour in 226 consecutive patients with histopathologically confirmed ocular adnexal lymphoproliferative tumour

	Orbit		Conj		Lacr		Eyelid		All				
	Pr	Sec	Pr	Sec	Pr	Sec	Pr	Sec	Pr	Sec	All	%	% l
RLH	7	0	11	0	13	0	2	0	33	0	33	15	na
MALT	na	1	41	1	10	2	0	0					
ENMZL	33	5	0	1	0	0	5	1					
Subt MALT + ENMZL									89	11	100	44	48
Follicular	11	2	5	3	3	2	4	1	23	8	31	14	15
DLBCL	10	3	0	0	3	0	1	1	14	4	18	8	9
Mantle	3	3	0	2	2	3	1	3	6	11	17	8	8
SLL/CLL	1	1	1	2	1	1	2	3	5	7	12	5	6
Lymphopl	3	1	0	1	0	1	0	0	3	3	6	3	3
Burkit	1	0	0	0	0	0	0	0	1	0	1	<1	<1
Pr cut follicular	0	0	0	0	0	0	0	1	0	1	1	<1	<1
Pr cut DLBCL	0	0	0	0	0	0	0	1	0	1	1	<1	<1
Myc fungoides	0	0	0	0	0	0	0	1	0	1	1	<1	<1
CD30+ T cell	0	0	0	0	0	0	0	1	0	1	1	<1	<1
T cell NOS	0	1	0	0	0	0	0	0	0	1	1	<1	<1
Lymph papul	0	0	0	0	0	0	0	1	0	1	1	<1	Na
T cell hyperpl	0	0	0	0	0	0	1	0	1	0	1	<1	Na
NK/T cell	0	0	0	1	0	0	0	0	0	1	1	<1	<1
Subtotal (%)	69 (80)	17 (20)	58 (84)	11 (16)	32 (78)	9 (22)	16 (53)	14 (47)	175 (77)	51 (33)	226	100	100
Total (%)	86 (38)		69 (31)		41 (18)		30 (13)						

Conj = conjunctiva, Lacr = lacrimal apparatus, Pr = primary, Sec = secondary, l = lymphoma, RLH = reactive lymphoid hyperplasia, MALT = MALT lymphoma, ENMZL = extra nodal marginal zone lymphoma, Follicular = follicular lymphoma, DLBCL = diffuse large B cell lymphoma, Mantle = mantle cell lymphoma, SLL = small lymphocytic lymphoma, CLL = chronic lymphocytic leukaemia, Lymphopl = lymphoplasmacytic lymphoma, Burkit = Burkit lymphoma, Pr cut follicular = primary cutaneous follicular lymphoma, Pr cut DLBCL = primary cutaneous diffuse large B cell lymphoma, Myc fungoides = mycosis fungoides, CD30+ T cell = CD30 positive T cell lymphoma, T cell NOS = T cell lymphoma NOS, Lymph papul = lymphomatoid papulosis, T cell hyperpl = T cell hyperplasia, NK/T cell = NK/T cell lymphoma, Na = not applicable.

OFP-17-003
A case of epidermotropic and folliculotropic T-cell lymphocytosis: Drug-induced Mycosis-like reaction or pilotropic T-cell dyscrasia?

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Method: A 31-year-old white female patient presented with a generalized maculopapular pruritic rash, 2 weeks after the onset of a Lamotrigin treatment. She also presented with multiple adenopathies, blood eosinophilia and hyponatremia. The clinical differential diagnosis included Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) and Mycosis Fungoïdes. A biopsy from the right forearm was performed.
Results: On microscopic examination, the epidermis showed orthokeratosis, perifollicular parakeratosis and rare epidermal acidophilic bodies. A basal linear exocytosis of lymphocytes, with perinuclear clear halo, was noted, some mimicking small Lutzner cells. The lymphocytes were mostly concentrated at a follicular infundibulum, or scattered in the superficial dermis with scarce neutrophils. They were CD3, CD4 and CD8 positive (CD4/CD8 ratio estimated at 2) and CD7 negative. Alcian Blue stain showed no mucinosis. A descriptive diagnosis of folliculotropic T-cell lymphocytosis was hence made; Drug-induced Mycosis-like reaction could not be excluded. Lamotrigin was discontinued. The complete resolution of her symptoms and the disease-free 6-month follow-up confirmed the DRES S syndrome and the non-neoplastic nature of the cutaneous infiltrate.
Conclusion: Folliculotropic T-cell lymphocytosis within a DRESS syndrome can mimick Mycosis Fungoïdes. Drug-related lymphoid cutaneous reactions remain extremely controversial when considered in the absence of the clinical information and evolution.

OFP-17-004
Broad spectrum of histological findings in five cases of epithelioid cell histiocytoma

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Objective: Epithelioid benign fibrous histiocytoma, also known as epithelioid cell histiocytoma (ECH), is a rare and distinctive variant of fibrous histiocytoma. We identified five cases in our database diagnosed between 2005 and 2014. These are worth reporting due to their variety of histological features that may lead to misinterpretations in differential diagnosis.
Results: In first two cases, an exophytic dermal nodule surrounded by an epidermal collarette was observed. The main component was polygonal epithelioid cells with abundant eosinophilic cytoplasm and a chondromyxoid stroma. Case 3 was composed of a lesion with prominent hemangiopericytoma-like pattern characterized by numerous small vascular structures scattered between epitheloid cells. In case 4, the striking histopathological feature was the extensive mucin deposition surrounding spindle, epithelioid, and rare xanthomatous cells. In the last one, spitzoid cellular morphology and stromal hypereosinophilic collagen bundles were the striking features. All lesions were immunohistochemically positivite for FactorXIIIa and CD68. Dermal melanocytic lesions were excluded based on negativity of melanocytic markers.
Conclusion: The light microscopic findings of ECH can mimic melanocytic, vascular, epithelial, or other histiocytic lesions. Combination of histological and immunophenotypic findings is crucial for proper diagnosis. It is important for practicing pathologists to be aware of this entity and its various histological patterns.

OFP-17-005
E-cadherin expression in lymph node metastatic melanoma

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Objective: Loss of E-cadherin expression has been associated with malignant progression of neoplastic cells through loss of cell-cell contact and thereby allowing cancer cells to detach and migrate. It is observed from in early stage and radial growth phase melanoma in metastatic melanoma in a percentage higher than 80 %.
Method: We studied 20 patients (11 females, 9 males) with regional lymph node metastatic melanoma (primary melanomas: Nodular and Superficial Spreading Melanoma), within a range of age between 41 and 83 years old. In our study we evaluated the immunohistochemically E - cadherin expression in formalin-fixed, paraffin-embedded tissue in metastatic melanoma cells of lymph nodes.
Results: Expression of E - cadherin in 100 % melanoma cells. The expression was complete membranous, strong in a percentage of 60 % (12 patients) and moderate in a percentage of 40 % (8 patients).
Conclusion: Even though there is loss of E - cadherin expression in the majority of similar studied cases in the literature, in our study E - cadherin was expressed in a percentage of 100 %.

OFP-17-006
P53/Tp53 status in keratoacanthomas

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Objective: Keratoacanthoma (KA) is a common benign keratinocytic skin neoplasm that is located to sun exposed areas. It typically develops rapidly and undergoes complete spontaneous regression. P53 induces apoptosis and may be related to regression of KAs. We wanted to study P53 expression through stages of KA development–during proliferation, maturation and regression.
Method: 124 KAs were characterized with respect to age of the lesions, in addition to phenotypic criteria such as cellular atypia, infiltration and fibrosis. Tp53 mutations were detected by capillary electrophoresis and P53 protein levels assessed by immunohistochemistry.
Results: Tp53 mutations were detected in 49/124 cases (39.5 %). Increased levels of p53 protein were correlated with Tp53 gene mutation. A significant correlation was seen between high p53 protein levels and cellular atypia, infiltration and age of the lesions.
Conclusion: This is the first report showing extensive mutation of the Tp53 gene in KAs, and its association to increased p53 levels. Higher p53 protein levels in older lesions suggest a role for p53 in the late stage of keratoacanthomas, suggesting a p53-dependent apoptosis pathway related to regression. This is further substantiated by the significance restricted to non-mutated lesions.

OFP-17-007
Metastatic basal cell carcinoma of the skin: Report of two cases

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Objective: Basal cell carcinoma (BCC) shows locally invasive behavior with extremely rare metastases. Herein, we report two cases of metastatic basal cell carcinoma.
Method: Analysis of skin-biopsies database covering a 15-years period (2000–2014).
Results: Among 6657 BCCs, there were two with microscopically proven metastases (0.03 %). A 68-years old male, with the history of scalp irradiation (for tinea capitis treatment) at the age of 12, developed metastases in multiple bones, and infiltrative BCC was found in sacrum biopsy. He had first basal cell carcinoma discovered at the age of 58, and experienced 22 excisions during the 8-years-period for recurrent BCC located in the occipital and parietal region. Tumour diameter-range was 6–102 mm (average

36.3 mm, median 31.5 mm). First seven biopsies showed tumour in the reticular dermis, while most of the remaining tumours invade subcutaneous fat, muscles, epicranial aponeurosis or parietal bone. All scalp tumours were infiltrative or morpheaform histologic type. Second patient was an 82-year-old male with BCC on the ear lobe and metastasis in retroauricular lymph node. Tumour was 35 mm in diameter, infiltrative type.
Conclusion: Location, multiple recurrences, infiltrative type and exposure to ionizing radiation could be associated with (albeit small) risk of metastatic BCC.

OFP-17-008
Application of biophotonics to the study of scar tissue
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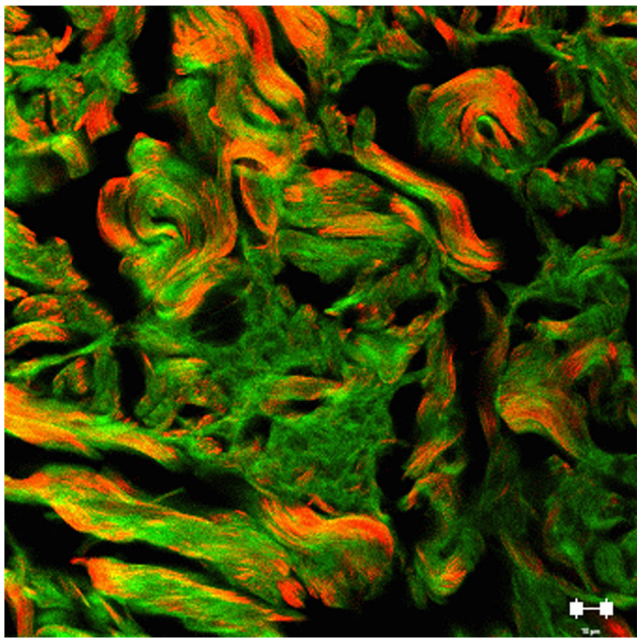
Objective: The integrated application of modern techniques such as Second Harmonic Generation (SHG) and fluorescence lifetime imaging (FLIM) with mathematical image analysis enable us to visualize details not seen by conventional light microscopy. The aim of this study was to investigate whether this could also be true for the investigation of scar tissue.
Method: 32 routine histological preparations of keloids, hypertrophic and normal scars were studied. Two-photon fluorescence and SHG was obtained by a multiphoton microscope and a Mai Tai Ti- Saphire laser at 940 nm. 3D reconstructed patchwork images were created and computerized image analysis was done. For FLIM we used a system composed of a confocal microscope and a FLIM detection system. The samples were excited by a laser diode at 405 nm.
Results: Texture variables derived from the co- occurrence matrix of the computerized fluorescence images showed significant differences between normal scars, hypertrophic scars and keloids. Lifetimes of collagen in central areas of all scar types were significantly longer than in the periphery. There was a significant positive correlation between the fluorescence lifetimes of red blood cells and collagen fibers among the cases.
Conclusion: In summary, SHG and FLIM techniques reveal in routinely processed scar tissue morphological characteristics, which cannot be detected by conventional light microscopy.

Combined picrosirius fluorescence and SHG imaging of a keloid:



OFP-17-009
EGFR and Cyclin D1 in nodular melanoma: Correlation with pathohistological parameters and overall survival
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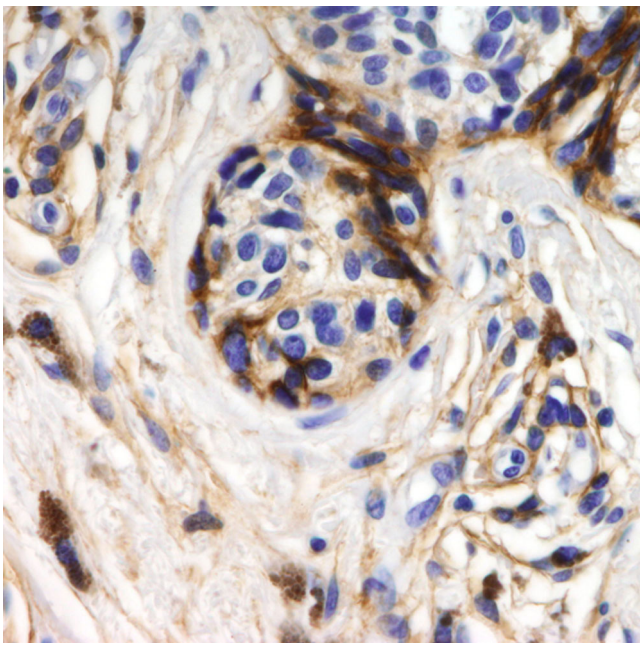
Objective: We aimed to investigate protein expression of membrane and nuclear EGFR, cyclin D1 and the corresponding gene status and correlate the obtained results with clinicopathological parameters and overall survival of patients in nodular melanoma (NM).
Method: Immunohistochemical and FISH analyses were performed on tissue microarrays constructed from 110 NM samples, 30 compound nevi and 38 dysplastic nevi.
Results: NM samples demonstrated 24 % of strong cyclin D1 and 37 % of strong ki67 protein expression compared to the 3 and 0 % of strong cyclin D1 and ki67 expression in the control group.Membrane EGFR expression was detected in 50 % of NM cases, while EGFR gene amplification was detected in only 4 % of NM cases. Multiple NM samples presented simultaneous membrane and nuclear EGFR expression.
Conclusion: We demonstrated negative correlation between tumour thickness and membrane EGFR expression. It was also observed that membrane EGFR 3+ NM samples presented ulceration significantly more often than membrane EGFR negative (0) NM samples. In univariate analysis, performed on 44 patients with follow-up data, both nuclear and membrane EGFR overexpression showed a correlation with a shorter overall survival. Nuclear EGFR (++,+++) showed 3,06 and membrane EGFR (2+,3+) showed 2,76 greater mortality risk compared to patients with low and negative nuclear and membrane EGFR expression ($p < 0,05$).

mEGFR 3+ positive melanoma:



Poster Sessions

Sunday, 6 September 2015, 09.30–10.30, Restaurant
PS-01 Poster Session Breast Pathology

PS-01-002
WT1 is expressed in a continuum of breast lesions extending from simple mucinous cysts to mucocele-like lesions, mucinous DCIS and invasive mucinous carcinoma
S. Shousha*, N. Ali
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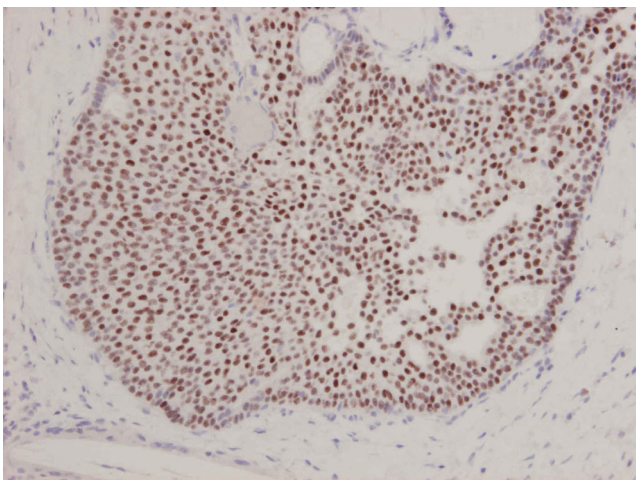
Objective: WT1 is expressed in around 60 % of invasive mucinous carcinoma of the breast, and, as previously shown, in around 80 % of mucocele-like lesions. We extended our study by investigating WT1 expression in simple mucinous cysts, presumably precursors of mucocele-like lesions, and mucinous DCIS, presumably precursors of invasive mucinous carcinoma, to see if there is a continuum of WT1 positive breast lesions.
Method: The study included 34 mucocele like lesions, many also containing simple mucinous cysts, 4 mucinous DCIS and 10 benign non-mucinous lesions. Sections were stained for WT1 using immunohistochemistry, and for mucin using alcian blue/ PAS.
Results: Thirty one (91 %) out of 34 mucocele like lesions were WT1 positive. WT1 was also expressed in all mucinous cysts containing acidic mucin and in all 4 mucinous DCIS. WT1 was not expressed in non-mucinous cysts, ductal hyperplasia, columnar cell change, flat epithelial atypia, fibroadenomas or in lactational change. However, WT1 was noted in a rare normal looking or mildly hyperplastic duct.
Conclusion: WT1 is expressed in a continuum of breast lesions extending from an occasional normal-looking duct to simple mucous cysts, mucocele like lesions, mucinous DCIS and invasive mucinous carcinoma, this may help in understanding the pathogenesis of mucinous carcinoma.

WT1 positive mucinous DCIS:



PS-01-004
Incorporating tumour grade enhances immunohistochemistry Internal Quality Assurance Program testing in breast cancers: a Canadian experience
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Objective: The objective of this study is to determine whether the current internal quality assurance program for HR (ER, PR and Her2) testing of breast cancer can be refined by incorporating clinic-pathologic factors such as tumour grade.
Method: All breast cancer patients ($n = 662$) tested for HR in Newfoundland during the first 6 months of recommencing testing at Eastern Health IHC laboratory (post Cameron inquiry) were included. Data on age at diagnosis, tumour type, stage, and grade, lymph node status, fixation time, Allred score, and HR status (ER, PR, and Her2) were collected.
Results: 80.2, 69.9 and 15.9 % of breast cancers were ER, PR and Her2 positive. Only 18/189 (9.5 %) of grade 1 and 2 cancers were ER-/PR-. Of the Her2 positive cancers, 6.2 % (3/48) were grade 1 and 52.1 % (25/48) were grade 2 cancers, respectively. A significant statistical association between high-grade tumours and negative ER and PR immunostains was found ($P < 0.0001$). Positive Her2 immunostains were also associated with high-grade tumours ($P < 0.0001$).
Conclusion: Including pertinent clinic-pathologic information into an IHC Internal Quality Assurance Program Testing in breast cancers is both feasible and important. Our findings show that incorporating tumour grade enhances identification of erroneous breast marker results.

PS-01-005
The value of Nottingham Prognostic Index in four molecular subtypes of breast cancer
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Objective: The aim of this study is to present the prognostic value of the NPI in the four different subtypes of breast cancer (BC).
Method: In this retrospective study (2007–2010), 192 breast cancer patients have been evaluated. All of the patients underwent surgical treatment based on previously diagnosed breast cancer. The morphological and histopathological examination of the surgical specimen have determined the assessment of the NPI and the additional immunohistochemical analyzes were used in order to separate four molecular subtypes of breast cancer: Luminal A and B, HER2+ and Triple-.
Results: The age of the patients was 28–83 years (mean 50,24 years). The NPI was higher in Luminal B (80 patients, 41,7 %), HER2+ (36 patients, 18,7 %) and triple negative BCs (25 patients, 13 %) compared with Luminal A BCs (51 patients, 26,6 %, $p < 0,01$). The tumour size (pT) was bigger in HER2+ and Triple- BCs compared with the tumour size of Luminal A BCs ($p < 0,05$). Histologic grade (G) was positively associated among Luminal A and other less differentiated subtypes ($p < 0,01$) while the lymphonodal metastases were usually present in Luminal B and HER2+ BCs compared with Luminal A ($p < 0,01$) and in HER2+ BCs, compared with triple- BCs ($p < 0,05$).
Conclusion: This study provides well evidence for the use of NPI supporting the individual treatment management on four different subtypes of BCs.

PS-01-006
Expression of p40 in breast tissue and lesions
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Objective: The demonstration of myoepithelium plays an important role in the distinction between benign, preinvasive and invasive malignant mammary lesions. Certain types of breast lesions show occasional lack or reduction of staining for myoepithelial markers. In this study, we analyzed such entities for the expression of a novel marker, p40, and correlated this to the p63 staining profile.
Method: P40 and p63 immunostaining was analyzed in a selected set of benign sclerosing and (11) adenomyoepithelial lesions (10), high grade

ductal carcinomas in situ (15), cytokeratin 5-positive, estrogen receptor-negative invasive carcinomas (20) and associated normal breast tissues.
Results: Normal structures showed analogous positivity using p40 and p63 (diffuse and strong) in 35/35 cases. Both antibodies gave a similar labeling in 38/38 lesions reported to show altered expression of myoepithelial markers; they demonstrated losses of staining focally in a parallel manner. The expression of p40 was seen more frequently (18/19) than that of p63 (8/19) in the tumour cells of cytokeratin 5-positive carcinomas and the staining was also more marked.
Conclusion: Our data support that the two antibodies can be used alternately for the demonstration of the myoepithelium, but there seems to be a difference in the labeling of at least a subset of tumour cells.

PS-01-007
Effects of histamine on the development of MNU-induced mammary tumours
A. I. Faustino-Rocha*, A. Gama, P. A. Oliveira, H. Vala, R. Ferreira, M. Ginja
*CITAB, Dep Veterinary Sciences, Vila Real, Portugal

Objective: Breast cancer is frequently diagnosed worldwide. Histamine acts as mediator in several cancers. Ketotifen is a mast cells stabilizer drug that inhibits their degranulation. This work aimed to evaluate the effects of histamine on the development of MNU-induced mammary tumours.
Method: Procedures followed the European Directive 2010/63/EU. Twenty animals were equally divided into two experimental groups: ketotifen and control. At 7 weeks of age, all animals received an intraperitoneal injection of N-methyl-N-nitrosourea (MNU). Animals from ketotifen group received ketotifen in drinking water (1 mg/Kg; 7 days/week; for 18 weeks). At the sacrifice, mammary tumours were fixed and histologically evaluated.
Results: During the protocol one ketotifen-treated animal died. At the end, eight animals from ketotifen group developed 19 mammary tumours (2.4 tumours per animal), while six animals from control group developed 21 mammary tumours (3.5 tumours per animal). Animals from control group developed one benign lesion and 20 non-invasive carcinoma; all lesions from ketotifen-treated animals were malignant, however they did not develop any comedo carcinoma that was the lesion of the highest grade of malignancy found in this work.
Conclusion: Inhibition of histamine release by ketotifen seems to reduce the number and malignancy of MNU-induced mammary tumours. Funding: CI&DETS, FCT and QREN/FEDER (Ovislab ICT-2013-05-004-5314 ID-64757), (PTDC/DES/114122/2009).

PS-01-008
Expression of estrogen receptors-alpha and beta in chemically-induced mammary tumours
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Objective: Estrogen receptors (ERs)-α and β are important for stimulating the growth and differentiation of human mammary tumours, respectively. This work aimed to evaluate the expression of ERs-α and β in rat chemically-induced mammary tumours.
Method: Procedures followed the European legislation (2010/63/EU). Fifteen seven-week-old female Sprague-Dawley rats received an intraperitoneal injection of N-methyl-N-nitrosourea (MNU) (50 mg/Kg). At sacrifice, mammary tumours were fixed and histologically evaluated. Sections were incubated with ER-α and β primary antibodies and the percentage of immunopositive cells was determined.
Results: During the experimental protocol four animals died, all survived animals developed mammary tumours: 30 benign, 2 preneoplastic and 39 malignant lesions. All histological patterns expressed ERs-α and β. The mean expression of ER-α (55.14 % ± 13.26) was lower than the expression of ER-β (70.06 % ± 18.51) ($p < 0.05$). The expression of both receptors was not statistically different among lesions, however it was higher in preneoplastic lesions, followed by malignant and benign ones ($p>0.05$).
Conclusion: All MNU-induced mammary tumours in rats expressed ERs-α and β, being a good model of ER-positive human mammary tumours. Once the expression of ER-β was higher, tumours' differentiation was stimulated and its proliferation was inhibited. Funding: CI&DETS, FCT and QREN/FEDER (Ovislab ICT-2013-05-004-5314 ID-64757), (PTDC/DES/114122/2009).

PS-01-009
MicroRNA expression profiles in phyllodes tumour and fibroadenoma of the breast
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Objective: MicroRNAs (miRNAs) are short assembly of non-coding, single-stranded RNAs, which are important gene regulators acting on cellular functions. Deregulation of miRNA has been implicated in various diseases, including cancer. There are some miRNAs known as oncogenes or tumour suppressors in breast cancer. We analyzed miRNA profiles of phyllodes tumours (PT) and fibroadenoma (FA) cases.
Method: miRNA microarray analysis was performed on 13 PT cases (3 malignant, 3 borderline, 7 benign) and 7 FA cases by using the FFPE samples. A total of 400 ng RNA from each sample was used and labeled with PANArray™ miRNA expression profiling kit (PANAGENE Inc). The kit is a PNA-based microarray for expression profiling of 158 miRNAs. Hybridization images were captured by the GenePix4000B scanner. The expression level ratio of 1.5 or more was considered as overexpressed and 0.5 or less as underexpressed.
Results: Among 158 cancer and stem cell-related miRNAs, miR-155 (1.68-fold) and miR-200c (1.61-fold) were overexpressed in the borderline and malignant PT groups compared with the benign PT and FA groups ($p < 0.05$).
Conclusion: Even though there was no significant difference in miRNA expression among PT and FA cases, both miR-155 and miR-200c were upregulated in high grade (borderline and malignant) PT cases.

PS-01-010
Loss of PTEN expression is associated with aggressive behavior and poor prognosis in middle eastern triple negative breast cancer
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*King Faisal Specialist Hospital, Dept. of Pathology and Laboratory Medicine, Riyadh, Saudi Arabia

Objective: To explore the significance of the role of PTEN in middle eastern triple negative breast cancer.
Method: We analyzed PTEN alteration in a tissue microarray format containing more than 1000 primary breast cancers with clinical follow up data. Tissue Microarray sections were analyzed for protein expression and copy number change using immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH).
Results: Loss of PTEN immunostaining was observed in 77 % of the cases. PTEN loss was significantly associated with large tumour size ($p = 0.0030$), high grade ($p = 0.0281$), tumour recurrence ($p = 0.0333$) and Triple negative breast cancers ($p = 0.0086$). PTEN loss in Triple negative breast cancers was significantly associated with rapid tumour cell proliferation ($p = 0.0396$) and poor prognosis ($p = 0.0408$). PTEN deletion was found only in 60 cases (6.4 %) of cases.
Conclusion: Loss of PTEN protein expression occurs at high frequency in Middle Eastern breast cancer. PTEN inactivation may potentially lead to an aggressive behavior of tumour cells through stimulation of tumour cell proliferation.

PS-01-011

Mammary myofibroblastoma: A rare case of a benign spindle cell tumour of the mammary stroma

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Objective: Myofibroblastoma of the breast is a benign mesenchymal neoplasm that occur more commonly in older men with gynaecomastia and postmenopausal women.

Method: We report a case of a 54 years old woman, with 12 mm right palpable nodule.

Results: After core biopsy that showed stroma with infiltration of tumour cells, positive for estrogens but negative for cytokeratins, lumpectomy was performed. Macroscopic examination of the specimen showed a solid, well circumscribed pseudo-encapsulated tumour. Microscopically in H&E the tumour was cellular composed of bipolar spindle cell with oval nuclei which were arranged in fascicles intermingled with bundles of collagen. There were also entrapped adipocytes of variable size, without epithelial elements within lesion. There were no areas of necrosis. Tumour cells were positive for vimentin, estrogens and Bcl-2, focal positive for desmin and negative for CD 34. Cytokeratins, S-100 and smooth muscle actin were negative. Ki-67 was positive in <2 %. Diagnosis of myofibroblastoma was given after correlating histopathological and immuno-histochemical findings.

Conclusion: The diagnosis of MFB is difficult in needle core biopsy, especially if one is faced with unusual variants that could be misdiagnosed as malignant. The correlation of histology and immunohistochemistry is helpful to establish the diagnosis of MFB.

PS-01-012

Radiation-induced angiosarcoma of the breast with MYC amplification: A case report

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Objective: We report a case of radiation-induced angiosarcoma of breast, developed 10 years after primary breast high grade DCIS, treated with quadrantectomy, Tamoxifen and radiotheraphy, in a 64-year-old female.

Method: We describe the clinical presentation and comment on the histologic diagnosis and the therapeutic approach.

Results: The patient presented with a reddish thickening of the periareolar skin of the left breast, measuring 10 × 6 cm. In 2004, she was diagnosed with a high grade DICS (DIN3), hormone responsive with HER-2 negativity; she underwent mammary quadrantectomy, and was administered Tamoxifen and radiotheraphy. A skin biopsy was performed, revealing a poorly differentiated vascular proliferation. The patient underwent a mastectomy with dermoepidermal graft. Histologically the neoplastic population consisted of highly atypical hobnail and spindle cells, with high mitotic index (24mitoses/10HPF). Extensive necrosis and areas of hemorrhage were evident. Immunohistochemistry showed positivity for vimentin, CD31 and CD34; Mib1 labeled 80 % of the neoplastic elements. FISH analysis documenting C-MYC amplification supported the diagnosis of radiation-induced angiosarcoma. 10 months later, the patient is disease-free.

Conclusion: This report confirms that secondary radiation-induced angiosarcoma is often associated with MYC amplification, documenting its diagnostic relevance. Mastectomy seems to be the best treatment option.

PS-01-013

Reliability of preoperative core needle biopsy for determing ER, PR, HER2 status and Ki67 expression in invasive breast cancer

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*Clinical Center of Vojvodina, Center for Pathology, Novi Sad, Serbia

Objective: We evaluated the concordance of hormone receptors (estrogen- ER and progesterone- PR), HER2 status and Ki67 expression between core needle biopsy (CNB) and surgical specimens (SS).

Method: ER, PR, HER2 and Ki67 expression were determinated by immunohistochemistry on preoperative CNB and subsequent SS in 54 patients with invasive breast cancer with no chemotherapy between. All patients were treated at the Institute of Oncology of Vojvodina for both of procedures. Cutoff value for Ki67 high expression was 14 %. The analysis of the concordance was performed using the kappa (k) coefficient (95 %CI).

Results: Concordance rates for ER, PR and HER2 were 96,4, 90,7 and 94,5 % respectively. Ki67 expression was slightly higher in CNB than in SS samples (61,1 vs. 44,4 %). An almost perfect concordance was identified for ER ($k = 0$, 88; 95 %CI: 0,71–1,0) and also for HER2 ($k = 0{,}81$; 95 %CI: 0,60–1,0). There was a substantial concordance for PR ($k = 0{,}75$; 95 %CI: 0,55–0,96), while for Ki67 moderate concordance was registered ($k = 0{,}46$; 95 %CI: 0,24–0,68).

Conclusion: CNB was accurate in determining ER, PR and HER2 status in invasive breast cancer. The concordance rate of Ki67 was less consistent. We should be aware of the problem of false test results in Ki-67 assesment in CNB and the potential impact on systemic treatment.

PS-01-014

The role of tru-cut biopsy in the diagnosis of breast lesions

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*UMF Targu Mures, Dept. of Pathology, Romania

Objective: The aim of this study was to evaluate the role of tru-cut biopsy (TCB) in the diagnosis of breast lesions.

Method: This retrospective observational non-interventional study included 169 patients in whom TCB was performed for the diagnosis of a breast lesion between 2010 and 2014 in the Surgery Department.

Results: All the TCB were optimal for microscopic evaluation. Histopathology revealed 115 (68 %) malignant lesions, 45 (27 %) benign lesions and 9 (5 %) suspicious lesions. One hundred percent of malignant and precursor lesions (including in ductal situ carcinoma, lobular neoplasia and suspicious lesions) were followed by surgical procedures (mastectomy/wide local excision), and only 14 out of 45 benign lesions (31 %) were followed by surgical procedures. Based on the histopathological diagnosis on TCB, there were 115 (68 %) true-positive cases, 22 (13 %) true-negative cases, 1 (0,6 %) false-positive case and no false-negative cases. TCB exhibited a sensitivity of 99 %, specificity of 96 %, a positive predictive value of 99 %, a negative predictive value of 100 % and an overall diagnostic accuracy of 99 %.

Conclusion: TCB is an accurate, reliable and safe method of establishing the diagnosis in breast lesions; it also provides all the necessary details to guide the clinician in designing an optimal therapeutic strategy for patients with breast lesions.

PS-01-015

Immunohistochemical expression of CD31 in high grade HER2+ invasive breast carcinomas

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Objective: CD31 is an adhesion molecule expressed by endothelial cells, leukocytes and platelets. Its expression by non-endothelial neoplastic cells has been correlated with "vascular mimicry" (VM), a phenomenon where neoplastic cells form tubular channels mimicking endothelial cells. VM is more pronounced in more aggressive tumours. The HER2/neu gene is amplified in 20–30 % of breast carcinomas, and has been correlated with features of aggressive clinical course. The aim of the present study was to examine the expression of CD31 in high-grade HER2+ breast carcinomas.

Method: Immunohistochemical analysis for CD31 was performed in 20 invasive breast carcinomas, no special type (NST), grade 3, HER2+.
Results: Heterogenous expression of CD31 (membranous immunostaining) was observed in 2/20 (10 %) cases, both in the invasive and the in situ component (DCIS), and was not correlated with VM. The DCIS component was of high nuclear grade. In one of the cases where the invasive carcinoma was negative, the adjacent DCIS was focally positive with strong immunostaining.
Conclusion: The expression of CD31 by neoplastic cells in breast carcinomas is not frequent and is not correlated with VM. It is possibly correlated with the "plasticity" of cancer cells, which exhibit simultaneously various immunophenotypes from epithelial to mesenchymal, including endothelial.

PS-01-017
The coexistence of breast columnar cell lesions in low grade invasive carcinoma and tubular carcinoma: Immunohistochemical study of Bcl2 expression and cyclin D1
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Objective: Collumnar cell lesions (CCL) are a type of intraductal proliferative lesion of the mammary gland.The group includes columnar cell changes (CCC) and flat epithelial atypia (FEA). FEA is at the center of scientific interest as a frequent early lesion in the low grade breast carcinoma pathological pathway which is of clinical significance as a precursor to cancer of the mammary gland.
Method: We examined 76 retrospective samples of low grade invasive carcinoma and tubular carcinoma from the archives of the CGB Laboratory. We observed the presence of different types of CCL and two types of microcalcifications in the biopsy materiál - ossificans and crystalline type. We performed immunohistochemical staining with antibodies to cyclin D1 and Bcl2 in 20 cases. (10 cases of FEA and 10 cases of CCL without atypia).
Results: The coexistence of different CCL and low grade invasive carcinoma was statistically significant. Expression of Bcl2 and cyclin D1 had no specific statistical relationship with FEA and CCL without atypia.
Conclusion: Our finding is consistent with and confirms the theory of the low grade estrogen dependent carcinoma pathway. Measurement of BCL2 expression and cyclin D1 in order to distinguish between FEA and CCL without atypia however proves to make no contribution.

PS-01-018
An unusual type of primary breast lymphoma
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Objective: Primary breast lymphoma is a rare entity, counting for less than 2.2 % of extranodal lymphomas and less than 0.5 % of breast malignancies. More than 70 % of them are of B-cell lineage. Primary Hodgkin's lymphoma of the breast is even rarer.
Method: A 54-year-old woman with two nodular, solid, painful left breast lesions was referred to the Emergency University Hospital Bucharest. Clinical examination revealed inflammation and ulceration of the overlying skin along with axillary erithema and enlarged axillary lymph nodes.The aspect was suggestive for inflammatory breast cancer.A core biopsy was performed, but proved to be inconclusiv, although it could not exclude a malignancy.Based on these findings the patient received anti-inflammatory medication and 2 weekslater she was scheduled for lumpectomy with axillary lymphadenectomy.
Results: Microscopic examination showed a nodular lymphoid malignant proliferation that infiltrates the adjacent mammary tissue. A proliferation of eosinophiles, plasma cells, giant pleomorphic lacunar Reed-Sternberg cells, Hodgkin cells and anaplastic multinucleated giant cells were observed to replace the normal architecture of the breast. Imunohistochemical investigantions (CD30, Pax5, CD15, CD20, CD3) were consistent with classic Hodgkin's lymphoma.
Conclusion: This report presents a curious case of primary breast lymphoma that clinically posed as an inflammatory breast cancer. Further immunohistochemistry investigations guided the diagnosis of primary Hodgkin's lymphoma of the breast.

PS-01-020
Toker cells of the nipple: Morphological and immunohistochemical characterization of 82 cases
I. Várkonyi*, T. Parris, E. Werner Rönnerman, K. Helou, A. Kovács
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Objective: To identify and characterize incidence of Toker cells (TC) in nipple epidermis in 82 patients: invasive breast cancer (IBC) (n = 63), ductal carcinoma in situ (DCIS) (n = 4), prophylactic mastectomy (PM) (n = 13), two patients with metastasis of malignant melanoma in the breast. Paget's disease was not included.
Method: FFPE samples from the nipples of 82 patients were examined by immunohistochemistry (IHC) using cytokeratin 7 and 19 antibodies.
Results: TC in the nipple epidermis were identified in 36/82 cases (44 %): IBC (87 %), DCIS (0 %), PM (46 %), malignant melanoma (0 %). TC were observed in the lower 1/3 of the epidermis in about 90 % of the malignant cases and in PM. In IBCs containing TC in the nipple epidermis, the average distance to the tumour from the nipple was 27.3 mm in comparison with 38 mm in cases without TC. The average number of TC in IBC per IHC slide was 44 and only 18 in the PM group.
Conclusion: TC may represent CK7+ intraepithelial extension of lactiferous duct cells or abortive mammary ductile cells. The number of TC is more prominent in cases of underlying carcinoma, and this number increases if the tumour is located in close proximity to the nipple.

PS-01-022
Alternatively spliced MALAT1 transcripts are independent prognostic factors in human breast cancer
D. Meseure*, K. Drak Alsibai, M. Trassard, S. Vacher, A. Nicolas, E. Marangoni, A. Morillon, I. Bieche
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Objective: Identification of cancer-associated long non-coding RNAs (lncRNAs) is pivotal in understanding molecular mechanisms implicated in carcinogenesis. MALAT1 is an abundant lncRNA with regulatory and structural functions (nuclear speckles). MALAT1 mutations and dysregulation have been recently observed in carcinomas. However, its role in breast cancer is unknown. The aim of this study was to examine the expression pattern of MALAT1 and to evaluate its biological role and clinical significance in invasive breast carcinomas (IBC).
Method: We performed RT-PCR, RNA-FISH and RPPA methods to quantify transcript and/or protein levels of the wild type MALAT1 gene, two major alternatively spliced MALAT1 variants and candidate genes involved in MALAT1 functions in IBCs.
Results: Wild type MALAT1 was overexpressed in 17 % of IBCs and significantly correlated with high histopathological grade and positive hormone receptors. Two major alternatively spliced MALAT1 pre-mRNAs were underexpressed respectively in 18 and 22 % of IBCs. Survival analysis revealed that patients with low alternatively spliced MALAT1 had shorter MFS.
Conclusion: We identified in IBCs a complex expression pattern of MALAT1 wild type and variants transcripts indicative of nuclear speckles disruption and associated with shorter MFS.

PS-01-023

A rare case of secretory breast carcinoma: Correlation of aspiration cytology and histology

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Objective: Secretory carcinoma of the breast is an extremely rare neoplasm (<1 %) which shows distinct features at cytology and histology. It is still rarer in adults where it is potentially more aggressive than in childhood. Recent researchs showed that secretory carcinoma belongs to the phenotypic spectrum of basal-like breast carcinomas. Diagnosis of this carcinoma at fine needle aspiration cytology is difficult.
Method: A 55 years old woman with a breast mass underwent fine needle aspiration biopsy.
Results: The aspirate was highly cellular and consisted of sheets, clusters and single cells with abundant cytoplasm and intracytoplasmic vacuoles in a background of mucinous and eocinophilic globules of secretory material. Some of the cells were binucleated or multinucleated and showed emperipolesis. Histopathologic examination of the mass showed a tumour with solid, microcystic and ductal patern associated with PAS positive diastase resistant intracellular and extracellular abundant secretory material. Immunohistochemically, tumour was negative for estrogen receptor, progesterone receptor and HER2, positive for CK5/6 and EGFR.
Conclusion: The authors were discussed the differences in morphology at fine needle aspiration cytology of secretory carcinoma of the breast from other breast carcinomas, correlation with histopathology and its utility of making a preoperative diagnosis.

PS-01-024

Characteristics of breast cancer stem cell population in invasive ductal carcinomas with different phenotype

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Objective: To study characteristics of stem cell phenotype (CD44+/CD24-low) distribution in ductal invasive carcinomas - in tumours with different malignancy degree, in relation to primary tumour size and lymph node status, and in tumours of different molecular subtype.
Method: 393 postoperative invasive ductal breast carcinoma materials investigated in 2008–2012 were used for the study. Association of CD44/CD24 expression in different tumour phenotypes, between clinicpathological parameters and different biological characteristics were performed. Pearson correlation and $\chi 2$ tests were used for quantitative analysis.
Results: Amount of CD44 positive cases progressively increased with tutor grade ($p < 0.001$). Expression of CD44 regularly reflected aggressive behavior and metastatic potential of cancer subtypes, except Her2 + subtype ($p < 0.001$). CD 24 as an independent marker does not reflect a clear correlation between aggressive behavior and metastatic potential of tumours ($p = 0.01$). Stem cells phenotype (CD44+/CD24-low) positivity was in direct correlation with tumour grade and metastatic potential, except Her2 + subtype ($p < 0.001$), also with tumour size ($p < 0.001$), presence of metastatic lymph nodes and high proliferative activity (Ki-67) ($p < 0.001$).
Conclusion: Cells with CD44 +/CD24-low phenotype are involved in tumour progression and development of metastasis. CD44 alone can be used as an independent marker of tumour progression.

PS-01-025

Nucleotide variants in the HER2 gene region encoding herstatin, the endogenous pertuzumab

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Objective: The monoclonal antibody pertuzumab inhibits signaling from HER2 heterodimers and is currently used in the treatment of breast cancer (BC). Herstatin (p68-HER2 protein) is produced through alternative splicing of the HER2 gene and acts as an endogenous HER inhibitor similar to pertuzumab. Herein, changes in the gene region encoding the carboxy-tail of herstatin, including intron 8, were investigated.
Method: Informative data from 1612 paraffin BC DNA samples were obtained by using highly-multiplexed custom panels and massively parallel sequencing. Variant metrics and annotations were retrieved with the Ion Reporter v.4 software.
Results: In total, 166 nucleotide variants were observed in exon-intron8 in 121 breast carcinomas (121/1612, 7.5 %) and were mostly (138/166, 83.1 %) located in the herstatin-tail intron8 region corresponding to 52 nucleotide positions. Variants were mostly C/T transitions (72/138, 52 %). Moreover, in intron8 region of herstatin two different polymorphisms (rs139636338 and rs4252625) were observed. These changes were found more often in HER2 positive than negative carcinomas (Pearson $p = 0.002$).
Conclusion: Nucleotide variations are observed in a subset of breast carcinomas in the HER2 gene region encoding Herstatin. It will be of interest to further investigate whether these changes affect the endogenous or pharmaceutical inhibition of the HER signaling pathway.

PS-01-026

Is the positivity of the sentinel lymph node influenced by the molecular profile of the primary invasive breast tumour?

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Objective: The aim of the study is to assess the influence of the molecular profile of the primary breast tumour on the positivity of the sentinel lymph node (SLN).
Method: A retrospective study was performed by accessing the molecular profile of 55 consecutive patients identified in the database between 2012 and 2014, diagnosed with invasive breast carcinoma, in which SLN biopsy was performed for staging. The molecular profile included the assessment of the ER, PR, ki 67 and HER2 status in the invasive component (according to the St Gallen International Expert Consensus). Statistical analysis was performed using GraphPad Prism, Fisher's exact test and Pearson's correlation tests.
Results: Our 55 cases were imunohistochemically classified as: 24 Luminal A (43.64 %), 17 Luminal B-Her 2 negative (30.91 %), 6 Luminal B-Her2 positive (10.91 %), 1 as Her2 positive type (1.82 %) and 7 as triple negative (12.73 %). The statistical analysis revealed that ER ($p = 0.66$), PR ($p = 0.26$), ki 67 ($p = 0.5$), Her2 receptor ($p = 0.41$) and the molecular type of the primary tumour ($p = 0.5$) did not significantly influence the positivity of the SLN.
Conclusion: The molecular profile of the primary breast tumour cannot independently predict SLN involvement.

PS-01-027

Which clinical and histological parameters can predict positivity in axillary sentinel lymph node biopsy for invasive breast carcinoma

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Objective: The aim of the study is to identify the clinical/histological features of the primary invasive breast carcinoma that can predict positivity of the axillary sentinel lymph node (SLN) in order to avoid this procedure (associated with a certain risk of long-time morbidity) especially in low-risk breast cancer patients.
Method: We retrospectively reviewed all the invasive breast carcinomas identified in the database (2012–2014) in which SLN biopsy was routinely performed for staging. Statistical analysis was done using GraphPad Prism, Fisher' and Pearson's tests.

Results: 80 consecutive patients with invasive breast carcinoma previously diagnosed on a core biopsy were included in the study (mean age 54.88). A total of 218 SLN were examined. Presence of metastases was revealed in 23.75 % of the cases, out of which 47.36 % were also associated with extracapsular extension. In this series, the histological type ($p = 0.7$), grade of the primary tumour ($p = 0.09$), multifocality ($p = 0.3$), tumour diameter ($p = 1$), patient's age ($p = 0.11$), location of the tumour ($p = 1$), presence of necrosis ($p = 0.5$), lympho-vascular invasion ($p = 0.4$), microcalcifications ($p = 0.3$) did not statistically influence the positivity of the SLN.
Conclusion: Based on the clinical/histological features of the primary breast tumour, SLN biopsy remains the method of choice for the evaluation of the axillary status in breast cancer.

PS-01-028
A case of lobular breast carcinoma with extracellular mucin production
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Abstract: Invasive lobular carcinomas (ILC) of the breast typically demonstrate intracytoplasmic mucin, whereas extracellular mucin production is by default a feature of ductal origin carcinoma. We present a unique case of classical type ILC with focal extracellular mucin production. A 72-year-old woman presented with an ulcerated mass in the right breast. An ultrasound-guided needle core biopsy was performed. Histologically, sections showed architectural and cytological features of classical lobular carcinoma. Focally, a pool of extracellular mucin was detected, while neoplastic cells were floated within. Special stain for Alcian-Blue was used to confirm the mucin production. Immunohistochemical study for E-Cadherin showed complete loss of staining in all the neoplastic cells, including the cells within the mucin. Estrogen receptor (ER) showed 50 % (++/+++) positivity, whereas progesterone receptor (PR) was positive in less than 1 % of the tumour cells. HER2 was scored 1+ and Ki67 was counted 25 %. The findings suggest that the presence of extracellular mucin does not exclude a diagnosis of lobular carcinoma. To the best of the authors' knowledge, only 3 cases of infiltrating lobular carcinoma displaying extracellular mucin have been reported in the literature.

PS-01-029
Incidence of other previously diagnosed primary malignant tumours in breast cancer patients: A retrospective statistical evaluation in 2007–2014
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Objective: To analyze other previously diagnosed primary malignant tumours in breast cancer patients during an 8 year period 2007–2014.
Method: We performed a retrospective search of other primary malignancies in 4305 breast cancer patients using our own database at the Dept. of Pathology.
Results: The incidence of other primary malignant tumours ($n = 234$, including two male patients), occurring before the breast carcinoma was detected, increased from 3 to 7 % during 2007–2014. The most striking increase was found among the gynecological tumours (endometrium/ovarian adenocarcinomas) and malignant melanoma. The number of lymphoma/leukemia cases, urothelial/renal cell carcinomas, head & neck region tumours, malignant soft tissue tumours did not show a significant increase, while thyroid gland carcinomas and lung cancer showed a slight increase. The number of gastrointestinal malignancies showed an irregular, but relatively high incidence during this time period.
Conclusion: Second primary malignancies in breast cancer patients are becoming an issue of concern worldwide. Breast cancer patients with other primary malignancies need special treatment strategies, regarding the previously administered radio-and/or chemotherapy to avoid excessive cytotoxic harm due to cumulative effect of all applied therapies.

PS-01-030
Her2/neu in local metastases and primary focus of breast cancer
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Objective: Targeted therapy of breast cancer is based on results of immunohistochemical evaluation of Her2/neu status of primary tumour, but in some cases Her2/neu rate of metastases is dissimilar. The aim of this study is to evaluate and characterize difference of Her2/neu status between primary breast cancer and locoregional metastases.
Method: Postoperative tissue samples of primary lesion and local metastases of breast carcinoma by 88 patients without neoadjuvant therapy before operation were included in this study. All tissue specimens were stained for Her2/neu by Ventana immunostainer. Patients were divided into four groups on the basis of the Her2/neu rate of the primary tumour: 1 – 0 (50 cases), 2 – 1+ (9 cases), 3 – 2+ (17 cases), 4 – 3+ (12 cases). In each group Her2/neu levels of primary and metastatic tumours were compared. Wilcoxon test was used for statistical analysis.
Results: The mean values of Her2/neu rate in metastases were: 0,33 in first, 0,85 in second, 0,75 in third and 2,13 in fourth group. Statistically significant ($p < 0,01$) was shift in third group only.
Conclusion: The tendency to reduction of Her2/neu level in local metastases in patients with 2+-rate of primary cancer was revealed. In other groups there was no significant change of Her2/neu status in metastases.

PS-01-031
The follow-up of non-metastatic breast cancer: Tunisian experience about 50 cases
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Objective: The survival of patients affected by breast cancer is increasing greatly through the last decades. This study is about a new challenge which is how to manage these patients after cancer treatment.
Method: We undertook a retrospective study on non-metastatic breast cancer patients treated by surgery, chemotherapy and radiotherapy. We analyzed epidemiological, clinical, histological features and evolution profile of all patients and we focused on the particularities of their follow-up.
Results: Our study group included 50 patients with an average age of 51, 3 years. They were clinically followed up every 3 months the first 2 years and every 6 months the 3 following years. Mammography and ultrasound were done every year. Chest X-ray was required in 42,9 % of cases, CA 15-3 in 59,1 % of cases, abdominal ultrasound in 34,7 % of cases and thoracoabdominopelvic computed tomography in 22 % of cases. Local recurrence and metastases occurred in 0,82 and 4,97 % of cases per year respectively. Delayed breast cancer reconstruction was performed in 20 % of cases.
Conclusion: According to our study, the follow up of breast cancer, a cornerstone in the management of breast cancer, is still not optimized and needs specified national recommendations.

PS-01-032
Assessment of the effectiveness of neoadjuvant chemotherapy for breast cancer by analysis of cell density and pathological response
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Objective: The aim of this study was determine efficacy parameters of neoadjuvant breast cancer chemotherapy (BC) by changes in cell density gradient in the tumour.
Method: The study included 31 patients diagnosed with breast carcinoma. After whole slide scanning by Pannoramic 250r (3DHistech,

Budapest) of HE slides before and after neoadjuvant chemotherapy, we located the areas within the tumours and calculated the prescise quantity of tumour cells per sq.mm. Morphometric analysis was performed using the Pannoramic Cell Quant software (3DHistech, Budapest). For each case we analyzed a total number of tumour cells in more than 1 mm2 sample and Ki67 was evident in at least 10 fields of view.
Results: Mean cell dencity before chemotherapy was 6213 cell/mm2, after 4052. There was good correlation with pathology response graded based on the Miller-Payne system in 84 % cases (Pearson criteria = 0.84 [$p < 0.001$]).
Conclusion: Effectiveness of neoadjuvant chemotherapy for breast cancer and pathology response could be evatuated using digital data (scanning, image analysis) to achieve more precise result.

PS-01-033
Prognostic value of histology grade and ki67 index in breast cancer (T1-2 N0 M0)
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Objective: We analyzed histology grade of breast carcinoma and proliferative activity (% Ki67-positive cells) to establish prognostic value of this measure using TMA approach.
Method: The study included 980 patients diagnosed breast carcinoma T1-2N0M0. After whole HE slide scanning by Pannoramic 250 (3DHistech, Budapest), we located the 2 mm in diameter areas within the tumours at each slide and punched them from block to form TMA recipient block. The Ki67 stained TMA slides calculated for precise quantity of tumour cells per sq.mm, which was the sum of negative and Ki67 positive cells. Morphometric analysis was performed using the Pannoramic Viewer software (3DHistech, Budapest). For each case we analyzed a total number of tumour cells in a 1 mm2 sample and Ki67 was evident in at least 10 fields of view
Results: Low risk of recurrence T1-2N0M0 (G1+G2, Ki-67 < 5 %) = 18 % of patient. High risk of recurrence T1-2N0M0 (G3+G2, Ki 67 >20 %) = 32 % (no recurrence in 8,5 years follow-up > 90 %) in detail see A. Prat, J. S. Parker, C. Fan Ann Oncol (2012) 23 (11): 2866–2873.
Conclusion: By analysis of breast carcinoma was established that G1+G2 with Ki67 less than 5 % allow to take patient low risk group of disease and G3+G2 more than 20 % Ki67 positive cells means high risk population of T1-2 N0M0 breast carcinoma.

PS-01-034
The latest ASCO-CAP HER2 guidelines: What has changed?
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Objective: Herceptin therapy of breast carcinoma is dependent on HER2 status. In 2013 the American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP) updated their 2007 HER2 interpretation guidelines. We have explored how these changes impact on HER2 evaluation results.
Method: All our 145 breast cancer cases with a 2+ or 3+ HER2 immunohistochemical score (years 2013 and 2014) were evaluated separately following both the 2007 and 2013 ASCO-CAP HER2 FISH interpretation criteria.
Results: Of the 145 cases, 2007 and 2013 guidelines provided discordant HER2 amplification results in 14 instances. Specifically, 10 nonamplified cases according to 2007 criteria were placed in the equivocal category by 2013 criteria, 3 equivocal cases were upgraded to positive for amplification, and 1 negative case was moved to the amplified category.
Conclusion: In our hands, the 2013 updating of HER2 interpretation guidelines results in an increased number of cases needing FISH evaluation. New criteria make evaluation more laborious, since more cases require signal counting while the percentage of cluster signal cases remains unchanged. Implementation of the new guidelines increases the number of equivocal cases and unveils few instances of HER2 amplification.

PS-01-035
Pathogenetic regularities of epithelial-mesenchymal transition in breast cancer carcinomas
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Objective: The aim was to study the ultrastructural and immunohistochemical features of EMT in 127 mammary glands removed for cancer.
Method: Methods of electron microscopy, immunohistochemical identification of pancytokeratin, E-cadherin, vimentin, alpha-smooth muscle actin were used.
Results: The key feature of EMT is the separation of tumour cells due to irregularities in their intercellular adhesion due to the loss of E-cadherin. This feature is maximally expressed in medullary breast cancer, when membrane expression of E-cadherin is significantly decreased up to the absence. In infiltrating ductal carcinoma membrane expression of E-cadherin is detected in a large complexes of tumour cells and becomes cytoplasmic, or disappears in small groups of cells invading the stroma. Ultrastructural manifestations of EMT were homotypical. Separation of tumour cells was accompanied by the acquisition of fibroblast-like shape with invasion into the stroma, indicating their mesenchymal origin. In some cases of infiltrating breast carcinoma tumour cells expressed vimentin.
Conclusion: The most characteristic feature of EMT in breast cancer is the presence of clusters of myofibroblasts in the stroma. EMT process is accompanied by the simultaneous expression of epithelial and mesenchymal markers. However, there is no fixed sequence of reducing the expression of epithelial markers and increasing the expression of mesenchymal ones.

PS-01-036
Primary chondrosarcoma of the breast: A rare case report
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Objective: Malignant mesenchymal tumours of the breast other than angiosarcoma are rare and comprise <0.5 % of breast tumours. Primary chondrosarcoma of the breast is an extremely rare entity and only less than 20 cases are reported as single case reports in literature until date. We present here a rare case of primary breast chondrosarcoma.
Method: Case Report: A 50-year-old female patient presented to the surgical outpatient department complaining of a large lump in her left breast of 6 months duration. FNA cytology revealed malignant chondroid cells. The mass was removed with a wide local excision. Grossly, the tumour was received in multiple pieces together measuring 150 × 84 mm. Histological examination showed malignant chondroid and chondromyxoid proliferation. Further careful and detailed examination did not show any malignant epithelial components. Immunohistochemistry revealed positive vimentin and negative cytokeratin. A final diagnosis of chondrosarcoma of the breast was reached.
Conclusion: Primary chondrosarcoma of the breast is an extremely rare condition. It's origin is obscure, and speculations abound. Misplaced mesenchymal nests, chondroid differentiation of tumours of mesenchymal origin, and pluripotent cells undergoing chondroblastic differentiation have been proposed. Extensive sectioning of the tumour and immunohistochemistry are essential to rule-out metaplastic carcinoma and malignant phyllodes tumour.

PS-01-037

Ultrastructural research of drug induced apoptosis in anthracyclineresistant breast cancer

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Objective: The purpose of this study was to investigate the intensity of apoptosis in tumours, removed surgically at various times after treatment, in patients after cisplatin. Sixteen cases of infiltrating ductal breast cancer in III stage of disease were studied.
Method: The study used the method of transmission electron microscopy.
Results: In each ultrathin slice the number of apoptosis in 30 tumour cells was counted. In tumours of patients who did not receive chemotherapy, and have undergone preoperative course or more than 2,5 months before, apoptosis occurred in individual fields of vision (0–3 %). In patients treated with cisplatin for 1–2 months before surgery, apoptosis intensity was higher, and in 3 cases was 13–16 %.
Conclusion: Intensity of cisplatin-induced apoptosis in breast cancer peaks at certain periods. The peak intensity of apoptosis is observed in 1–2 months after treatment. In some cases, activation of apoptosis, induced by cisplatin, appears on III stage of disease, and has no significant impact on life expectancy of patients.

PS-01-038

Capabilities of immunohistochemical method in predicting the course of mammary gland cancer

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Objective: The goal of our research was to find dependence of prognostic marker expression (ER, PgR, HER-2/neu, p53, VEGF, Ki-67, bcl-2) on age and on presence of metastases in mammary gland cancer, and to identify correlation in groups with metastases or without them.
Method: To explore the dependence on age we compared general allocations based on intensity of a certain marker expression (nonmetering metastases) between a group <35 and 35–50 years old group, a group <35 and >50 years old, also between a 35–50 years old group and >50 years old. To analyze the difference in marker expression between subgroups with metastases and without them in every age group and difference between age group nonparametric test $\chi 2$(chi-squared) was used.
Results: All markers with high confidence level can be used as prognostic regarding risk of development of metastases in patients of different age. Exeptional were ER and PgR markers in the age group <35 years old, ER - in 35–50 years old group. Increased level of expression with age was typical only for ER and PgR markers: for ER expression - difference was reliable in 35–50 years old group and >50 years old group, in groups <35 and >50 years old; for PgR - between 35 and 50 years old group and>50 years old group.
Conclusion: It was discovered that expression of markers p53 and Ki-67 reliably differs in groups with presence of metastases independent from age. The latter are more reliable as prognostic for younger than 35 years old group.

PS-01-039

Triple Negative Breast Carcinoma (TNBC) and Androgen Receptor (AR) expression

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Objective: Triple negative breast carcinoma (TNBC) is a subtype of breast carcinoma, with high invasiveness, aggressive behavior and poor prognosis. Hormonal or HER-2 targeted therapies are ineffective for TNBCs, and conventional chemotherapy remains the main therapeutic option. The identification of new target therapeutic molecules could be helpful for these patients. Androgen receptor (AR) has been associated with triple negative breast cancer pathogenesis, but its role has not been clearly identified. The percentage of AR expression in TNBC varies in the literature, ranging from 25 to 75 %.
Method: We have studied 24 cases of triple negative breast carcinomas in relation to their AR expression. The majority were ductal (NST) (17 cases, 4 of them with basal immunophenotype), 1 case of papillary, 3 cases of apocrine, 2 cases of medullary, and 1 case of mucinous carcinoma
Results: In 10 (41.6 %) cases we detected intense nuclear positivity for AR, ranging from 5 to 99 % of neoplastic cells. Notably, the apocrine carcinomas showed the higher staining intensity and the higher percentage of positive cells. Also, nuclear AR expression was displayed in cells of normal ductal-lobular units.
Conclusion: Our results suggest that AR positive carcinomas constitute an eventual subgroup of TNBCs which could possibly benefit from using AR as a therapeutic target.

PS-01-040

Mixed ductal/lobular invasive breast cancer arising within fibroadenoma: Case report

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Objective: Breast cancer arising within fibroadenoma is very rare and its usual histological appearance is that of lobular carcinoma in situ followed by ductal carcinoma in situ. We report an unusual case of mixed type invasive breast carcinoma arising within fibroadenoma.
Method: A 38-year-old woman with a palpable right breast mass, that was clinically and mammographically benign, underwent excision biopsy.
Results: On gross pathology we identified a well-circumscribed, encapsulated nodule measuring 4,5 × 4,5 × 3 cm. The cut surface contained gelatinoid yellowish material and had focal cystic and solid areas of fibroelastic composition. On microscopic examination, we identified mixed type invasive breast cancer (with features of both invasive carcinoma of no special type (NST) Grade III and pleomorphic lobular carcinoma) of 2 cm diameter arising within a fibroadenoma. By immunohistochemistry, tumour cells showed low estrogen receptor expression and were progesterone receptor positive. HER2 was 2+ by immunohistochemistry and negative by FISH. Ki-67 index was 60 %. tumour cells were positive for E-cadherin, with loss of it in the lobular areas. The patient underwent sentinel lymph node biopsy that was negative.
Conclusion: Clinicians should be aware of this rare clinical entity. Special caution should be taken in patients older than 35 years presenting with fibroadenomas.

PS-01-042

Immunohistochemical detection of cancer stem cells in different molecular subtypes of breast cancer

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Objective: Cancer stem cells are defined as small population of cancer cells with ability to differentiate, self renew and replicate the original tumour in vivo. The aim of the study is to evaluate the expression of CD44, CD24, CD133 and CD117 stem cell markers in different molecular subtypes.
Method: Tissue samples from 28 cases of invasive breast cancers were divided into 4 major molecular subtypes (luminal A, luminal

B, Her2 enriched and triple negative), and correlated with immunohistochemical expression of stem cell markers and clinicopathological parameters.
Results: Fourteen of the cases were classified as Luminal B, 9 were Luminal A, 4 were HER 2 and one was triple negative. Forty six percent of tumours were CD44+/CD24-, 18 % were CD133+, 14 % were CD117+ and 28 % were immunonegative for all 4 markers. Stem cell markers were expressed in 75 % of Her2 enriched 43 % of Luminal B and 37 % of Luminal A subtypes. They were also expressed in one triple negative case. Stem cell markers were correlated with larger tumour size (63 %), higher histologic grade (56 %), stage (87 %) and metastasis in lymph nodes (69 %).
Conclusion: Cancer stem cells revealed varying expression in different molecular subtypes and may have certain significance in predicting prognosis in breast cancers.

PS-01-043
Morphological and immunohistochemical features of breast cancer in young women
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Objective: Over the past 3–4 decades, epidemiological data suggest an increasing incidence of breast cancer in young women. The aim of this study was to evaluate the clinical, pathological and some molecular features of breast cancer in young women.
Method: A retrospective study was performed in order to identify patients younger than 35 years diagnosed with breast cancer in a period of 2 years. We analyzed the clinico-pathological characteristics and the immunohistochemical profile of these tumours.
Results: We have identified ten cases of breast tumours in women younger than 35 years: 9 primary carcinomas and 1 secondary tumour. The youngest patient was 19 years old. 5 carcinomas were larger than 2 cm and 3 tumours were poorly differentiated (G3). Axillary dissection was performed in five cases but nodal metastasis were identified in only 2 cases. One patient was diagnosed in our department with brain metastasis from breast carcinoma. Lymphovascular invasion was present in most cases, while perineural invasion was identified in only three cases. Most primary tumours were ER+/PR+ except one case which was ER-/PR-. HER2 protein was overexpressed in three cases.
Conclusion: Breast cancer in young women seems an aggressive malignancy, being associated with adverse pathological factors and requiring adapted management strategies.

PS-01-044
Breast cancer subtypes based on estrogen receptor, progesteron receptor, Her2 expression and Ki-67 proliferation: Clinicopathological evaluation
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Objective: To compare the clinicopathological features in breast cancer subtypes defined by immunohistochemistry expression of estrogen receptor (ER), progesteron receptor (PR), Her2 and Ki-67.
Method: We have retrospectively analyzed surgical specimens of 337 patients with invasive breast cancer. Subtypes of breast cancer were evaluated using conventional immunostaining: ER, PR, Her2 and Ki-67. Patients were classified into following groups: luminal A (ER/PR+, Her2-), luminal B (ER/PR+, Her2+), Her2+ (ER/PR-, Her2+) and triple-negative/basal-like (ER/PR-, Her2-).
Results: 76.2 % carcinomas were classified as Luminal A, 10.4 % as Luminal B, 6.2 % as Her2 + and 5.4 % as triple-negative/basal-like subtype. Luminal A subtype was associated with G2 tumours, lobular type, T1 status and the lowest rate of regional lymph node involvement. Luminal B subtype correlated most common with G2 and T1 status, ductal type of carcinoma, but higher Ki-67 index and more frequent lymph node metastases. Her2+ and triple-negative/basal-like subtypes showed predominantly G3 and T2 status, other histological types than ductal and lobular and high regional lymph nodes involvement.
Conclusion: The breast cancer classification on subtypes is very informative and it has predictive and prognostic value. Although further follow-up of these patients is needed, these facts are useful in identifying patients with increased risk of regional metastases and recurrence.

Clinicopathological characteristics by molecular subtypes of breast cancer:

Subtype	Luminal A		Luminal B		HER2 Enriched		Triple Negative/ Basal-like	
	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%
	n=257	76.2%	n=35	10.4%	21	6.2%	18	5.4%
Age (mean)	60.82		58.03		58.33		60.83	
< 45	30	11.7%	6	17.1%	5	23.8%	3	16.7%
≥45	227	88.3%	29	82.9%	16	76.2%	15	83.3%
Histological type								
Ductal	196	76.3%	32	91.4%	17	80.9%	15	83.3%
Lobular	33	12.8%	3	8.6%	/	/	/	/
Other	28	10.9%	/	/	4	9.5%	3	16.7%
Gradus								
1	49	19.1%	2	5.7%	/	/	/	/
2	148	57.6%	22	62.9%	7	33.3%	4	22.2%
3	60	23.3%	11	31.4%	14	66.7%	14	77.8%
Ki-67 index								
(mean percentage)		13.3%		28.4%		43.5%		45%
Tumor Size								
< 2cm	136	52.9%	18	51.4%	7	33.3%	7	38.9%
2 - 5 cm	110	42.8%	17	48.6%	12	57.2%	8	44.4%
> 5 cm	11	4.3%	/	/	2	9.5%	3	16.7%
Lymph node status								
positive	71	27.6%	14	40%	10	47.6%	6	33.3%
negative	186	72.4%	21	60%	11	52.4%	12	66.7%
Distant metastatases								
present	5	1.9%	1	2.9%	2	9.5%	1	5.6%
absent	71	27.6%	8	22.8%	6	28.6%	9	50%
N/A	181	70.5%	26	74.3%	13	61.9%	8	44.4%

* in 6 patients we were not able to determine subtype of invasive carcinoma

PS-01-045

Evaluation of changes in the Hormone receptor, Her2 status and Ki-67 proliferation following administration of neoadjuvant chemotherapy in breast cancer

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Objective: To evaluate the changes in the hormone receptor (HR), HER2 status and Ki-67 proliferation in locally advanced breast cancer patients after neoadjuvant chamotherapy (NAC).
Method: We investigated 36 breast cancer patients for estrogen receptor (ER), progesterone receptor (PR), HER2 status and Ki-67 proliferation of their lesions before and after NAC. The changes in statuses of HR, HER2 and Ki-67 in operated tumour tissue were compared with initial core biopsies. HR, HER2 and Ki67 expression were determinated by immunohistochemistry. Patients with HER2 IHC 2+ were further examined by CISH.
Results: 2 (5.5 %) patients who were ER positive prior to treatment showed ER negativity after. In 3 (8.3 %) patients PR became negative after neoadjuvant chemotherapy. Changes in ER and PR were not statistically significant ($p = 0.056$ and $p = 0.083$ respectively). Conversion of HER2 occured in 4 of 36 patients (11.1 %): in two from positive to negative and in two from negative to positive. Ki-67 index decreased significantly from 35.9 % in specimens prior to NAC, to 26.1 % in specimens obtained post-NAC. ($p = 0.89$).
Conclusion: Our results indicate that HR, HER2 and Ki-67 from same tumour tissue demonstrate differences after NAC. These changes may affect the therapeutic management so we recommend monitoring status of biologic markers before and after NAC.

PS-01-046

Homologous recombination proteins are directly affected by BMI-1 silencing in human breast cancer cell line

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Objective: BMI-1 is recruited to DNA breaks sites and participates in the damage-induced ubiquitination of H2AX, allowing to infer a role for BMI-1 in response to DNA damage. In mammalian cells, a major repair pathway to double-strand breaks is homologous recombination (HR). However, the role of BMI-1 in homologous recombination is still poorly understood. Thus, the aim of this study was to evaluate the effect of BMI-1 silencing in homologous recombination protein markers.
Method: MCF-7 cells are constitutively positive for BMI-1 and silencing was performed using siRNA + Lipofectamine RNAiMAX. Using double-staining immunofluorescence we analyzed homologous recombination markers and evaluated BMI-1 silencing impact on their immunolocalization.
Results: BMI-1 silencing resulted in the reduction of nuclear expression of BRCA-1 and BRCA-2 and the translocation of RAD51 from nucleus to cytoplasm. ATM expression changed from nucleus to nucleus and cytoplasm after silencing while ATR stained nucleus and cytoplasm in control but only nucleus in silenced samples.
Conclusion: Our study demonstrates that BMI-1 directly affects the homologous recombination markers, playing an important role in development and progression of breast cancer.

PS-01-047

A new role for CCL2 in breast cancer: A modulator of local iron homeostasis

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Objective: Tumour cells display increased iron uptake, regardless of intracellular levels. Tumour-associated lymphocytes and macrophages putatively contribute to iron supply. CCL2, a leukocyte chemoattractant, was described to be regulated by intracellular iron status in neuroinflammation.
Method: CCL2, CD68 and FPN immunohistochemistry was performed in 252 TMA spots from 101 primary samples (52 invasive ductal carcinomas, 17 ductal carcinomas in situ (DCIS) and 32 reduction speciments). The number of CCL2-expressing macrophages and CD68-positive cells were assessed. Hemosiderin deposits were detected with Perls' Prussian Blue staining.
Results: CCL2 expression was increased in tumour cells and associated macrophages. CCL2 in epithelial cells and macrophages was positively correlated with iron deposition in stromal cells. The number of CD68+ cells and its CCL2 expression were positively correlated with tissue iron deposition. CCL2 expression in epithelium was positively correlated with FPN expression in stromal cells. CCL2 in macrophages was positively correlated with their FPN expression and negatively correlated with FPN in epithelial cells, in DCIS.
Conclusion: CCL2 was correlated with increased tumour iron content and export in inflammatory cells, reinforcing their contribution to tumour iron nutrition. We report the existence of a positive feedback loop, implying autocrine and paracrine CCL2 signaling in breast cancer iron-associated alterations and progression.

PS-01-048

Link between N-cadherin and HER-2/neu expression in invasive lobular breast cancer

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Objective: Cadherin switch from epithelial to mesenchymal type is an important feature of epithelial-mesenchymal transition, which stimulates metastasis in breast cancer. Increase of N-cadherin expression promotes adhesion of cancer and stromal cells, and their further invasion to stroma. N-cadherin participates in signal pathways PLCγ, PI3K and MAPK. The latest increases MMP-9 expression and promotes Erk1/2 activation that lead to cancer cells invasion. The same signaling pathway acts in presence of HER-2/neu receptor that lead to high proliferation of cancer cells.
Method: 250 cases of invasive lobular breast cancer were studied. The immunohistochemical method with use of Monoclonal Mouse Anti-Human N-cadherin (Clone IAR06, Monosan, the Netherlands) and Rabbit Monoclonal Anti -HER2/neu antibody (Clone 4B5, Ventana) was applied.
Results: Coexpression of N-cadherin and HER-2/neu was found in 72 (29 %) cases. We revealed the positive moderate correlation between N-cadherin and HER-2/neu expression ($V = 0.41$, $p < 0.05$).
Conclusion: N-cadherin and HER-2/neu both participate in signaling pathway RAS/MAPK/Erk. Epithelial-mesenchymal transition connects with high metastatic potential of tumour and high proliferation of cancer cells as well.

PS-01-050

Breast benign papillary lesion clinically simulating malignancy: Analysis of two cases

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Objective: Breast benign papillary lesions consists of the proliferation of ductal epithelium supported by fibrovascular stroma. Morphological interpretation of papillary lesions of the breast is challenging. In addition, the clinical presentation of benign and malignant lesions are overlapping.
Method: The retrospective analysis of clinical and histopathological testing of two cases.
Results: First case. A 37-year old female with ulcerated tumour for 2 years in the right breast. Second case. A 23-year-old patient with right nipple enlargement and erosion.
Conclusion: The clinical diagnosis of papillary lesions is still challenging. The precise histopathological examination is important for optional breast surgery.

Table 1:

	First case	Second case
Clinical diagnosis	Invasive carcinoma T4bNxM0 of the right breast	Nipple erosion/Paget's disease of the right breast
Core biopsy	Papillary structures with epithelial hyperplasia, apocrine metaplasia, but without atypia	Was not performed
Gross pathology	Breast conserving surgery: cystic solitary papillary lesion 3x2x1.8cm with ulceration of overlying skin	Excision biopsy: nipple tissue sample 0.4x0.3cm
Microscopic pathology	Papillary hyperplasia of ductal epithelium with apocrine metaplasia. Hyperplastic epithelium extend to the skin surface with following erosion of epidermis	Papillary hyperplasia of ductal epithelium. Hyperplastic epithelium extend to the nipple surface with following erosion of epidermis
Immunohistochemistry	Smooth muscle actin, p63, CK5/CK6 positive	Smooth muscle actin, p63, CK5/CK6 positive
Final diagnosis	Papilloma with skin ulceration	Adenoma of the nipple/florid papillomatosis of the nipple

PS-01-051
Three cases of Metaplastic Cell Carcinomas of the Breast (MBCs)
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Objective: The term metaplastic carcinoma refers to a group of neoplasms characterized by differentiation of neoplastic epithelium into squamous and/or mesenchymal-like elements. It is a very rare carcinoma of the breast (incidence about 0,2 %, as referred in the literature). We present three cases of MBCs, a pure squamous cell carcinoma, a fibromatosis-like metaplastic cell carcinoma and a spindle cell carcinoma.
Method: In our laboratory we received surgical specimens of three women, two of them aged 50 and one aged 85. The mean diameter of the tumours was 3,5 cm., with a whitish, fleshy gross appearance and infiltrating margins.
Results: Histopathologically, the cells had squamous and spindle cell morphology. Immnohistochemically, they were ker AE1/AE3 +, ker 3412+, ker 5/6+, e-cadherin+ and ER-, PR-, c-erbB-2-. There are no well-defined prognostic markers.
Conclusion: Differential diagnosis is broad, including phyllodes tumour, metastatic carcinomas and sarcomas. They behave aggressively with a poor overall prognosis, due to frequent metastases in visceral organs. There are no well-defined protocols for therapy. Complete surgical excision along with adjuvant chemotherapy and/or radiotherapy have been proposed.

PS-01-053
Idiopathic granulomatous mastitis: One diagnosis of exclusion with the question that it poses
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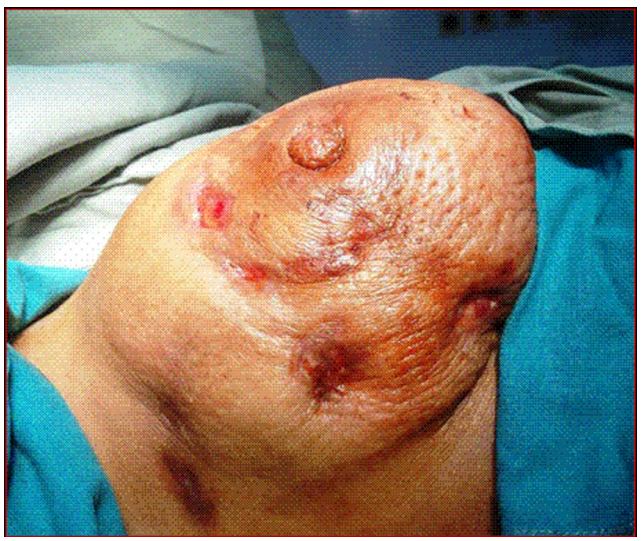
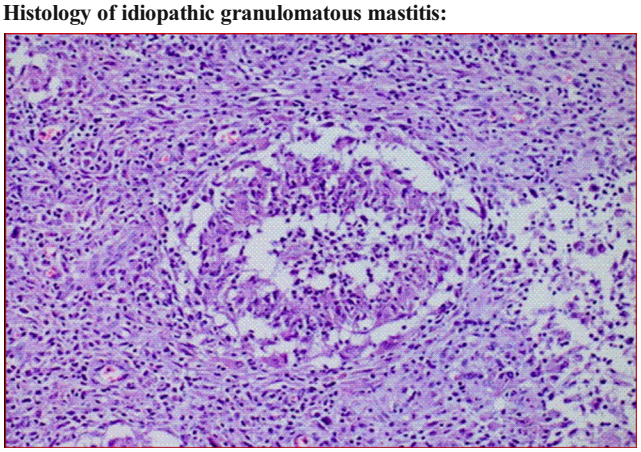
Objective: We present a case of 24 year old woman, who presents with bilateral granulomatous breast inflammation with abscess formation and fistula tracts that end in multiple draining openings in periareolar skin. We put emphasis on the differential diagnosis, because similar changes may be seen in autoimmune diseases, use of oral contraceptives, after pregnacy and lactation, and most importantly may present as background of invasive breast carcinoma.
Method: The additional work-up of the specimen includes special stains as Ziel-Nilsen, PAS, Grocott and immunohistochemistry with CK AE1-AE3.
Results: The mentioned above markers were all negative, wich excludes infectious agents and cocurrent carcinomaq thus supporting the diagnosis idiopathic granulomatous mastitis.
Conclusion: The idiopathic granulomatous mastitis is a diagnosis of exclusion, that requires broad differential diagnosis, detailed anamnesis and sufficient amount of tissue for histologic examination. Careful examination should be performed to exclude breast cancer.

Gross view of idiopathic granulomatous mastitis:



Histology of idiopathic granulomatous mastitis:



PS-01-054

Prognostic importance of NF-kB in breast cancer

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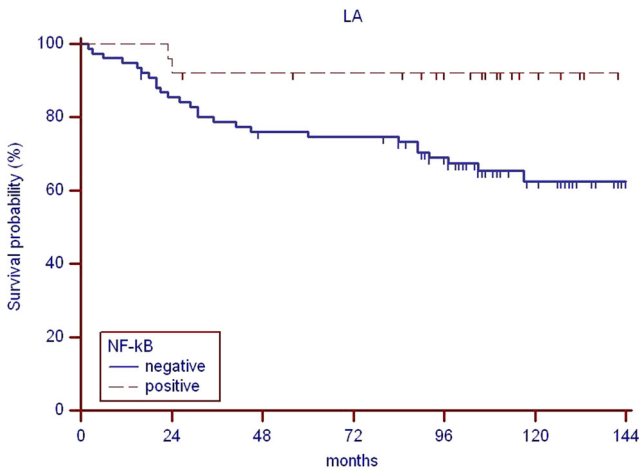
Objective: Nuclear factor κB (NF-κB) is transcriptional factor involved in cancerogenesis and metastatic spread of tumours cells. The aim of this study was to evaluate expression of NF-κB in breast cancer and to correlate the immunohistocemical expression of this marker with clinicopathological parameters and patient outcome.
Method: This retrospective study included 208 consecutive newly diagnosed ductal invasive breast cancer patients operated at Department of Surgery, Clinical Hospital Center Rijeka, Croatia between 2000 and 2004 with long term follow up over 10 years. Immunohistochemical staining for NF-kB was done on tissue microarray and expression in more than or equal to 10 % nuclei of entire tumour area was considered positive.
Results: NF-kB was positive in 31 % of tumours. Activation of NF-kB showed inverse correlation with expression of estrogen receptor ($p = 0.005$) and positive correlation with expression Ki-67 proliferation index ($p = 0{,}015$). We found better overall survival in NF-kB positive tumours in luminal A subtype ($p = 0.021$).
Conclusion: Our results could be explained as consequence of possible tumour suppressing effect of NF-kB. We think that the practical relevance of NF-kB as prognostic indicator and potential target for specific therapies deserve further investigation.

Overall survival for patients with Luminal A (LA) subtype according NF-kB positivity:



PS-01-055

A breast hamartoma: Fibroadenolipoma

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Abstract: Breast hamartomas are rare benign tumour-like nodüles composed of mammary glandular tissue, fibrous stroma, and fat mixed in various proportions. It was first described in 1971 as lipofibroadenoma, fibroadenolipoma or adenolipoma, based on the predominant component of the breast tissue. The lesion often gives the impression of "breast within breast." Hamartomas are typically found in women who are premenopausal and in the fourth and fifth decades of life. Our case was a 30-year old woman. She was admitted to clinic, complaining of a mass in her left breast since 3 months. Ultrasonographic examinations revealed a 4 cm mass diagnosed as fibroadenolipoma. Gross examination included a soft, circumscribed, lobulated mass with cleft-shaped cystic areas bordered by a thin fibrous pseudocapsule. Microscopic findings were composed of disorganized lobules with interspersed ducts in a background of collagenous stroma and mature fat limited by a pseudocapsule.There was no cytologic atypia or significant mitotic activity. Complete surgical excision is curative for this lesion. However, researchers have reported local recurrence within the first year after surgery in an adolescent patient whose tumour had been incompletely excised.

PS-01-056

Non-Hodgkin's lymphomas in breast

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Abstract: Non-Hodgkin's lymphomas diagnosed at the breast can be primary or secondary. Both are relatively rare, they represent about 0.6 % s breast cancer. Eighty-year-old female patient with swelling and pain in her right breast attended to our outpatient clinic. On the ultrasound examination, lobulated countered, 3 × 7 cm sized solid mass was determined on the right upper outer quadrant. Histopathologic examination is recommended with the diagnosis of inflammatory breast cancer. In the histomorphological study of biopsy material, 3–4 times large in size mature atypical lymphocytes, formed infiltration between adipose tissue and the striated muscle tissue under the squamous epithelium, showing intense apoptosis and necrosis, containing nucleoli clarity, large nuclei and narrow cytoplasm and neoplastic infiltration consisting of mitotic figures was observed. In the immunohistochemical studies of this atypical lymphocytes, diffuse immunoreactivity with CD20 and CD79a was observed. In the remaining non-neoplastic lymphocytes CD-3 staining was observed. Ki-67 proliferative index was assessed as 95–98 %. Atypical lymphocytes was also observed with FNA. In light of these findings and patients histomorphological and immunohistochemical data 'Non-Hodgkin's malignant lymphoma (Diffuse Large Cell B Cell) was diagnosed. Patient was diagnosed with the same diagnosis from the right tonsil specimen and after 1 year right breast metastasis is observed. Diffuse large B cell lymphoma (DLBCL) is the most common subtype of metastatic breast lymphoma.

PS-01-057

Collision tumour of the breast: Coexistent invasive ductal carcinoma and multicentric adenomyoepithelioma

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Objective: To report the first case of a collision tumour between an invasive ductal carcinoma and a multicentric adenomyoepithelioma of the breast.
Method: A 73-year-old woman was admitted for tumorectomy and excision of a 1 cm subcutaneous nodule of the left breast. Within the tumorectomy, a 2,2 cm ill-defined white indurated lesion was identified.
Results: On microscopic examination, the 2,2 cm lesion consisted of a grade 3 invasive ductal carcinoma, with intra- and peri-tumoural ductal carcinoma in situ (DCIS) of high nuclear grade. No lympho-vascular tumour emboly was observed. Estrogen and progesterone receptors, as well as HER2 status (score 1+), were negative. The 1 cm subcutaneous nodule and other nodules found around the carcinoma turned out to be multiple adenomyoepitheliomas. Focally, the invasive ductal carcinoma and an adenomyoepithelioma collided. At this site, numerous DCIS foci with comedo-necrosis were intimately in contact and admixed with the adenomyoepithelioma. The myoepithelial cells were p63 and Smooth Muscle Actin positive, unlike the invasive ductal carcinoma and the DCIS.
Conclusion: We hereby report the first case of a collision tumour between an invasive ductal carcinoma and a multicentric adenomyoepithelioma. This stresses the importance of investigating the most suspect nodule within a multicentric adenomyoepithelioma, while considering the possibility of a colliding invasive carcinoma.

PS-01-058

Glycogen-rich clear cell carcinoma of the breast showing carcinomatous lymphangiosis and extremely aggressive clinical behavior

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Objective: Herein, we describe the first documented case of glycogen-rich clear cell carcinoma (GRCC) with lymphangitic carcinomatosis.
Method: A 62-year-old postmenopausal Japanese woman presented with a palpable mass in the right breast. Ultrasonography revealed a well-marginated, hypoechoic mammary tumour and systemic CT detected no other suspicious lesions.
Results: The cut surface of the mastectomy specimen contained a lobulated, solid tumour, measuring 34 × 32 mm. Histologically, this tumour was composed of medullary invasive growth of carcinoma cells with central necrosis and hemorrhage. Polygonal carcinoma cells possessed abundant, clear and/or finely-granular cytoplasm, containing PAS-positive diastase-labile glycogen, and irregularly-shaped, hyperchromatic nuclei with prominent nucleoli. Mitotic figures were numerous (65/10HPFs). Marked lymphatic permeation and vascular infiltration, confirmed by D2-40 and/or CD31 immunostaining, were detected. This cancer was of the 'triple negative' subtype with a high MIB-1 index (70.1 %). Metastases were identified in 12 regional lymph nodes. Unfortunately, local recurrence was detected on palpation a month after surgery and multiple lung, liver, bone and lymph node metastases were identified on CT scans.
Conclusion: The biological behavior and prognosis of breast GRCC remain controversial. Our present case with the unusual feature of extraordinary intramammary vessel invasion, as well as rather high stage and grade, followed a very rapid and aggressive clinical course.

PS-01-059

Massive myoepithelial hyperplasia (myoepitheliosis) with lumpy deposits of basement membrane material closely associated with apocrine adenosis and ductal carcinoma in SITU of the breast

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Objective: Myoepitheliosis is a benign mammary lesion characterized by a multifocal proliferation of myoepithelial cells growing into and/or around small ducts and ductules. Herein, we report a unique case of apocrine ductal carcinoma in situ (DCIS) arising from apocrine adenosis with massive myoepitheliosis producing excessive basement membrane material.
Method: A 68-year-old woman presented with an induration in the right breast. Fine needle aspiration cytology of the lesion indicated apocrine cancer, and lumpectomy was performed.
Results: Histologically, the lesion was composed of a lobulated aggregate of tubules having both epithelial and myoepithelial proliferations with stromal fibrosis. The epithelial cells had extensive apocrine metaplasia with varying degrees of nuclear atypism. In some parts, the epithelial cells having large nuclei with coarse chromatins and conspicuous nucleoli were arranged in solid and cribriform patterns with focal necrosis. Marked myoepithelial hyperplasia accompanied these epithelial lesions in not only a periductal but also an intraductal pattern. Furthermore, myoepithelial cells frequently showed a transition to lumpy deposits of amorphous basement membrane material.
Conclusion: There may be a paradoxical link between excessive myoepithelial cell proliferation and breast cancer development, whereas tumour-suppressing functions of these myoepithelial cells might be inhibiting a cancer invasion by the DCIS in spite of its marked cellular atypicality.

PS-01-060

Breast cholesterol granuloma: A benign mimicker of malignancy

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Objective: Breast cholesterol granuloma (BCG) is a rare benign condition that clinically and radiologically simulates malignancy. It appears as a mass lesion consisting of granulation tissue, rich in cholesterol crystals surrounded by foreign body giant cells.
Method: We present a case of a 71-year-old woman with a 2 cm mass lesion of the upper, outer quadrant of her left breast. Mammography revealed a well circumscribed, round mass with microlobulated margins and scattered coarse calcifications. Cytologic evaluation was positive for atypia and lumpectomy followed. A surgical specimen encompassing a 2 cm partially cystic mass, with smooth fibrous walls and brownish friable content was received. At the periphery of the lesion diffuse, grayish fibrous areas were also observed.
Results: Microscopically, the mass consisted of granulation tissue with irregular arrays of cholesterol crystals surrounded by foamy histiocytes and foreign body giant cells, along with fibrosis. Mammary duct ectasia was noted in the surrounding parenchyma.
Conclusion: BCG is a rare, benign breast lesion of unclear pathogenesis. It is presumably related with rupture of ectatic ducts or breast macrocysts into surrounding parenchyma. The main significance of this entity is that it mimics malignancy and histological examination is necessary for the final diagnosis.

PS-01-061

High prevalence of solid papillary carcinoma with neuroendocrine differentiation in breast lesions detected by the clinical symptom of bloody nipple discharge

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Objective: Bloody nipple discharge (BND) is an important clinical symptom in mammary disorders, especially cancers. However, the association between this symptom and carcinomas with neuroendocrine features has not been sufficiently investigated or well understood.
Method: We clinicopathologically studied 89 cases using biopsy and/or resection in 144 patients who came to the hospital for a thorough examination of symptomatic BND.
Results: Of these 89 cases examined histologically, 24 (27 %) were solid papillary carcinomas (SPCs) and immuno-expressed chromogranin A and/or synaptophysin in >50 % of cells. Moreover, these solid papillary neuroendocrine carcinomas (SP-NECs) made up 44 % (24/55) of the mammary cancers found because of the BND. The frequency of diagnosing malignancy preoperatively in 24 SP-NECs was 4 % by nipple discharge cytology, 40 % by fine needle aspiration cytology, 62 % by core needle biopsy and 67 % by mammotome biopsy. The 24 SP-NECs were subclassified into SPC in situ (9 cases), SPC with microinvasion (7 cases) and SPC with invasion (8 cases).
Conclusion: NECs relevant to SPC, often under-diagnosed preoperatively, accounted for an important share of breast conditions associated with BND. It is, therefore, worth keeping this type of mammary cancer in mind when performing medical examinations on patients with BND.

PS-01-062

Microinvasive neuroendocrine carcinoma arising from central papilloma of the breast

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Objective: Herein, we describe the first case of a mammary neuroendocrine tumour (NET) histologically recognized as originating from a central papilloma.
Method: A 43-year-old premenopausal Japanese woman presented with a clinical symptom of bloody nipple discharge. Ultrasonography revealed a sharply elevated hypoechoic mass in a dilated large duct immediately beneath her left nipple, suggesting an intraductal papilloma.
Results: The cut surface of the lumpectomy specimen contained a circumscribed gray-whitish tumour in a prominently dilated lactiferous duct. Histopathologically, this intracystic tumour was supported by arborized and/or intricate fibrovascular cores lined with myoepithelial cells within a proliferation of two different epithelial cells: benign ductal cells and carcinoma cells. Benign ductal cells closely lining the myoepithelial cells were cuboidal to columnar in shape with relatively dark-staining nuclei. There was pseudoinvasion at the periphery of the lesion. Carcinoma cells had a predominantly solid growth, were polygonal or occasionally spindle-shaped, and had fine-granular cytoplasm and ovoid nuclei with fine-granular chromatin. Carcinoma cells showed microinvasion and vascular infiltration with no intraductal spreading through surrounding ducts of the intracystic tumour. Immunohistochemically, chromogranin A and synaptophysin were diffusely-positive in carcinoma cells.
Conclusion: This report adds to our limited knowledge of the natural history of breast NETs and the mechanisms underlying their development.

PS-01-063
Molecular profiles of invasive breast carcinomas
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Objective: We established the molecular profiles of invasive breast carcinomas with immunohistochemical ERBB2moderate expression.
Method: 90 cases diagnosed with breast carcinoma and immunohistochemical ERBB2moderate expression were selected from the Pathology Department of Emergency Clinical County Hospital of Constanta. The molecular profiles were established using immunohistochemical expression of ER, PR and Ki-67. Identification of ERBB2 gene status was done by chromogenic or fluorescence in situ hybridization (CISH/FISH).
Results: The mean age of patients studied was 58.69 ± 10.21. The majority of patients (82 %) were diagnosed with invasive ductal carcinomas. ERBB2 gene status reveled no gene amplification in 68 % cases, low level amplification in 22 % cases and high level amplification in 7 % cases. Tumour heterogeneity was observed only in 3 % of cases. The estrogen receptor status presented positive expression in 70 % of cases and progesterone receptor positive expression was detected in 75 % of cases. According to Ki67 proliferation marker expression in 72 % Ki67 was positive in >10 % of tumoural nuclei and in 28 % Ki67 was positive in <10 % of tumoural nuclei. Only 6 % of cases were categorized as triple negative breast cancer.
Conclusion: Daily management of patient with breast carcinomas remains critically dependent on careful pathological evaluation supplemented by ER, PR and ERBB2 test.

PS-01-064
Evaluation of receptor status (ER, PgR) in breast cancer: A validation study of tissue microarrays
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Objective: We studied ability of tissue microarrays technique as alternative to analysis of whole sections (WS) for breast carcinomas.
Method: The study included 229 patient with breast carcinoma T1-2 N0 M0 treated within 2000–2009 years. After whole slide scanning TMA blocks was constructed using 2 mm punches and TMA master device (3DHistech, Budapest). TMA results of immunohistochemistry (IHC) testing for Estrogen receptors (ER), Progesterone receptors (PgR) were compared retrospectively with the results of WS.
Results: We found excellent agreement between the two methods for ER and PgR IHC evaluation, using the Allred score. There was only 1 disagreement case (positive in TMA and negative in WS).
Conclusion: For breast cancer TMAs (with big diameter core) are an efficient and reliable alternative to WS IHC staining for ER and PgR. This technique allow reduce time, reagent and finally cost of each type of analysis.

PS-01-065
Well-differentiated neuroendocrine tumour of the breast with recurrence due to needle tract seeding
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Objective: Herein, we describe the first case of a mammary neuroendocrine carcinoma (NEC) showing a relapse related to needle implantation.
Method: A 60-year-old postmenopausal Japanese woman presented with slight skin retraction in the right breast. Ultrasound-guided 16-G automated core needle biopsy (CNB) of the irregular, hypoechoic breast mass yielded a pathological diagnosis of carcinoma.
Results: The cut surface of the lumpectomy specimen contained a poorly-marginated, gray-whitish solid tumour, measuring 12 × 10 mm. Histologically, this tumour was composed of a solid and/or trabecular invasive growth of carcinoma cells with a highly vascular stroma. Polygonal carcinoma cells possessed fine-granular cytoplasm and round-to-ovoid nuclei with fine-granular chromatin. We detected small subcutaneous scars with disseminated carcinoma cell clusters, causally-related to the preoperative CNB, away from the main tumour. Immunohistochemically, the carcinoma cells were positive for chromogranin A and NCAM. The patient received anastrozole as endocrine therapy, but refused adjuvant radiation. She had become aware of a mass at the skin puncture site for the previous CNB 4 years after surgery. We pathologically confirmed the recurrent NEC involving the skin and subcutaneous tissues.
Conclusion: To reduce the clinical impact of tumour displacement, we need to consider preventive radiation therapy for needle pathways, their excision and/or use of vacuum-assisted biopsy devices.

PS-01-066
Primary neuroendocrine tumour of the breast: A rare pathological finding
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Objective: Primary neuroendocrine tumours (pNET) of the breast make up less than 0.1 % of the breast cancer, but their outcome is among the worst. They chiefly affect middle aged women and usually do not involve the axillary lymph nodes at diagnosis. Surgery is the first therapeutic option. Also, adjuvant chemotherapy is highly effective due to their chemo-sensitivity.
Method: We present a case of pNET of the breast, NGS = 7 in a middle aged Caucasian woman. Histopathological and immunohistochemical examinations were performed.
Results: Microscopic evaluation indentified limited areas of in situ ductal breast carcinoma; the tumour demonstrates positivity for synaptophysin and chromogranin in more than half of the malignant cells, very strong diffuse positivity with ER(89 %) and 40 % positivity for PR. Her2/Neu aspect was borderline(2+) with negative in situ hybridization test. The

patient does not have any other synchronous neuroendocrine tumour and no specific signs or symptoms.
Conclusion: pNET of breast can be demonstrated only using immunohistochemical assays, but since neuroendocrine markers are not a usual component of breast panel, this feature must be at least suspected on usual hematoxylin-eosin slides. Positive diagnosis is important, since this tumour is particularly aggressive and bears a poor prognosis. *Dragusin and Pop are first authors in equal proportion.

PS-01-068
Evaluation of HER2 in breast cancer: A validation study of tissue microarrays
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Objective: We studied ability of TMA technique as alternative to analysis of whole sections (WS) for breast carcinomas.
Method: The study included 229 patients with breast carcinoma T1-2 N0 M0 treated within 2000–2009 years. After whole slide scanning were constructed TMA blocks using 2 mm punches and TMA master device (3DHistech, Budapest). TMA results of immunohistochemistry of HER2 were compared retrospectively with the results of WS.
Results: General distribution of HER2 status for WS was: negative (0+1) 85,5 %, unequal (2+) 6,07 %, positive (3+) - 8.41 %, for TMA cores negative (0+1) 82,6 %, unequal (2+) 7,04 %, positive (3+) - 10,33 %. When we compared each cases for HER2 there was moderate agreement with negative (score 0) and positive(score 3+) case around 70 % and poor agreement in HER2 (1+2+ category) - only 50 % 25 % including both false negative and false positive estimations. We thought such kind disagreement in individual group was due to using different primary antibodies (all not FDA-approved) in previous years compared with PATH WAY® rmAb 4B5 (Ventana) antibody which was used for TMA slides.
Conclusion: For breast cancer TMAs could be reasonable alternative to WS. Especially for Her2 testing, should be used only FDA approved systems and this technique allow reduce time, reagent and finally cost of such type of analysis.

PS-01-071
The change in the immunophenotype during the progression of the breast cancer
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Objective: Breast cancer represents heterogeneous disease based on morphology, prognosis and the response to the therapy. Intratumoral heterogeneity of the primary tumour is important for the development of the metastatic disease and the change in immunophenotype during disease progression highlights the importance of sampling metastatic tumour tissue for the optimal therapy strategy. The aim of this study was to determine and compare immunophenotype in primary and metastatic breast cancer.
Method: In the small pilot study we reviewed pathological features and biomarker expression of estrogen receptor (ER), progesterone receptor (PR), human epidermal receptor 2 (HER-2), Ki-67 proliferation marker (Ki-67) that were assessed for the primary tumour and the matched metastases.
Results: The change in immunophenotype was observed in 11 out of 26 patients (42 %), 23 % of ER and PR became negative, 0.1 % of HER-2 became positive. The 6 out of 8 (75 %) luminal A changed to luminal B (Her-2 negative) and 1 (13 %) luminal A to luminal B (Her-2 positive). Three out of four tumours in luminal B (HER-2 negative) group changed immunophenotype (1 to luminal A, 1 to luminal B (HER-2 positive and 1 to triple negative). One out of 5 triple negative breast cancers changed immunofphenotype to luminal B (HER-2 positive) in second local reccurence.
Conclusion: The observation of the immunophenotype change in the present study during the cancer progression demonstrates development of the tumour mass mostly composed of different cells than the primary tumour. The therapeutic implications may derive from providing new information to the oncologist based on immunophenotype of the tumour.

PS-01-073
Primary breast lymphoma: Clinicopathological analysis of 18 cases
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Objective: The purpose of our study was to investigate clinical presentation, histopathological features, and treatment modalities of PBL.
Method: This retrospective study concerned data of 18 cases of PBLs collected at Salah Azaiez Institute of Tunisia from 2000 to 2015. Patient's details including age at diagnosis, sex, presenting symptoms and signs, histopathological examinations and outcome were retrieved from the medical records.
Results: The series included 14 women and 4 men. The mean age of patients was 42 years. The presenting clinical symptoms were dominated by breast mass. Diagnostic imaging techniques included breast ultrasonography and mammography in all cases. All patients underwent surgical resection of tumour. The mean tumour size was 6,7 cm. Frozen section was helped confirm the diagnosis of lymphoma in 9 cases. Histological diagnoses were three cases of low grade lymphoma and 15 cases of high grade lymphoma. The predominant histological type was diffuse large B cell lymphoma. All tumours immunophenotype were CD20+. Sixteen cases were treated by chemotherapy with surgery. One case was received radiation treatment and chemotherapy and surgery. One case received radiation treatment with surgery. Complete remission was observed in three cases.
Conclusion: There is no consensus on the question of how to best treat PBL: chemotherapy, radiotherapy or combined therapy.

PS-01-076
DNA repair pathway in BRCAX and BRCA1/2-associated hereditary triple-negative breast cancers
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Objective: Tumours from patients with BRCA1/2 germline mutations are known to be especially sensitive to DNA cross-linking agents (e.g., platinum drugs) and to poly(ADP-ribose) polymerase (PARP) inhibitors. The purpose of this report is to compare the expression of genes engaged in DNA damage repair pathway in triple-negative hereditary breast cancers without pathogenic mutations in BRCA1/2 (BRCAX) and hereditary triple-negative breast cancers with BRCA1/2 mutations.
Method: Total RNA was extracted from 30 formalin fixed and paraffin embedded consecutive hereditary triple-negative breast cancers. A real-time PCR arrays based on UPL probes were designed and used to profile the expression of 90 most important DNA repair genes including e.g., BRCA, PARP, CHEK, ATM, XRCC, ERCC, PALB2, PTEN, RECQL, RAD and FANC family.
Results: The expression profile of studied genes was highly similar between BRCAX and BRCA1/2-associated triple-negative breast cancers. Only expression of USP1 gene (ubiquitin specific peptidase 1) was significantly downregulated (1.8 fold change, $p = 0.03$) in BRCAX group.
Conclusion: Similarity of expression profile of genes engaged in DNA damage repair between both groups suggests that identification of BRCAX patients with triple-negative cancers based on family history can increase the proportion of patients with triple-negative breast cancer who may be eligible for therapy using PARP inhibitors and platinum drugs.

PS-01-078

Breast metastases from extra-mammary solid tumours: Clinicopathologic characteristics of 15 cases

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Objective: Breast metastases (BM) from extra-mammary neoplasms are rare. The most common origin are lymphomas/leukemias and melanomas. Our goal is to study the clinicopathological features of BM of malignant solid tumours.
Method: We identified 15 cases of BM from solid tumours. The clinicopathologic characteristics were reviewed.
Results: All but three patients were women, median age: 55 years. Twelve patients had prior history of cancer: In 3 the initial presentation was as BM. Ten patients developed metastases in other organs after diagnosis of BM. The median interval from diagnosis of the primary tumour to the BM was 14,2 months. Fourteen cases were presented as single BM. Macroscopically, all tumours were well defined. Average diameter: 1.8 cm (0,5–4,5 cm). Primary tumours were: melanoma (3), kidney carcinoma (3), ovarian carcinoma (2), lung carcinoma (2), colon adenocarcinoma (1), oropharyngeal-SCC (1), medullary-thyroid carcinoma (1), ASPS (1), and anaplastic ependymoma (1). Thirteen patients with follow-up: median 26,9 months: 9 died and 4 alive. The median survival from diagnosis of BM: 8.43 months.
Conclusion: Metastatic tumours in the breast are rare. Given a breast single nodule in patients with known extramammary malignancy, we should suspect a metastasis. The diagnosis of BM carries a poor prognosis, with a very low survival.

PS-01-079

Different clinical involvement of RASSF hypermethylation in breast cancer subtypes

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Objective: Breast cancer is a heterogeneous disease that comprises several tumour subtypes with different prognosis. The 2013 St. Gallen Consensus Conference on breast cancer provided mostly evidence-based, of the classification of breast tumours into the categories luminal A-like, luminal B-like/HER2-negative, luminal B-like/HER2-positive, HER2-positive and triple-negative tumours. The analysis of new molecular factors is crucial to obtain further insights into the mechanisms involved in the tumourigenesis of each tumour subtype. In this study the presence of hypermethylation of an important Ras-effector of RASSF (RAS-association domain family) and its clinical value has been studied in breast cancer subtypes.
Method: The hypermethylation of genes was analyzed in 198 breast tumours of different subtypes by means of methylation-specific PCR and this hypermethylation was confirmed by bisulfite-sequencing. Different patterns of RASSF expression for distinct tumour subtypes were detected by immunohistochemistry.
Results: The hypermethylation of this gene was much more frequent in luminal subtypes than in non-luminal tumours ($p = 0.001$). This alteration is associated with better prognosis in multivariate statistical analysis ($P = 0.039$).
Conclusion: The hypermethylation of certain genes is different in luminal and non-luminal tumours and can be promising genes with clinical involvement in breast cancer.

PS-01-080

Estrogen and progesterone hormone receptor status in HER2 positive breast cancers

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Objective: The aim of this retrospective study was to evaluate the difference between estrogen and progesterone hormone receptor status in HER2 positive breast cancer cases.
Method: 144 consecutive breast cancer cases diagnosed between 2012 and 2014 in the Clinical hospital Acibadem Sistina were included in this retrospective study. Representative samples of tumour tissue were used for the immunohistochemical analysis and in situ hybridization. For the evaluation of hormone receptors, primary antibodies and detection system from Dako were used and the slides were stained using Dako autostainer Link 48. HER2 status was evaluated using Hercep test from Dako. On equivocal HER2 cases, dual color CISH was performed using HER2 and CEN-17 probes.
Results: Our results showed that only 23 % of the HER2 positive cases revealed positivity for progesterone receptor as well ($p < 0,05$), whereas 57 % of these HER2 positive cases were also positive for estrogen receptor ($p>0,05$).
Conclusion: These data suggest that HER2 overexpression might have negative influence on progesterone receptor expression in breast cancer patients. Further follow up studies should be performed in order to assess the prognostic significance of these findings.

PS-01-082

Clinicopathological features and Mib-1 (Ki-67) value in estrogen receptor-negative breast ductal carcinoma: Experience of Salah Azaiez Institute

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Objective: The main aim of the present study was to correlate the morphological features of estrogen receptor negative ductal breast carcinomas with pathological data and other prognostic variables. Proliferative activity using MIB-1(Ki-67) will be investigated and correlated with pathological data.
Method: A total of 450 operable breast cancer patients, diagnosed from January 2010 to December 2014 were retrospectively reviewed and 141 patients with ER–negative tumours were identified. Only 60 cases were evaluated.
Results: All the 60 patients were female with an age range from 33 to 74 years. Most of the tumours are ≥ 2 cm in size (46/60 cases; 76.6 %). There were 34/60 cases (56,6 %) with lymph node metastases. A high proportion of tumour was graded 3 (35/60 cases; 58.3 %) followed by grade 2 (22/60 cases; 20.2 %) and only 3 cases of grade 1 (5 %). All of cases showed PR negative, while 33.3 % of cases (20/60) were c-erbB2 positive. MIB-1 was positive (>20 %) in 40 (70 %) of 60 ER negative breast tumours.
Conclusion: MIB-1 was found to be positive in more than 50 % of ER negative tumours. Given that tumours with high proliferative index occurs in patients with poor clinical outcome, MIB-1 is a potentially reliable prognostic marker in this hormonally resistant subtype of breast cancers.

Sunday, 6 September 2015, 09.30 – 10.30, Restaurant
PS-02 Poster Session Endocrine Pathology

PS-02-002
Carcinosarcoma of adrenocortical origin
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Objective: Carcinosarcomas are defined as malignant neoplasms showing both epithelial and mesenchymal differentiation. We report a case of a carcinosarcoma of adrenal gland origin.
Method: An 81 year old patient presented with large adrenal mass without history of hypertension and was led into surgery.
Results: The adrenal gland weighted 480 gr and its dimensions were 11 × 8 × 7 cm. The gland was entirely occupied by a large neoplasm with necrotic areas. Histological examination revealed a biphasic neoplasm with distinct epithelioid and spindle areas. The epithelioid areas consisted of nests or sheets of polygonal cells with eosinophilic cytoplasm, moderately atypical nuclei with eosinophilic nucleoli and multiple mitosis. The epithelioid cells expressed MelanA, Synaptophysin, Vimentin and CD56 while they were negative for Chromogranin, Inhibin, Calretinin, SALL-4, OCT3/4 and characteristically negative for cytokeratins. The spindle areas consisted of intersecting fascicles of cells with moderately atypical nuclei with mitotic activity and large areas of geographic necrosis. No heterologous differentiation was noted. The spindle cells expressed Desmin and Smooth Muscle Actin but failed to express Myogenin, MyoD1, MelanA or Synaptophysin. The immunomorphological findings were typical of leiomyosarcoma.
Conclusion: Adrenocortical carcinosarcoma is an extremely rare and aggressive neoplasm. Detailed immunophenotyping helps to differentiate it from the extra-adrenal carcinosarcomas.

PS-02-003
Corticomedullary mixed tumour of adrenal gland
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Objective: We report a 37-year-old woman, operated due to a tumour mass in left adrenal gland, with clinical symptoms of hypertension despite therapy, insulin resistance, metabolic syndrome, obesity. Laboratory evaluation showed normal cortisol and catecholamine levels. Histopathological examination revealed a corticomedullary mixed tumour of adrenal gland.
Method: The patient underwent a laparoscopic adrenalectomy of the tumour, which was identified by computed tomography. Macroscopically, it is a well-circumscribed tumour (2.5 × 1.5 cm) with a thin, fibrotic capsule, yellowish-orange, homogeneous. Immunohistochemistry was also performed.
Results: The tumour was composed of an admixed population of both adrenal cortical cells and pheochromocytes. The adrenal cortical component is composed of enlarged cells with eosinophilic, slightly granular cytoplasm with round to oval nuclei. The pheochromocytes display finely granular, basophilic cytoplasm. The nuclei are larger and ovoid in shape. Immunohistochemical studies were positive both for cortical cells (inibin-α, synaptophysin, melan-A and calretinin) and medullary cells (S-100 and chromogranin A).
Conclusion: Adrenal gland can be thought of as two separate organs, the adrenal cortex and the adrenal medulla, each with distinct structure, function, and embryologic origin. Corticomedullary mixed tumour is a rare adrenal tumour, reported in not more than 20 patients to date.

PS-02-004
Clinicopathological features of primary thyroid lymphoma: A study of 7 cases
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Objective: Primary thyroid lymphoma (PThL) is an uncommon neoplasm accounting for 5 % of all thyroid gland malignant lesions. Pathology features compared with CT, ultrasound exam and cytology findings were analyzed. The patients were 6 women (79, 78, 76, 73, 65, 62-years-old) and 58-year-old man. Total thyroidectomy were performed in 2012–2014.
Method: The diagnoses were confirmed by IHC.
Results: Patients presented with mass lesion (7), with rapidly enlargement (4), and compression symptoms(3). Tumour size ranged from 5 to 12 cm in maximal dimension. PThL involved one lobe (1 case), both lobes(6), with extension to adipose tissue(6), skeletal muscles (3), paratracheal tissue (3), trachea(1), v.jugularis interna (1), skin(1). Cytology findings identificated lymphoma in 1 case, in 2 - anaplastic carcinomas were suspected. 2 MALT-lymphoma and 5 DLBCL (3 centroblastic and 2 anaplastic type) were found. All cases of DLBCL shows CD20(+),CD5(-),CD10(-),BCL6(+) phenotype. Plasmacytoid features were seen in 1 MALT-lymphoma, in 3 DLBCL. All PThL occurs in the settings of chronic lymphocytic thyroidities, 4 of 5 glands with DLBCL had areas of MALT-lymphomas.
Conclusion: PThLs occur predominantly older aged women. Plasmacytic differentiation or plasmacytoid features are common. Specificity of CT, ultrasound exam and cytology findings were low for diagnosis of the PThL.

PS-02-005
Adrenocortical carcinoma with concomitant myelolipoma
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Objective: Patients with concomitant adrenocortical carcinoma and myelolipoma are extremely rare and in the best of our knowledge there is only one case reported in the available literature. We present a case of incidentally discovered nonfunctioning adrenocortical carcinoma with concomitant myelolipoma. The patient was 72 years old man with benign prostatic hyperplasia, severe prostatitis and cystitis, which was a reason for attending physician.
Method: Echosonography revealed right adrenal gland mass confirmed by computed tomography. The patient underwent unilateral adrenalectomy and operative material was received at the Institute of Pathology in Skopje for histological analysis.
Results: The adrenal gland weighed 113 g and measured 8 × 6 × 3,5 cm. On cut surface a binodular well circumscribed tumour mass measuring 5,5 × 3,5 × 3,5 cm was seen. It was partly light brown and partly white-gray colored. A central hemorrhage was present in one half of the tumour which revealed microscopically to be adrenocortical carcinoma. On microscopic examination we found cortical carcinoma showing cytologic atypia, necrosis, hemorrhage, 6 mitoses/10 HPF and venous invasion in one half of the tumour mass and collision myelolipoma in the other half.
Conclusion: Although extreme rare an adrenocortical carcinoma with concomitant myelolipoma should be included in differential diagnosis of adrenal gland masses.

PS-02-006
Cystic lesions of the adrenal gland
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Objective: Adrenal cystic lesions are uncommon but due to improved radiologic imaging techniques their appearance seems to increase. We analyzed the

clinical and radiological findings of 10 patients with adrenal cysts and we analyzed the pathological features of the operative material.
Method: Standard dissection procedure of the operative material and paraffin embedded tissue sections were made, stained by HE and immunohistochemicaly with CD34, CD 31, CKWS and AE1/AE3.
Results: The mean age of the patients was 40,6 years. The female to male ratio was 2,3:1. All the cysts were diagnosed as cystic lesions by imaging techniques except one. The most present clinical symptom was abdominal pain. The diameter of the cysts measured from 2 to 7 cm. Four of the cysts were diagnosed as pseudocysts and six as endothelial. They all were well circumscribed, six were multilocular and 4 filed with blood. Six were lined by CD34 and CD31 positive cells, and four had no lining cells. Nests of adrenal cells were found in 6 cases and calcification in three cases.
Conclusion: Adrenal cysts showed nonspecific clinical and radiologic finding, and were more often present in female. Endothelial cysts were more common cysts in our study.

PS-02-007
Ile105Val polymorphism in GSTP1 and the risk for thyroid carcinomas in a population from Central Bulgaria
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Objective: Thyroid carcinoma (TC) is one of the most frequently endocrine malignancy in Bulgaria. The mechanism of thyroid carcinogenesis is still not fully elucidated. The exposure to ionizing radiation may produce genotoxins, potentially detoxified and eliminated by glutathione S-transferases. We conducted a case-control study to explore the possible role of Ile105Val (+315A>G) GSTP1 SNP in TC.
Method: We genotyped for Ile105Val (+315A>G) GSTP1 SNP 49 patients with TC and 126 non-affected by the disease controls from the region of Stara Zagora, Bulgaria usind PCR-RFLP method.
Results: We found that the genotype and allele frequencies differed significantly between patients with TC and control individuals ($p < 0.0001$ for both). The genotype distribution determined 10.56-fold higher risk (OR = 1.56, 95 % CI: 4.05–27.40, $p < 0.0001$) of developing thyroid cancers in carriers of variant G allele containing genotypes (AG+GG) compared to those with AA genotype. Similarly, the variant G allele was associated with 2.60-fold higher risk for this malignancy than the more common A allele. The genotype distribution was not associated with clinical characteristics and survival of the patients with TC.
Conclusion: Our results suggest that GSTP1 could increase disease risk susceptibility and could act as a risk factor for thyroid carcinoma in individuals from the region of Stara Zagora, Bulgaria

PS-02-008
Histological variants of papillary carcinoma: Report of 52 cases
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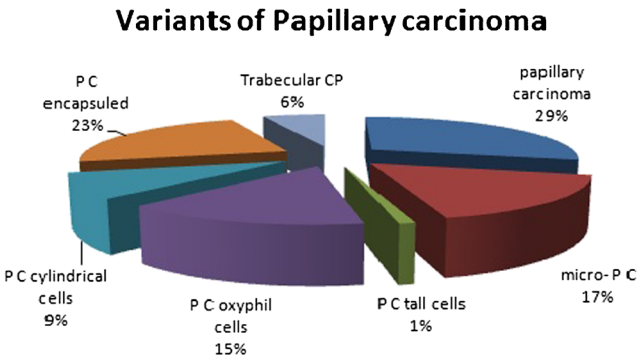
Objective: Papillary carcinoma accounts for 60 to 70 % of thyroid cancer. WHO defines papillary carcinoma as follows: Differentiation vesicular papillary and follicular architectures with nuclear changes of characteristics Several variants, or non-influential on prognosis, have been described over the years.
Method: Total thyroidectomy (THT) is the surgical procedure as practiced in our recruitment. All surgical specimens were entrusted benefited from a microscopic study after which an immunohistochemical study was performed with a variable antibody panel. Indirect immunoperoxidase is the technique used in our laboratory.
Results: During the period 2012–2013 we counted 52cases papillary carcinoma. The distribution of the variants of papillary carcinoma is dominated by the follicular variant: CPV representing 29 % of all cases and 23 % are encapsulated CPV remaining sub- morphological type of excellent prognosis. Our series does not have the variants of diffuse sclerosing variant of CP Obneil cells. The variant of the CP-type "tall cell" represents 1 case in our series, it remains pejorative, it was a male patient aged 16.
Conclusion: The variants of papillary carcinoma correspond to real clinicopathological variables entities diagnostic difficulties. The net increase in the CP in its follicular variant is explained in part by a better understanding of this variation, and partly by the considerable contribution of immunostaining with antibodies that the HMBE1 showed its diagnostic specificity in thyroid pathology.

Distribution of variants of papillary carcinoma:



PS-02-009
An unusual coexistence of papillary thyroid carcinoma with primary thyroid lymphoma
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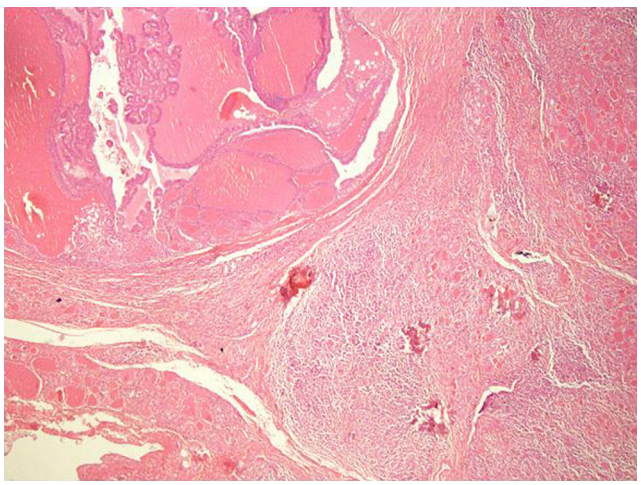
Objective: Papillary thyroid carcinoma (PTC) is the most frequent thyroid cancer, whereas primary thyroid lymphoma is distinctly rare.
Method: Right-sided, measuring 4.3 × 2.2 cm nodule was examined by fine-needle aspiration biopsy.
Results: By the presence of a rich population of monomorphic non-cohesive large lymphoid cells and absence of thyroid follicular cells, a cytodiagnosis of lymphoma included a differential diagnosis of lymphocytic thyroiditis was made. Subsequent histologic examination revealed CD45 / CD20 / Bcl-6 positive, cytokeratin / CD3 / CD5 / CD30 negative tumour cells arranged diffusely in the whole thyroid coexisting with a separate 1.3 × 1.0 cm nodule of PTC in the right lobe.
Conclusion: The goal of this case is, a cytodiagnosis of this extremely rare coexistence was possible by adequate sampling both of these discrete nodules preoperatively.

The coexistence of Thyroid papillary carcinoma (upper left) and primary thyroid lymphoma (lower right) H&E, x100:



PS-02-010

Well-differentiated neuroendocrine tumour of the pancreas: Case report and review of literature

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Objective: Pancreatic neuroendocrine tumours (PanNETs) are uncommon and represent 2–4 % of all clinically apparent pancreatic neoplasms.Males and females are equally affected. PanNETs may arise at any age, but most occur between the ages of 30 and 60 tes. We present a rare case of well-differentiated neuroendocrine tumour of the pancreas extending to the stomach, and lymph nodes.
Method: The patient was a 38-year-old woman. She visited our hospital with epigastric pain. Endoscopic ultrasound and computed tomography (CT) scan revealed a hypoechoic and heterogeneous mass measuring 87 × 61 mm in the tail of the pancreas. On initial, the case was diagnosed by biopsy, and the distal pancreatectomy, splenectomy, partial gastrectomy, adipose tissue and lymph nodes were performed.
Results: The cat surface of the tumour was white, lobulated, with cystic change. Histologically, the architecture revealed insular, trabecular and solid or cribriform nets morphologies. The cytonuclear atypical and mitotic figures were moderate. The massive tumour invaded into the serous and muscles of the stomach without invasion of the spleen. Perineural and vascular invasion were noted. In addition 02/16 lymph nodes were positive for metastasis. Tumours cells positively stained for chromogranin A and synaptophysin. Positivity of the ki67 was less than 20 %.
Conclusion: Pancreatic NETs are rare tumours that, depending on subtype and histologic features, vary in clinical aggressiveness. The most important prognostic factor is whether or not the tumour can be removed surgically. Other significant prognostic for patients with an islet cell tumour / pancreatic endocrine neoplasm include the size of the tumour, the presence or absence of blood vessel invasion, the presence or absence of metastases to lymph nodes or other organs.

PS-02-011

Phosphohistone-H3 antibody in oncocytic adrenocortical adenoma: A case report

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Objective: Most common primary adrenocortical neoplasms are adenomas (ACA), tumours with perfect prognosis. Adrenocortical carcinomas (ACC) are rare (0,5–2 per million annually) and carry poor 5-years survival rate of 38–46 %. Therefore, distinction between ACA and ACC is of utmost importance.
Method: We present the case of a 40-year-old woman with incidentally found 3.5 cm in diameter, purely oncocytic adrenocortical tumour (OACT) presenting extremely bizarre, pleomorphic cells and nuclei. No necrosis, vascular nor capsular invasion was found. Unfortunately, mitotic count in such tumours can be very difficult as some degenerating/bizarre nuclei can resemble atypical mitoses. According to Lin-Weiss-Bisceglia system even one atypical mitosis results in diagnosis of oncocytic ACC. Ki67 proliferative index was scored 6–7 % in hotspots, high for ACA. Reticulin stain showed reticulin network disruption that can occur in both ACA and ACC. Finally, phosphohistone-H3 antibody was used and a few, typical mitoses were stained.
Results: Oncocytic ACA was diagnosed. In the commentary close follow-up based on high Ki67 proliferative index was advised.
Conclusion: We suggest using phosphohistone-H3 antibody to differentiate degenerating/bizarre nuclei from atypical mitoses in OACT.

PS-02-012

Carney complex: Report of a case

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Objective: We report a case of a 53 year old man with multiple vertebrae fractures and osteoporosis under medical treatment with denosumab for the past 4 years. He had a previous history of relapsing cardiac myxomas and large bowel adenomas. Spotty pigmentation of lower limbs and nevi of thorax was found in physical examination. Dexamethasone suppression test showed ACTH independent Cushing syndrome and CT revealed nodular lesions in both adrenals, multiple nodules in the thyroid gland and diffuse testicular calcification.
Method: We received left and right adrenal glands, within a 3 month interval, weighing 23 and 16,5 gr respectively. Confluent micronodular brown lesions were observed in cut sections.
Results: Microscopically we observed nodules of large eosinophilic cells with brown pigment, nuclear pleomorphism with focally giant nuclei and low mitotic activity, features compatible with primary pigmented nodular adrenal disease. Myxomatous areas in the adrenal cortex and adjacent fat were also found. Molecular genetic test revealed a point mutation in the PRKAR1A gene.
Conclusion: Carney complex is a rare autosomal dominant syndrome and careful screening of the first degree members should be conducted and short and long term follow up controls are important since the syndrome has malignant potential and occasional ominous prognosis.

PS-02-014

Epstein-Barr virus reactivation stimulates the expression of activation-induced cytidine deaminase in PBMCs from Graves' disease patients and healthy controls

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Objective: Graves' disease is an autoimmune hyperthyroidism caused by excessive thyrotropin receptor antibody (TRAb). Epstein-Barr virus (EBV) persists mainly in human B lymphocytes. We have reported that TRAb predisposed EBV infected cells (TRAb(+)EBV(+) cells) can produce TRAb in response to EBV reactivation. TRAb is recognized to be IgG class antibody; thus, class-switch recombination through activation-induced cytidine deaminase (AID) is required to produce TRAb. In this study, we examined the expressions of AID mRNA and protein in EBV reactivated cells.
Method: We separated peripheral blood mononuclear cells (PBMCs) of 9 Graves' disease patients and 9 healthy controls. We used these PBMCs and short-term cultured PBMCs as samples. The cultured PBMCs were then transferred to 33°C to reactivate persistent EBV as previously. We confirmed the subpopulation of sample cells by flow-cytometry. The expression of AID was examined by real-time PCR and immuno-histochemistry.
Conclusion: Flow-cytometric analysis revealed that B cell population enriched by short-term culture, and EBV reactivation was accompanied by increase of plasma cell frequency. We detected the increased mRNA and protein expressions of AID by EBV reactivation induction, which suggested that TRAb production from TRAb(+)EBV(+) cells in response to EBV reactivation is related to class-switch recombination by AID.

PS-02-015

Paraganglioma of appendix: Description of two rare cases with histological and immunohistochemical related differences, the former within a benign profile and the latter within a potentially malignant profile in a lymphnode metastatic case

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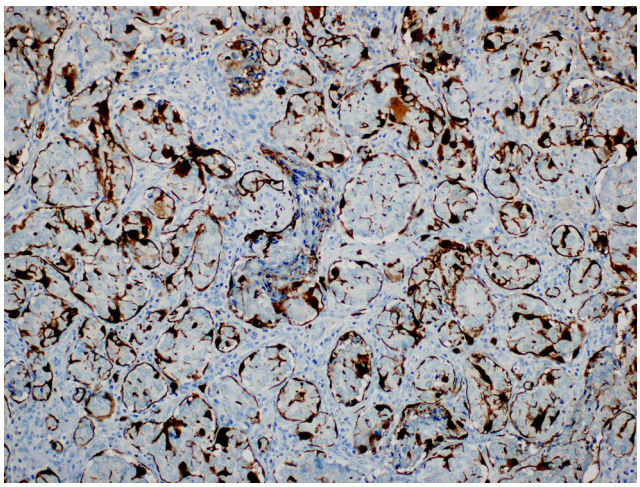
Objective: Paragangliomas (PGLs), either sympathetic or parasympathetic, are rare neuroendocrine tumours derived from neural crest cells. Sympathetic PGLs, mostly abdominal, produce catecholamine excess.
Method: We researched differences, in histology and immunohistochemistry (IHC), in tumour progression, based on lymphnode metastases, in 2, not functional, appendix PGLs. One was discovered during screening colonoscopy for colon cancer family history. The other was an "incidentaloma" in acute appendicitis. The former was larger, more locally extensive, metastasized in a local lymphnode.
Results: In both cases histology showed nests of polygonal granular cells, mixed with anastomoting or trabecular pattern. In the lymphnode metastatic case nested/trabecular pattern was less evident, with prevalence of solid/diffuse growth; sustentacular cells and hyaline globules were reduced or disappeared. IHC confirmed positivity of chromogranin, synaptophysin, CD56, focally CKAE1/AE3,CK7,CK20 of chief cells, and S100 in sustentacular cells. Differences in IHC expression were in CK focal positivity, S100 reduction/absence, and slight increase of Ki67 noted in nodal metastatic case.
Conclusion: No histological or immunohistochemical feature was alone able to identify metastatic potential. Data suggested that a multifactorial scoring system can help in discriminating tumours with a greater risk of metastasis. Because PGLs often metastasize late, use of criteria requires a long term follow-up and confirmation in larger series.

Tipical S100 positivity of sustentacular cell network (IHC LSAB 200x ori. ingr.):



PS-02-016
Abnormalities of thyroid C-cells in patients with PTEN-hamartoma tumour syndrome

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Objective: PTEN-hamartoma tumour syndrome (PHTS) is an autosomal dominant disorder caused by germline inactivating mutations of the PTEN tumour suppressor gene, including Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba (BRRS), and Proteus-like syndromes. Medullary thyroid carcinoma is not part of PHTS; a few studies however, have identified C-cell hyperplasia (CCH) in this syndrome. We report C-cell abnormalities in PHTS patients.
Method: We revised the H&E and calcitonin stained slides from 67 paraffin blocks (3 total thyroidectomy and 1 left lobectomy) of 4 PHTS patients.
Results: The PHTS patients, 3 female (CS) and 1 male (BRRS), had a mean age of 28 at thyroidectomy (25–34) for CS and 12 for BRRS. Germline PTEN mutations were at exons: 8, 2, 5 and 7 respectively. Thyroid findings were: microadenomas in all (100 %) patients, lymphocytic thyroiditis in 3 (75 %), follicular adenoma in 3 (75 %), papillary carcinoma in 2 (50 %), follicular carcinoma (FC) in another (25 %), parathyroid gland within thyroid in 1 (25 %), and adipose tissue another (25 %). CCH (cluster of ≥50 C-cells in a X100 field) was found in 3 cases (75 %), with multiple C-cell clusters of a lower proportion identified in all patients.
Conclusion: CCH of the thyroid should be included as a feature of PHTS.

PS-02-017
Hobnail/micropapillary variant of papillary thyroid carcinoma: Evidence of progression to undifferentiated carcinoma with molecular analysis

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Objective: We describe the hobnail/micropapillary variant (HMPV) of papillary thyroid carcinoma (PTC), a rare but very aggressive variant of PTC.
Method: Pathological and molecular study of 2 cases of HMPV of PTC.
Results: In case 1 (62-year-old man [pT3,pN1,M0]) and case 2 (53-year-old woman [pT3,pN1,M0]), both primary tumours showed a hobnail/micropapillary pattern in ≥20 % of neoplasm, tall/columnar cell areas, and positivity for TTF-1, TTF-2, thyroglobulin (TG), cyclin D1 and p53. Ki67 indexes: 4.6 and 5 %. Case 1 showed positivity for BRAFV600E and TERT C228T promoter mutations but negativity for NRAS, HRAS, KRAS, RET/PTC1, RET/PTC3 and PAX8/PPARgamma. After 11 years the patient died with cervical lymph node, bone and liver metastases. In liver metastasis, columnar cell PTC (positive for TTF-1, TG and BRAFV600E) merged with undifferentiated (UC) (positive for TTF-1 and BRAFV600E, negative for TG). Case 2 died after 6 years with local recurrence and disseminated metastases (lung, pleura, bone and liver). Recurrence showed an UC (positive for cyclin D1 and p53, negative for TTF-1 and TG) component with residual HMPV of PTC (positive for cyclin D1, p53, TTF-1 and TG). BRAF, TERT, NRAS, HRAS and KRAS were wild type (primary tumour/recurrence components).
Conclusion: Hobnail/micropapillary features in PTC evidence progression to UC with fatal outcome.

PS-02-018
The impact of age and diabetes on the rat isolated ileum contractile response to Metformin

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Objective: Metformin is recommended as first-line oral therapy for type 2 Diabetes Mellitus (T2DM). Diarrhea is an adverse gastrointestinal effect associated to metformin (non-diabetic diarrhea) but is also known as part of the symptomatology of the disease (diabetic diarrhea).
Method: The metformin-induced intestinal contraction in male Wistar control rats and in male Goto- Kakizaki (GK) ones, a non-obese T2DM animal model, was evaluated at two different ages: 3 and 12 months old. Ileum segments were isolated for functional studies and TNF-α quantification by ELISA and ileum histological section obtained for S100β protein immunostaining, an enteroglial inflammation marker.
Results: An increase in metformin efficacy was observed in 1-year-old GK rats, in comparison with control ones, underlying the so-called diabetic diarrhea. However there was a loss of 5-HT2 receptors contribution to metformin-induced intestinal contraction, with both age and disease.

Additionally high levels of TNF-α were observed in the aged Wistar rats' ileum, corroborating the pro-inflammatory state associated to aging. Finally, the S100β protein immunostaining was higher in GK animals at both ages, suggesting that a diarrhea with inflammatory characteristics might be present in diabetic animals.
Conclusion: In conclusion, diabetic diarrhea might happen by other mechanisms than those involving mediation by 5-HT2 receptors, namely inflammation associated to aging or Diabetes itself.

PS-02-019
Correlation between immunohistochemistry using anti-BRAF V600E (VE1) antibody, and BRAF V600E mutation by RT-PCR with COBAS 4800 in Papillary Thyroid Carcinoma (PTC): A study of twenty-six cases
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Objective: To study the correlationship and concordance between immunochemistry by the anti-BRAF V600E (VE1) antibody and mutation test of BRAF V600E by RT-PCR with COBAS 4800 (Roche) in 26 archival cases of papillary thyroid carcinoma.
Method: Archival formalin fixed, paraffin embedded tissues from 26 surgical cases of PTC of our institution were evaluated by BRAF V600E by immunohistochemistry with VE1 antibody (Roche) and also by RT-PCR with COBAS 4800 method (Roche).
Results: Four cases (16 %) were positive by both method, immunochemistry and molecular, with 100 % of concordance. The positive cases were in patients with worse oncologic stage, with extrathyroideal extension and presented a higher rate of loco-regional lymphoid involvement. The no mutated and negative for immunochemistry cases were organ-confined lesions at the time of diagnosis and have no lymphoid involvement.
Conclusion: There is high concordance (100 % in our serie) between RT-PCR with COBAS 4800 method (Roche) and immunochemistry by anti-BRAF V600E(VE1) antibody in PTC and the positive cases have a more aggressive clinical behavior. This result confirms that BRAF immunochemistry using anti-BRAF V600E(VE1) antibody can be used as surrogate marker of BRAF V600E mutation in PTC.

PS-02-021
Adrenocortical carcinoma: Clinicopathological and immunohistochemical study of 8 cases
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Objective: Adrenocortical carcinoma (ACC) is a rare and aggressive tumour. We report clinicopathological features and immunohistochemical evaluation of Ki67, p53, β-catenin, E-Cadherin, HER2, estrogen (ER), progesterone (PR) and androgen (AR) receptors.
Method: Medical records, pathological and immunohistochemical studies of eight cases of ACC.
Results: Eight patients (3 males and 5 females), mean age 48.4 years (34-71). The tumours were in TNM Stage II- 1 case, alive and well (A&W) at 90 months; Stage III- 6 cases, two dead of disease (DOD), two alive with disease (AWD) and two A&W; Stage IV- 1 case, DOD at 3 months. Mean follow-up was 32.1 months (3–102). Nuclear staining of β-catenin was observed in three cases (37,5 %): two DOD (3 and 15 months) and one with local recurrence at 7 months, AWD at 12 months. PR expression was observed in all cases. Nuclear p53 staining was positive in 5 cases. Mean Ki67 expression was 30 % (5–60 %). No E-Cadherin, HER2, ER or AR expression was noticed.
Conclusion: ACC is often diagnosed in an advanced stage. Ki67 and p53 were not associated with relapse or metastasis in our series. Nuclear β-catenin expression was observed in cases with worse outcome and appears to be an important prognostic factor.

PS-02-022
Primary osteosarcoma of the thyroid gland
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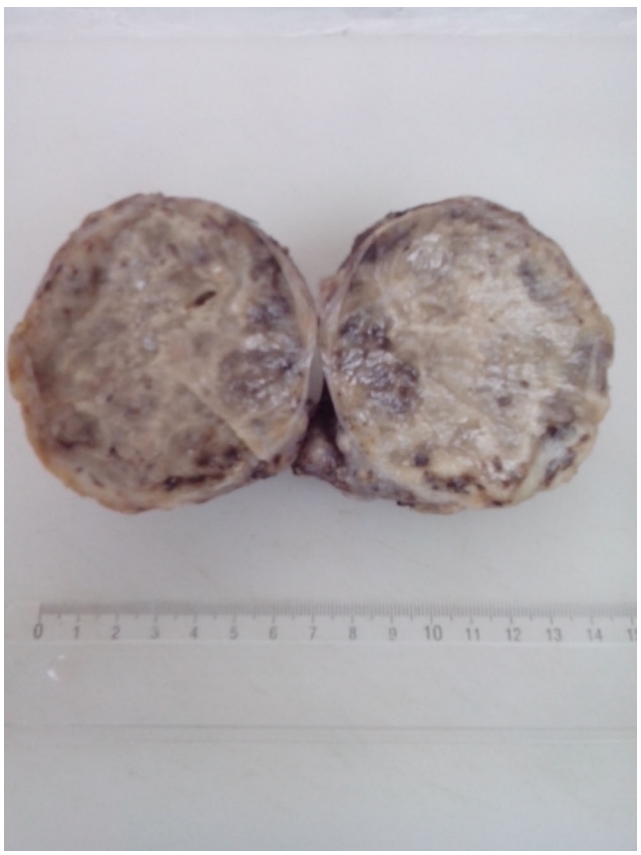
Objective: Primary mesenchymal tumours of the thyroid gland are extremely rare. One percent of the thyroid tumours are reported to be sarcomas, and the infrequency of these lesions is a reason for the difficulties in achieving right diagnosis.
Method: We report a case of primary thyroid osteosarcoma (PTO) in 54-years old female who underwent surgery of the thyroid left lobe, with an unexpected final diagnosis, focusing on the histopathological and immunohistochemical features, which helped in differential diagnosis.
Results: The surgical specimen was a thyroid lobe measuring 10 × 9 × 8, 5 cm. The cut surface showed gritty, grayish-white tumour with areas of hemorrhage which almost entirely infiltrate the left lobe, measuring 9 cm. The microscopic examination showed a high-grade malignant neoplasm with necrotic areas composed of polygonal and fusiform cells, numerous osteoclast-like giant cells and focal osteoid deposition. Immunohistochemical staining showed positive expression for vimentin and osteopontin, and negative immunostaing for cytokeratin 19, epithelial membrane antigen, thyroid transcription factor-1, calcitonin and thyroglobulin, with a high mitotic index (60 %) of the tumour cell nuclei, determinate by Ki-67 antibody. Thus, the diagnosis of PTO of a predominantly teleangiectatic variant was established, that was confirmed with additional CD34 immunohistochemistry.
Conclusion: PTO is extremely rare tumour that should be considered in thyroid pathology and immunohistochemistry is of decisive significance.

Primary osteosarcoma of the thyroid gland:



PS-02-023

Anaplasic thyroid carcinoma: Clinopathological study of 17 Tunisian cases

F. Tekari*, O. Adouni, O. Elamine, A. Goucha, S. Miladi, I. Bettaeib, S. Gritli, S. Touati, A. Gamoudi, A. El-May
*Salah Azaiz, Dept. of Pathology, Tunis, Tunisia

Objective: The aim of this study was to identify histopathology and clinical features of ATC and their relevance to prognosis.
Method: This retrospective study concerned data of 17 cases of ATC collected from 2000 to 2014 at Immuno-Histo-Cytology department of Salah Azaiz Institute of cancer in Tunisia.
Results: Mean patient age at diagnosis was 69 years and there were 7 men and 10 women. The signs of local compression were present in 7 cases. Cervical ultrasonography was performed for all patients. All the cases had intrathyroidal tumours. Ten patients presented lymph node metastasis. Of the 17 patients, 7 cases had distant metastases. The lung and the liver were the most site of distant metastasis. The mean tumour diameter was 7,9 cm. All tumours immunophenotype were Cytokeratine(+), Vimentin (+), ACE(+) and Tyroglobuline (-). 70,6 % of the tumours overexpressed P53 and median Ki67 proliferation index was 76,5 %. All the patients received surgical treatment, 10 received surgery alone, 5 received radiation treatment with surgery, and 2 received surgery plus radiation treatment and chemotherapy. At a median follow-up of 10 months, 14 patients died.
Conclusion: Despite technical advances in surgical technique, ATC still associated with dismal prognosis and remains a deadly disease.

PS-02-024

Microvascular density as assay for evaluation of thyroid Hürthle cell tumours

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Objective: The aim of this study was to investigate expression of Cytokeratin 19 (CK19), CD56, HBME-1, Galectin-3 (Gal-3) and to determine microvascular density (MVD) in benign and malignant Hürthle cell tumours (HCTs).
Method: We reviewed 30 cases of HCTs (20 carcinomas, 10 adenomas). Tissue microarray was constructed, containing minimum two tissue cores of each tumour, taken from the area right beneath the capsule. Immunostaining was considered positive if more than 10 % of tumour cells were positive irrespective of staining intensity, for CK19, HBME-1, Gal-3. Conversely, CD56 expression in less than 10 % of tumour cells was considered positive. Blood vessels were marked using CD31, pan-endothelial marker and counted applying modified Weidner method.
Results: Concerning expression of CK19, HBME-1, Gal-3, CD56 in HCTs no significant difference between adenomas and carcinomas was found ($p = 0.894$; $p = 0.176$; $p = 0.065$; $p = 0.450$ respectively). MVD was expressed as number of vessels per square millimeter, and it was higher in carcinomas (median = 215 /mm2) compared to adenomas (136/ mm2; $p = 0.028$). ROC analysis was performed. In case the number of blood vessels is equal or higher than 187/mm2, sensitivity is 75 % and specificity is 70 % for carcinoma.
Conclusion: MVD can serve as ancillary tool in diagnosis of HCTs, especially in those cases where capsular or vascular invasion is questionable.

PS-02-025

Angiosarcoma of the thyroid gland: Report of a rare case, with unusual histologic features

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Objective: Primary angiosarcoma of the thyroid gland is a rare and aggressive tumour. Herein, we present a case of a 78-year-old woman who presented with dyspnea and on imaging was found to have a large solitary thyroid mass.
Method: Intraoperative frozen section was performed indicating a high grade neoplasm. Total thyroidectomy followed.
Results: We received the thyroid gland weighing 148 gr. Upon gross examination a circumscribed, hemorrhagic tumour with maximal diameter of 6,9 cm, was noted at the right lobe. At the left lobe three colloid nodules were found. Microscopic examination revealed a high grade invasive neoplasm with extended necrosis. Cleft-like anastomosing spaces were recognized lined by epithelioid neoplastic cells, with large nuclei and prominent nucleoli. There were also multinucleated giant neoplastic cells. Immunohistochemistry showed positivity for CD31 and CD34 and negativity for pancytokeratin, EMA and TTF-1. The rest of the thyroid gland showed nodular hyperplasia. Based on the above, the diagnosis of high grade primary thyroid angiosarcoma was made.
Conclusion: Primary thyroid angiosarcoma is a rare neoplasm, being more frequent in mountainous areas, such as the region of Epirus where the present patient lives. Multinucleated neoplastic giant cells although very rare feature in angiosarcomas, were several in this case.

PS-02-027

BRAF V600E mutation status in anaplastic thyroid carcinoma

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Objective: A number of studies have shown that BRAF V600E mutant-specific antibody VE1 can identify BRAF V600E mutation in a spectrum of cancers. This study focuses on the utility of this antibody for BRAF V600E screening in anaplastic thyroid carcinomas (ATCs).
Method: 53 ATCs were studied using both BRAF pyrosequencing and VE1 antibody. When the tumour contained a differentiated element, each component was separately tested. The intensity of staining was graded from 0 (negative) to 3+ (strong).
Results: 15 of the 53 tumours were associated with differentiated carcinoma; 6 poorly differentiated carcinomas and 9 papillary carcinomas (PTCs). BRAF V600E was identified in 7 ATCs (13.2 %), 4 of which were associated with tall cell variant (TC) PTC. The TC component also showed BRAF V600E. All 7 ATCs and 4 TC PTC components were moderately to strongly positive for VE1. Additionally, seven and two ATCs showed 1+ and 2+ reaction, respectively, corresponding to wild type BRAF.
Conclusion: VE1 immunohistochemistry is a useful method for detecting BRAF when moderate to strong reaction is regarded as positive. In BRAF V600E mutated tumours, both ATC and PTC component were equally mutated, confirming the view that some of the ATCs are transformed from differentiated thyroid tumours.

PS-02-028

Pituitary adenoma and primary pigmented adrenal hyperplasia in the setting of Carney complex: Case report

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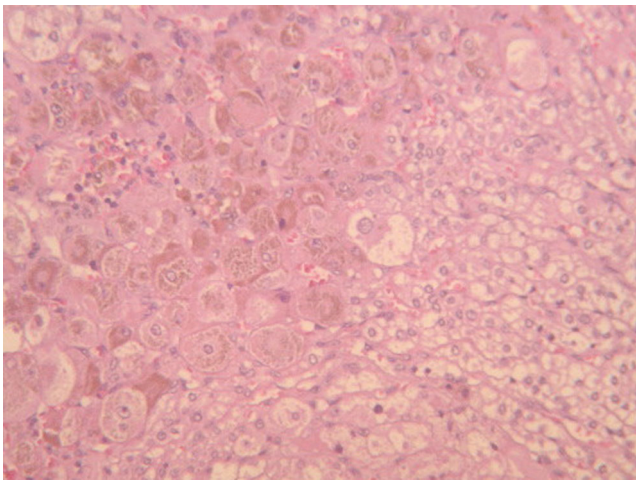
Objective: The aim of this report is to present a rare case of Carney's syndrome occuring in a 31 year-old caucasian male clinically characterized by Cushing`s disease. Thorough investigation of the patient revealed two mass lesions in the pituitary gland and adrenal gland.
Method: The tissue sections obtained from the pituitary and adrenal gland tumours were routinely processed and paraffin embedded. Thin sections were stained with hematoxillin and eosin and were analyzed using light microscope.

Results: The first operation was a transnasal microadenectomy and the pathology results showed the presence of basophilic pituitary adenoma. The second operation was adrenalectomy and the pathology results showed the presence of a unique morphologically distinct form of adrenal hyperplasia called primary pigmented nodular adrenal cortical hyperplasia.
Conclusion: Pituitary adenomas occuring in conjunction with adrenal gland hyperplasia are a rare findings that should prompt a search for other characteristic signs of Carney's complex. Careful evaluation of these rare patients should be performed, in order to prevent more serious complications in other involved organs.

Primary pigmented nodular adrenal cortical hyperplasia:



PS-02-029
E-cadherin and KI67 expressions in thyroid papillary microcarcinomas and their relationship between clinicopathologic parameters
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Objective: Thyroid papillary carcinomas are named as papillary mirocarcinomas (PMC) when the greatest dimension is under or equal to 1 cm. It has a favorable prognosis but some factors affect the prognosis adversely. In this study, we aimed to evaluate the relationship between KI67 and E-cadherin expressions in PMCs with some clinicopathological features such as age, gender, tumour subtype, dimension, precence of sclerosis and capsular invasion.
Method: A retrospective analysis of 102 patients with PMCs in Izmir Tepecik Education and Research Hospital was performed. E-cadherin and KI67 expressions were evaluated immunohistochemically.
Results: We observed capsular invasion in 26 (25.5 %) patients. The mean nuclear expression rate of KI67 was 2.56 % while cytoplasmic or membranous expressions of E-cadherin was 82.7 %. There were no significant correlations between with capsular invasion and E-cadherin (p = 0,431) or KI67 (p = 0,100) expressions. Contrary, there were significant correlations between capsular invasion and tumour dimension (p = 0,018), as well as capsular invasion and age of patients (p = 0,047).
Conclusion: In the present study, it was shown that both E-cadherin and KI67 expressions were not correlated with other prognostic factors of PMCs. In addition, we demonstrated that the most important prognostic factor of PMCs was still the precence of capsular invasion.

PS-02-030
A case report of very rare synchronous multicentric papillary and medullary carcinoma of thyroid gland
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Objective: To present interesting and rare case of synchronous multicentric papillary (PTC) and medullary carcinoma (MTC) of thyroid gland.
Method: A 70-year-old female with a 2-years history of multinodular goiter came to medical examination for progressive enlargement of thyroid nodules with compressive symptoms. Ultrasound examination found several nodules in both lobes, the largest was 35 mm in right lobe. FNAC was performed and the cytological finding was "suspicious for malignancy". TSH level in serum was increased, in contrary to T3 and T4. Concentration of calcium was normal, but CEA was twice above the limit.
Results: Patient underwent total thyroidectomy. Surgical specimens consisted of right and left lobe measuring 6 × 4.5 × 3 cm and 4.5 × 3.5 × 2 cm respectively. The cut surface was multinodular, showing cystic degeneration with papillary proliferations in right lobe. Histology revealed several unencapsulated foci of PTC with tipically nuclear feauters (12 and 2 mm in right; 12 and 5 mm in left) with invasion in surrounding soft tissue. In the right lobe was detected focus of MTC (8 mm), also without capsule, which showed positivity for chromogranin, synaptophysin and calcitonin immunostaining, but not for TTF1. Ki-67 proliferative index was 2 %.
Conclusion: Synchronous multicentric PTC and MTC is very uncommon entity and in literature is described only 20 cases.

PS-02-031
Ductal metaplasia in chronic lymphocytic thyroiditis - still a putative pitfall to be avoided: Case report
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*Universidade de Coimbra, Inst. de Anatomia Patologica, Portugal

Objective: Ductal metaplasia is a well known exocrine gland adaptation to continuous inflammatory stimulation, and, being not commom, morphology, immunophenotype and molecular alterations are well established, allowing the correct diagnosis.
Method: A 51 years old man had been diagnosed with hypothyroidism with clinically expressed auto-immune antibodies. Follow-up cythology demonstrated suspected nuclei for papillary carcinoma (PTC) on an ecographic multinodular thyroid.
Results: Total thyroidectomy was performed and several sections were observed after paraffin inclusion. Nodular pattern was observed with lymphoplasmocytic cells infiltration surrounding empty ductal structures of PTC- like cells. The diagnosis was sustained also by imunohistochemistry allowing PTC differential diagnosis.
Conclusion: Hashimoto nodular chronic lymphocytic thyroiditis was reported together with extended ductal metaplasia. This philogenetic adaptation has been recognized in thyroid and more cases are expected to be reported, after its recognition in others exocrine glands. The authors thank Prof M. Sobrinho-Simões for his diagnosis advise.

PS-02-032
Medullary microcarcinoma of thyroid in a children with MEN 2A: A case report
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*Tepecik Education Hospital, Dept. of Pathology, Izmir, Turkey

Objective: Medullary thyroid cancers (MTC) are rare tumours of neuroendocrin origin that arise from parafollicular C cells. MTC

represents 4–5 % of all thyroid cancers. MTC can be either sporadic, usually isolated to one thyroid lobe, or familial, the latter of which is defined as the cancer syndrome known as Multipl Endocrine Neoplasia type 2 (MEN 2). MEN 2 is result of the autosomally dominant missense gain of functin mutation in the RET proto - oncogen. Medullary thyroid carcinoma is the most common cause of death in MEN patient.
Method: We report a case of a boy with MEN 2 A whose operative specimen at prophlactic thyroidectomy showed medullary microcarcioma and C-cell hyperplasia.
Results: Medullary thyroid carcinoma occurs at a very young age in carriers ofgermline RET mutation. In patients with high - risk mutations prophilactic throidectomy is likely to be recommended.

PS-02-033
Cribiform-morular Variant of Papillary Thyroid Carcinoma (CMV-PTC): Report of a case with an aggressive clinical behavior
R. Oliveira*, A. Catarino, E. Mendonça, M. Olímpia Cid
*Hospital Prof. Doutor Fernando, Lisboa, Portugal

Objective: We present a case of CMV-PTC with a particularly aggressive clinical behavior, with extra-thyroidal extension and tracheal invasion.
Method: A 30-year old male presented with mulitnodular goiter. Ultrasound revealed an asymmetric thyroid, with a large hypo echogenic nodule in the right lobe, diagnosed as PTC with a fine needle aspiration biopsy. Total thyroidectomy was performed. During surgery it was observed that the tumour was adherent to the peri-thyroidal tissues and invaded the tracheal wall. Grossly, the right lobe was replaced by a firm, solid, gray-yellowish mass.
Results: The tumour had a heterogeneous morphological pattern with solid, cribriform and morular areas, interposed by fibrotic septa and sparse colloid; it was noticed some nuclear clearing. Beta-catenin was positive, with a strong nuclear/cytoplasmic expression. In light of this diagnostic entity, the investigation proceeded. A colonoscopy was performed, it revealed multiple colonic polyps.
Conclusion: CMV-PTC it's a rare neoplasm which is imperative to recognize because it will alert the clinician to investigate for familial adenomatous polyposis. In this case it was exceptionally important to distinguish it from other aggressive PTC variants, considering its extraglandular extension and lymphovascular invasion, in a manner that these features are more frequently associated with other aggressive variants of PTC.

PS-02-034
"PARTIAL" DeGeorge Syndroma: Autopsy case
V. Katic*, M. Mojsilovic, N. Jancic, M. Nedic, S. Jancic, D. Stojkovic
*Poliklinika Human Nis, Dept. of Pathology, Serbia

Objective: DeGeorgi Syndrome (DGS) is a birth defect that is marked by absence or underdevelopment of the thymus ans parathyroid glands. The child is born with a defective immune system and an abnormal low level of calcium (hypocalcemia) and parathormone in the blood. Having in the mind that "partial" DGS is discovered in autopsy, that the prevalence ranges from 1: 4000 to 1: 6395 and that clinical symptoms were induced by hypofunction of both parathyroid glands and thymus, we are reporting it.
Method: Autopsy.
Results: Female (small height), dead at 22 years of age in cerebral coma. Clinical symptoms were polymorphous and complex: recurrent viral and fungal infections, amenorrhea, parestesias, acches and cramps affecting legs, feet, abdomen and face, as well as the headaches and depression. The clinical diagnosis was idiopathic epylepsy. Two months before her death, both ionized serun calcium concentration (1.1 mg / dL) and the parathormone (9 pg / mL) were decreased. She was in a coma for 1 week and has died from muscular tetany. Autopsy finding: fibrosis of the parathyroid gland and thymus remnants, diffuse brain liquefactive necrosis, myocardial and ovarian fibrosis were found.
Conclusion: The authors have suggested out that the increased neuromuscular excitability is related to the decreased serum ionized calcium and that the recidivant viral and fungal infections were induced by the decreased thymus gland function, in other words by "Partial" DeGeorge syndrome.

PS-02-035
Comparative assessement of hormone immunoprofile between pituitary adenomas coming from Romania and Republic of Moldova
A. M. Cimpean*, E. Melnic, B. Balinisteanu, M. Coculescu, M. Raica, E. Foca
*'Victor Babes' University of Medicine, Timisoara, Romania

Objective: To compare the immunoprofile of pituitary adenomas from Romania and Moldova and to highlight similarities and differences regarding hormone profile between two regions.
Method: Group 1 included 94 cases coming from Romania and group 2 was composed of 86 cases collected from Republic of Moldova. Specimens were assessed by immunhistochemistry regarding all six hormones expressed in pituitary adenomas. An accurate statistic analysis has been performed.
Results: For group 1, 70 % of cases showed positivity for one hormone, 13 % were plurihormonal, while 17 % were negative. For group 2, 50,3 % of the cases expressed only one hormone and 12,5 % were negative for all hormones. The highest difference was observed for plurihormonal adenomas, found in about 37,2 % of cases for group 2 (2.86 times higher for

group 2 compared with group 1). GH-secreting adenomas characterized group "1", while group "2" had the highest percent of LH secreting adenomas, 55 % of cases being positive. Triple association was noticed in 4.25 % of cases of group 1 and in 8,13 % out of total cases, from group 2. Four hormones association was found in 15,56 % of the cases, exclusively for group 2.
Conclusion: We highlighted strong evidences of a particular and different immunoprofile of pituitary adenomas coming from Romania and Moldova.

Sunday, 6 September 2015, 09.30–10.30, Restaurant
PS-03 Poster Session Head and Neck Pathology

PS-03-002
Correlations between actin-binding protein expressions and clinico-pathologic variables in ameloblastoma
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*University of Malaya, Oro-Maxillofac Surgery and Medical Sciences, Kuala Lumpur, Malaysia

Objective: Actin cytoskeleton dynamics are critically implicated in cancer invasion and metastases. Actin-binding proteins cortactin, NWASP and WIP regulate actin assembly and reorganization during cell migration and invasion into the extracellular matrices. Altered expressions of these proteins have been implicated in human malignancies. This study addresses their role in ameloblastoma of the jaws.
Method: 87 paraffin-embedded ameloblastoma cases (20 unicystic, 47 solid/multicystic, 3 desmoplastic and 17 recurrent) were subjected to immunohistochemistry for expression of cortactin, NWASP and WIP.
Results: Cortactin (n = 73/87; 83.9 %), NWASP (n = 59/87; 67.8 %) and WIP (n = 77/87; 88.5 %) were heterogeneously expressed in ameloblastoma. Cortactin which functions as a scaffold for actin, demonstrated significantly higher expression levels in ameloblastomas from male patients. NWASP which mediates actin polymerization, was significantly elevated in the solid/multicystic subtype ($p < 0.05$). Age, ethnic and site showed no significant correlations.
Conclusion: Overexpression of cortactin and NWASP may be implicated in ameloblastoma tumourigenesis. Their enhanced expressions seem to favor ameloblastoma subtypes with a more aggressive clinical behavior.

PS-03-003
Intraparotid facial nerve schwannoma
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Objective: Intraparotid Facial nerve Schwannomas (FNS) are benign tumours that originate from Schwann cells, with a slow and predictable growth. FNS arise from either the extratemporal or intratemporal course of this nerve. Most of these tumours are intratemporal, whereas 9 % are located extracranially and usually appear as an asymptomatic parotid mass. Hence, it is difficult to establish a correct preopera-tive diagnosis. Although most patients do not present with facial nerve palsy, it is important to suggest this diagnosis preoperatively because post-operative facial nerve paresis or palsy is common, and these patients can be better informed of this complication before surgery.
Method: A 29-year-old woman, presented with gradually increasing mass in the parotid right region for several months of evolution. MR imaging showed a well-circumscribed lesion (2.0 × 1.5 cm.) in the upper right parotid gland. Fine needle aspiration cytology was suggestive of pleomorphic adenoma. The tumour was excised, trying to preserve the integrity of the nerve. The pathological diagnosis of the surgical piece disclosed a benign Schwannoma. The patient had a facial paralysis in the postoperative period.
Results: The tumour was histopathologically diagnosed as intraparotid facial nerve schwannoma (S100+).
Conclusion: - FNS is a very rare, benign tumour mimicking pleomorphic adenoma. Accounting for only 0.2–1.5 % of all parotid tumours. - FNS though rare should be also considered in the differential diagnoses of the slowly enlarging parotid swellings. - It is very difficult to preoperatively diagnose because it rarely produces any signs and symptoms.

PS-03-004
CD117, C-ERBB-2 Ekspression of head and neck and lung Squamous Cell Carcinomas (SCC)
H. Erdem*, H. Balta, B. Mollamehmetoglu
*University of Ordu, Dept. of Pathology, Turkey

Objective: To study the expression of CD117, C-erbB2 and its relationship with cell proliferation in head and neck and lung squamous cell carcinomas.
Method: Expression of CD117 and C-erbB2 were detected with immunohistochemical staining in 32 head and neck squamous cell carcinomas (including skin, tongue, larynx) samples and 6 lung squamous cell carcinomas samples.
Results: Statistically significant positive relationships were found between C-erbB-2 and tumour differentiation ($P < 0,05$). There was a significant correlation between C-erbB-2 and staining pattern ($P < 0,05$). There was a significant correlation between localization and tumour differentiation ($P < 0,05$). There was not a significant correlation between CD117 and C-erbB2 ($P = 0,426$). There was not a significant correlation between CD117 and localization and tumour differentiation (respectively: $P = 0,713$, $P = 0,181$).
Conclusion: C-erbB2 might have trigger effect in the tumour progression of squamous cell carcinomas.

PS-03-005
CD117, C-erbB2 receptors of nasal polyps
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Objective: CD117, C-erbB2 receptors participate in the pathologic process including tissue remodeling of inflammatory diseases in the upper and lower respiratory tracts. This study aimed at investigating the expressions of CD117, C-erbB2 protein in the nasal mucosa of nasal polyps.
Method: This study was conducted on a total of 77 paraffin-embedded nasal polyp samples. The expressions of CD117, C-erbB2 were examined by immunohistochemistry.
Results: Statistically significant positive relationships were found between C-erbB2 and localization ($p = 0,050$). Significant positive relationships were found between staining patern and localization ($p = 0,045$). Significant positive relationships were not find between CD117 and CErbB2 ($p = 0,153$) and localization ($p = 0,078$).
Conclusion: C-erbB2 was showed relationship localization and staining patern. In addition to, it can not relationship between C-erbB2 and CD117 in this study.

PS-03-006
Relationship between Bcl-2 and Ki-67 in chronic sialadenitis
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*University of Ordu, Dept. of Pathology, Turkey

Objective: The bcl-2 suppress apoptosis and programmed cell death in human tissue. This proto-oncogene encodes an inner mitochondria membrane protein.

Method: In this study anti-human bcl-2 antibody and Ki-67 that is reactive in formalin-fixed tissues was used with an avidin-biotin complex immunoperoxidase method to evaluate 18 cases of chronic sialadenitis. It was evaluated acinar, ductal glands and epimyoepithelial islands.
Results: Statistically significant positive relationships were found between Bcl-2 positivity in acinar glands and Ki-67 positivity in ductal glands (P = 0,016). Significant positive relationships were found between Ki-67 positivity in ductal glands and Ki-67 positivity in acinar glands (p = 0,010). Significant positive relationships were found between Bcl-2 positivity in ductal glands and Bcl-2 positivity in epimyoepithelial islands (p = 0,016). Significant positive relationships were found between Bcl-2 positivity in ductal glands and Ki-67positivity in epimyoepithelial islands (p = 0,017).
Conclusion: Bcl-2 positivity and ki-67 index showed positive correlation of acinar, ductal glands and epimyoepithelial islands in this study.

PS-03-007
"Undifferentiated" small round cell tumours of the sinonasal tract. Differential diagnosis update: A case report
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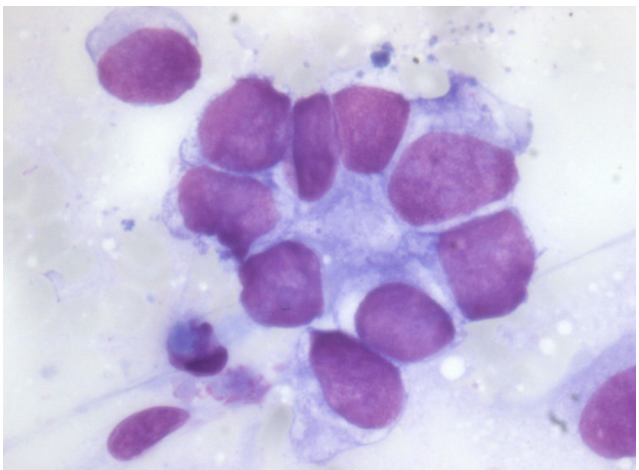
Objective: Olfactory neuroblastoma (OAN) is an extremely rare malignant neoplasm of the nasal cavity, peripherial primitive neuroectodermal tumours (PNET) are also rare in head and neck region. It is a great challenge to differentiate these two entities solely on the basis of pathohistology and cytological characteristics of tumour cells.
Method: We report the case of a 52 years old man who presented with a 27 years history of olfactory neuroblastoma of right nasal cavity with infiltration of the base of the skull, epipharynx, right orbit and frontal sinus. The patient went under radiotherapy. There was no sign of significant regression in 1988. Until 2014 he had no medical treatment, when he was rehospitalized with metastatic tumours in the right lung. We used cytology and immunocytochemistry for further examination.
Results: Tumour cells showed strong positive reaction for CD99 (> 90 % tumour cells). This result changed the diagnosis to PNET.
Conclusion: Besides the interesting fact of the long period of no progression and no dissemination of the primary disease, in this article we focus on the recognition that small blue round cell tumours cannot be differential diagnosed with certainty without immunocytochemistry or immunohistochemistry.

Transthoracic puncture of pulmonary lesion:



PS-03-008
Clinicopathological study of 52 cases of sino-nasal tumours
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Objective: We propose to study the epidemiological, clinical and pathological features of tumours of the nasal and paranasal sinuses.
Method: Our study is a retrospective included 52 cases of sinonasal tumours, collected at the Department of Pathology of the Military Hospital, between 2002 and 2013.
Results: Benign tumours represented 86 % of the cases (represented by inverted papilloma) against 14 % of cancers (represented by N/K lymphoma). The average age of all cases was 46, 5 years with male predominance. The average age of cases carrying sinonasal cancers was 50 years and the average age of patients with benign tumours was 25 years. The consultation period averaged 18 months. Nasal obstruction and rhinorhea were the predominant signs. Thirty four of patients underwent CT scan, which finded an hyperdense lesion in 9 %, an hypodense lesion in 6 % and osteolysis in 9 %. Treatment was curative in 95 % of cases. The mean of our patients was 03 years. We noted a good outcome in 39 patients, reccurences in 08 patients, and abdominal metastasis in a patient. Four patients were died.
Conclusion: Sinonasal tumours are rare and pose many difficulties both in etiology, diagnostic and therapeutic.

PS-03-009
Carcinoma ex pleomorphic adenoma of the parapharyngeal space: A case report
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Objective: Primary parapharyngeal space neoplasms are rare representing only 0.5 % of head and neck tumours. Herein, we report a case of non-invasive carcinoma ex pleomorphic adenoma (Ca-ex-PA) that occurred in the lateral parapharyngeal space.
Method: A 35-year-old man presented with a clinical diagnosis of a benign salivary gland mass located in the region of the right parapharyngeal space measuring 5.5 × 5 cm.
Results: The macroscopic appearance of the resected specimen was solid and completely encapsulated. Histopathological examination revealed a tumour almost completely consisting of a typical pleomorphic adenoma as well as some more cellular areas with duct-like structure and cell-rich mesenchymal tissues. The cellular component was characterized by nuclear atypia and a high mitotic rate. Immunohistochemically these areas were positive for S-100p, anti-p53, AR and HER2neu (3+). Based on these findings, a final diagnosis of adenocarcinoma NOS ex pleomorphic adenoma was made. Additional treatments were not performed because there were no evidences of capsule invasion and metastasis. Patient adapted a "wait-and-see" approach.
Conclusion: Ca-ex-PA of the parapharyngeal space is extremely rare and frequently misdiagnosed. Occasionally, extensive sampling is necessary to find the malignant component and rarely a benign remnant might not be found. HER2neu overexpression is helpful both for the diagnosis and any potential clinical management.

PS-03-010
Myoepithelial carcinoma of salivary gland arising in a pleomorphic adenoma with lung metastasis: A case report
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Objective: Salivary gland neoplasms composed exclusively or predominantly of myoepithelial cells are relatively uncommon. Herein we report a case of a myoepithelial carcinoma arising in a pleomorphic adenoma (PA) with subsequent lung metastasis.
Method: A 47-year-old woman presented with a 6-month history of a painless swelling of the left lateral pharyngeal space. The initial tumour was a PA. Four months later she complained for a chest pain. CT revealed multiple parenchymal lung nodules. Multiple biopsies were performed.
Results: Histological examination showed a malignant biphasic neoplasm composed of spindle cells with clear cytoplasm, a high mitotic rate and an infiltrative growth pattern in a background of a prominently myxoid stroma. Immunophenotypically tumour cells stained positively with anti-cytokeratin antibodies, S-100 protein, a-SMA, p63, Vimentin and anti-p53 (> 50 %).
Conclusion: Myoepithelial carcinoma may occasionally develop in a pre-existing PA but most often arises de novo. The immunophenotype was characteristic: tumour cells were immunoreactive with antibodies of myoepithelial differentiation. However, the combination of nuclear pleomorphism and mitotic activity was considered sufficient to justify the designation of myoepithelial carcinoma. To establish wherever a myoepithelial carcinoma has arisen in a PA may require microscopic examination of the entire tumour in order to demonstrate a small residual focus of pleomorphic adenoma.

PS-03-011
Keratocystic Odontogenic Tumour (KOT): Analysis of clinicopathologic and immunohistochemical findings for prediction of recurrence and election of surgical technique
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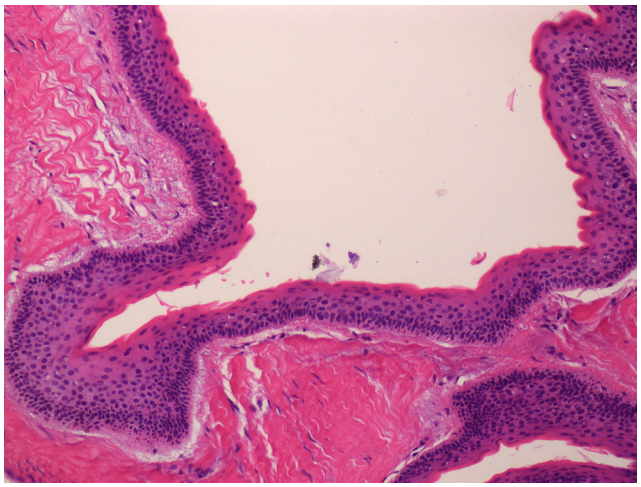
Objective: KOT is a tumour development with defined histoclinical characteristics that distinguishes them from other odontogenic cysts: Destructive behavior, risk of recurrence, association with Gorlin syndrome (GS), possible malignant transformation. There is considerable controversy regarding its management. The Objective is to determine prognostic factors for recurrence after simple enucleation by clinicopathological criteria.
Method: Retrospective study in our hospital during 2000–2003. We analyzed: localization, GS association, structure, cortical perforation, associated tooth, keratinization type, dysplasia, inflammatory component, cysts satellites, enucleation type, Ki67.
Results: Total 17 KOT: 35.3 % of recurrence after enucleation without adjuvant treatment. Mean follow-up period: 77.4 months. Mean time to recurrence: 64.9 months. We detect strong relationship between cortical perforation and the risk of recurrence (66.7 %). Others potential risk factors: associationGS (66.7 %recurrence), multilocular structure (33.3 %recurrence/18.2 %no-recurrence) and the presence of inclusion of the wisdom tooth (33.3 %recurrence/9 %no-recurrence). Factors such as degree of inflammation, cysts satellites, fragmented enucleation and Ki67 dont showed relationship. In no event shall observe dysplasia.
Conclusion: Essential to recognize the KOT histologically. Enucleation alone has demonstrated acceptable results with low morbidity in comparison with other more aggressive techniques. However, in cases with increased risk of recurrence such as multilocular cyst, cortical perforation and association with GS, could be indicated adjuvant therapy or more aggresive treatment.

KOT HE:



PS-03-012
The accuracy of frozen section in the diagnosis of thyroid lesions: About 490 cases
A. Khadhar*, F. Ben Abdallah, I. Msakni, B. Laabidi, R. Doghri, M. Yahia, N. Mansouri, I. Hlal, F. Bougrine, A. Bouziani
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Objective: In thyroid diseases, frozen section diagnosis is challenging but mandatory. The objective of this study was to compare the results of frozen section diagnosis and definitive histologic results and to propose ways to improve the performance of frozen section examination in thyroid lesions.
Method: We undertook a retrospective study in pathology department of the Military Hospital of Tunis including 490 patients undergoing thyroid surgery in a 5-year period (January 2008 to December 2012). We compared their frozen section examinations and the definitive histologic results.
Results: The frozen section diagnosis had a sensitivity of 61,1 % and a specificity of 100 %. The positive predictive value was 100 % while the negative predictive value was 97 %. The concordance was 74,4 %. The disconcordance, which was 25,6 %, was due to 12 false negative cases (2, 44 % of all cases), including 6 micropapillay carcinomas and 6 follicular variants of papillary carcinoma.
Conclusion: Frozen section is appropriate in deciding the extent of thyroidectomy in thyroid neoplasms. To improve its reliability, it is recommended to associate preoperative cytologic examination of samples. In addition, a closer collaboration between surgeons and pathologists is necessary.

PS-03-013
Death of mechanical asphyxia caused by non-neoplastic laryngeal lesion - a case report
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Objective: Mechanical asphyxia is an acute hypoxic state of the human body, developing as a result of mechanical obstruction which prevents respiration in the upper airways, trachea and lungs. We present a case of a 39 old man how died suddenly at home while dressing for work. He was complaining of shortness of breath and sore throat for a couple of months. Consultation with pulmonologist was carried out, which showed that he did not have lung cancer or other lung diseases. Consultations with other specialists were not made.

Method: We performed full forensic examination of the body with collection of anamnestic and criminological data, forensic autopsy, toxicological analysis and histological examination.
Results: During the internal examination of the body at the entrance of the larynx a pedunculated tumour formation was observed. It was obliterating completely the upper air ways. The histological examination revealed the tumour was a laryngeal polyp. The toxicological analysis was negative. Death was attributed to acute obstruction caused by the laryngeal polyp which led to mechanical asphyxia.
Conclusion: Laryngeal polyps rarely present with airway obstruction. This case shows the importance of a complete and thorough analysis of every patient with proper, on time diagnosis in order to avoid such complications.

PS-03-014
Leiomyosarcoma of the nasal cavity
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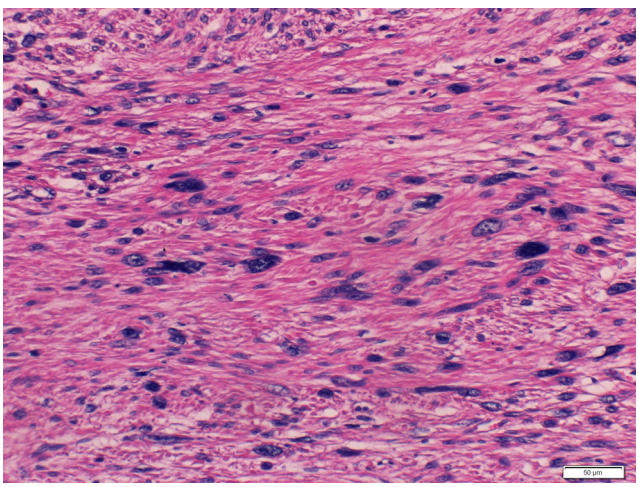
Objective: Leiomyosarcoma is a malignant smooth muscle tumour, which is most commonly found in the gastrointestinal tract, uterus and retroperitoneum. It is uncommon in the upper respiratory tract and even more rare in the nasal cavity. In the sinonasal tract, leiomyosarcoma is considered to be derived from smooth muscle of the vascular wall.
Method: We report a rare case of leiomyosarcoma arising in the nasal cavity.
Results: A 53-year-old woman sought treatment for nasal obstruction and facial pain. An endoscopic examination and computed tomography revealed a mass involving the posterior area of the right nasal cavity. The lesion was completely excised with adequate margins of uninvolved tissue. Macroscopically the surgical specimen consisted of two pieces of pale, gray, solid tissues measuring 35 × 30 × 30 mm. Section of the biopsy specimen stained with hematoxylin and eosin showed interlacing fascicles of highly atypical spindle shaped cells that have eosinophilic cytoplasm and elongated, blunt-ended hyperhromatic nuclei with frequent mitoses. The tumour cells were strongly immunoreactive for smooth muscle actin and h-Caldesmon. There was no immunoreactivity for S-100.
Conclusion: Leiomyosarcoma is an exceptional rare malignant tumour of the nasal cavity with no more than 20 cases reported so far, but the diagnosis is usually straightforward.

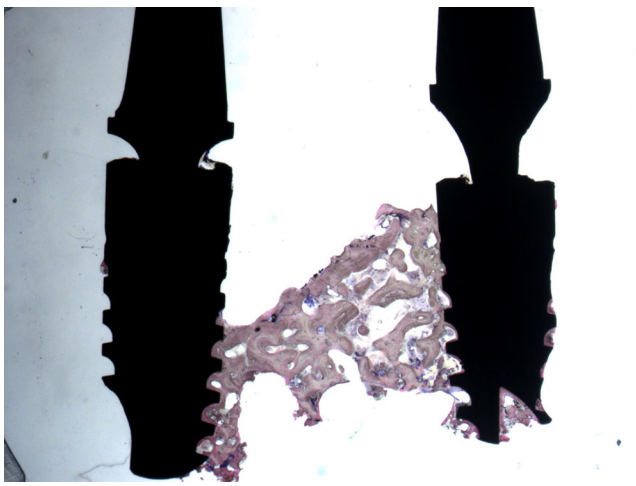
Atypical spindle shaped cells (HE 200x):



PS-03-015
Bisphosphonate-related osteonecrosis of the jaw around osteointegrated dental implants: Macroscopic and microscopic aspects on 12 osteoporotic patients
G. Favia*, A. Tempesta, L. Limongelli, V. Crincoli, A. Piattelli, E. Maiorano
*Policlinico P. Zza G. Cesare, Uoc Malattie Odontostomatologi, Interdisciplinare di Medicina, Bari, Italy

Objective: Peri-implant Bisphosphonate-related osteonecrosis of the jaw (PI-BRONJ) is a severe complication affecting oncologic and osteoporotic patients treated with bisphosphonates. This work highlights the different macroscopic and microsopic aspects of this recent pathological entity.
Method: Twelve osteoporotic patients (9 F, 3 M, average age: 72 years old) who received bisphosphonate came to our attention showing intraoral necrotic bone exposure around dental implants diagnosed as PI-BRONJ of different stages. All the affected sites underwent wide en-block surgical excision comprehending both bone and implants, with subsequent histological analysis.
Results: Macroscopically, we distinguished: “type 1” PI-BRONJ comprehending osteolytic forms with extensive osteolysis and inflammatory cell infiltration around implant fixtures that are also subdivided depending on the partial or total loss of implant osteointegration; “type 2” PI-BRONJ comprehending non-osteolytic forms with alveolar bone necrosis distant from implant fixture which is still well-osteointegrated. Microscopically, the histological examination of the decalcified and undecalcified samples highlighted areas of bone necrosis with large osteons and empty osteocytic lacunae, small and irregular Haversian canals, inflammatory cell infiltration and basophilic actinomyces-like bacterial colonies. The medullary spaces were replaced by fibrous connective tissue.
Conclusion: PI-BRONJ is a recent bisphosphonates complication that has to be taken into consideration by pathologists and dental practitioners.

Peri-implant Bisphosphonate-related osteonecrosis of the jaw (PI-BRONJ):



PS-03-016
Calcifyng epithelial odontogenic tumour (Pindborg's tumour): Confocal Laser Scanning Microscopic (CLSM) detection of micro-deposits of amyloid in 16 cases
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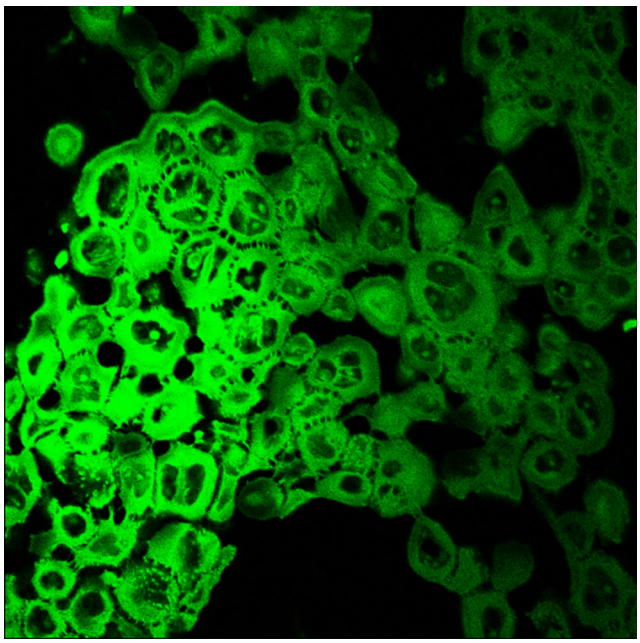
*Policlinico P. Zza G. Cesare, Uoc Malattie Odontostomatologi, Interdisciplinare di Medicina, Bari, Italy

Objective: The correct diagnosis of this benign odontogenic tumour, with its histological very atypical cellularity, mimicking a malignancy, could be easier by CLSM, with the early detection of the laser induced fluorescence of the micro-deposits of amyloid.
Method: Sixteen patients (mean age 31 years) reported from 1990 to 2014, underwent Rx-OPT, CAT-Scan, pre-operative FNAB and biopsy with histopathological analysis by optical and CLSM using standard stained slides (HE, Congo red).
Results: Rx revealed large (>4 cm) multilocular disomogeneous lesions with calcifications localized in mandibular angular region (13) and in posterior maxilla (3). Optical microscopy showed islands of atypical and dysplastic large epithelial cells with prominent intercellular bridges, suggestive for malignancy, surrounded by hyaline matrix and micro-calcifications. CLSM analysis revealed a strong red and green fluorescence localized mainly in spotty intra and extracellular localization constituted by small deposits of amyloid fibers, pathognomonic of this odontogenic benign tumour.
Conclusion: CLSM despite polarizing microscope and other techniques is more accurate and detailed to detect small and intracellular amounts of amyloid fibers and micro-calcifications, typical of this atypical and rare odontogenic tumour, allowing conservative surgical therapy.

CEOT at Confocal Laser Scanning Microscope:



PS-03-017
Mucoepidermoid Carcinoma (MEC) of minor salivary palatal glands: Clinico-pathological and prognostic correlations of 24 cases
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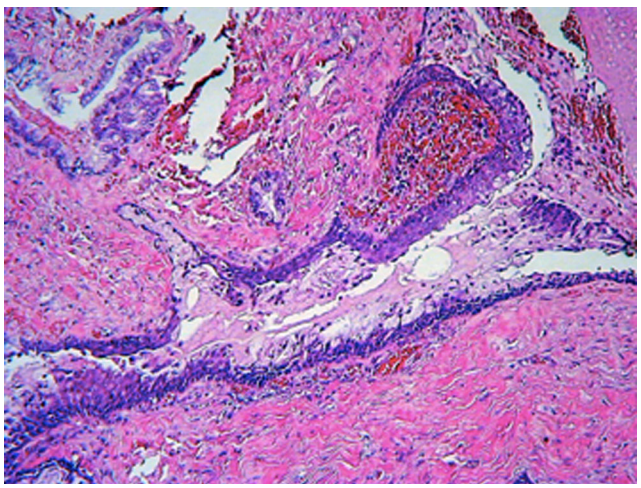
*Policlinico P. Zza G. Cesare, Uoc Malattie Odontostomatologi, Interdisciplinare di Medicina, Bari, Italy

Objective: MEC is a malignant tumour of salivary glands; on the basis of his histological prognostic scoring systems, 24 cases of MEC of minor salivary glands of the palate, treated between 1988 and 2008 were divided into low-grade (local recurrence) and high-grade types (nodal and distant metastasis) and clinico-pathological and prognostic correlations for this single localization were recorded.
Method: 24 patients affected by intraoral palatal MEC (mean 25 years, 60 %female) underwent spiral CT and MRI, pre-operative FNAB and biopsy and were classified into 18 cystic-low-grade and 6 solid high-grade, treated with wide surgical excision with 5 years of follow-up.
Results: Low-grade MEC present bluish-red, fixed nodules (mean 3 cm) with bone depression and cooping with well defined osteolytic areas. High-grade MEC present ulcerated vascular eso-endophytic nodular growth (3–6 cm) with underlying bone and sinus infiltration with indefinite margins; one patient had a local recurrence. Local metastasis were not detected.
Conclusion: MEC with palatal localization, is mainly low grade without recurrences when dimensional range is 1–3 cm; high grade palatal MEC with larger extension (3–6 cm) is locally aggressive but seems to have a better prognosis, with lower recurrence rates and metastasis respect to MEC of other minor and major salivary glands localizations.

Mucoepidermoid carcinoma:



PS-03-018
Papillary thyroid carcinoma associated with C-cell hyperplasia
T.-A. Georgescu*, M. Sajin, G. Simion, A. M. Lazaroiu, A. V. Dumitru, V. Axinte
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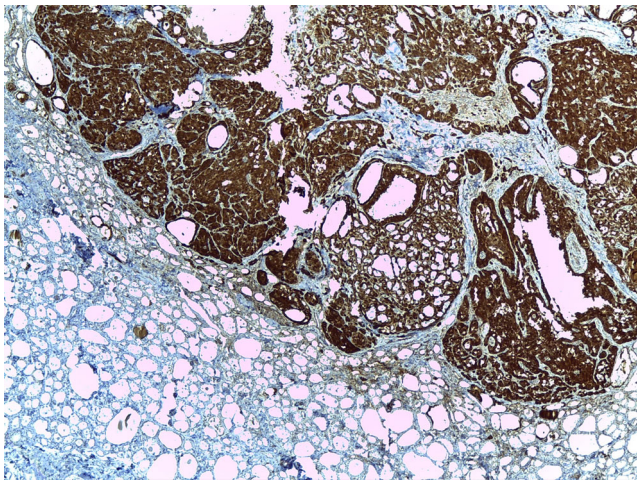
Objective: Papillary thyroid carcinoma is the most common type of thyroid carcinoma with apparently no benign neoplastic counterpart. Primary C-cell hyperplasia is mostly associated with MEN2, being considered the precursor lesion for medullary thyroid carcinoma. Secondary C-cell hyperplasia has been observed in the immediate periphery of nonmedullary thyroid neoplasms, in association with Hashimoto thyroiditis, secondary hyperparathyroidism, hypercalcemic states and after partial removal of the thyroid.
Method: We report a 74-year-old female with no family history of MEN2, presenting with a 2.8 cm painless nodule in the left thyroid lobe and slightly elevated calcitonin levels. The nodule was surgically removed and the intraoperatory diagnosis of papillary thyroid carcinoma concluded that a complete thyroidectomy was necessary.

Results: Histopathological evaluation of the left thyroid lobe confirmed the presence of papillary carcinoma, while the right lobe revealed a well-defined mass of focal, difuse and nodular C-cell hyperplasia, without atypical mitoses and with strong immunostaining for calcitonin. No regional metastases have been found.
Conclusion: Secondary C-cell hyperplasia has been described in association with various pathophysiologic conditions or adjacent to follicular tumours. We consider this incidental finding particularly interesting because C-cell hyperplasia occured within nonneoplastic thyroid tissue and in a completely different area than the coexisting papillary thyroid carcinoma.

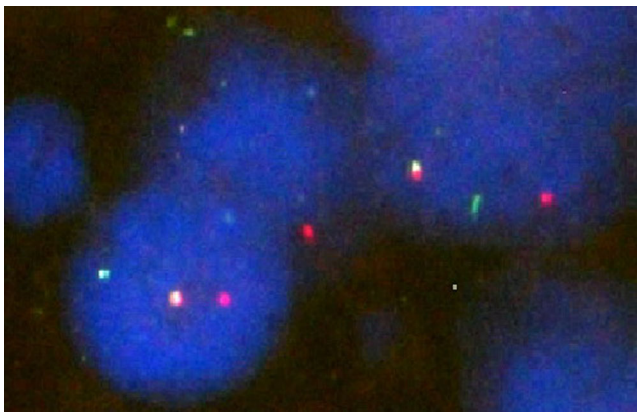
C-cell hyperplasia with strong immunostaining for calcitonin:



PS-03-019
Hyalinizing clear cell carcinoma of salivary gland: A case report
P. Constantinou*, N. Poulianitis, V. Pantelaion, G. Karagkounis, C. Vourlakou
*Evangelismos Hospital, Athens, Greece

Objective: Hyalinizing clear cell carcinoma (HCCC) is a rare salivary gland tumour made up of clear cells in a hyalinized stroma.
Method: A 60-year-old man presented with a mass lesion located in palate and right maxillary sinus. On gross examination, there was a firm mass measuring 6.5 × 4.5 cm (moderately advanced local disease) with extensive bone destruction.
Results: Microscopically, the tumour cells were arranged in solid cell nests, trabeculae or cords surrounded by a prominent hyalinized stroma. The majority of cells were round to polygonal with clear cytoplasm. There was another population of smaller cells with plump nuclei and granular eosinophilic cytoplasm. Both populations lacked nuclear pleomorphism and mitoses. Immunohistochemically the tumour cells were focally or diffusely positive for EMA, CK5/6, CK7, CK14, CAM5.2 and invariably negative for S100, SMA, MSA, and GFAP, ruling out myoepithelial differentiation. Fluorescent in-situ hybridization (FISH) break-apart assay for the EWSR1 gene rearrangement revealed that our case was positive, confirming the diagnosis of HCCC.
Conclusion: This carcinoma harbors a recurrent and consistent EWSR1/ATF1 fusion, which links this tumour to clear cell odontogenic carcinoma, and is not present in other clear cell mimics, which are involved in the differential diagnosis. HCCC demonstrates a squamous line of differentiation without myoepithelial marker expression.

Fluorescent in situ hybridization for Ewing's sarcoma breakpoint region 1 (EWSR1) gene rearrangement confirmed the diagnosis of HCCC as indicated by the separation of red and green signals:



PS-03-020
Case report of a follicular dendritic cell neoplasm in a cervical lymph node
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*Henry Dunant Medical Hospital, Dept. of Histopathology, Athens, Greece

Objective: Dendritic Cell Neoplasms (DCN) are rare tumours that previously were classified as lymphomas, sarcomas or histiocytic neoplasms. Currently the WHO classifies DCNs into five distinct entities: a) Langerhans' cell histiocytosis, b) Langerhans' cell sarcoma, c) Interdigitating dendritic cell sarcoma/tumour, d) Follicular dendritic cell sarcoma/tumour and e) Dendritic cell sarcoma, not otherwise specified.
Method: A 79-year old male patient admitted to our hospital with a cervical enlargement. We received a surgical specimen of a lymph node, m.d.: 2 cm, which on cut was whitish in hue and had a hard consistency. We performed an immunohistochemical evaluation with the following: LCA, CD20, CD3, κ and λ light chains, EMA, AE1/AE3, CD1a, FVIII, Desmin, CD21, CD4, CD8, CD68, bcl2, bcl6, MPO, S100, CD30, CD23, CD35, Vimentin and EBV.
Results: Histologically the lymph node architecture was completely destroyed and it was invaded by medium to large size neoplastic cells with cytoplasmic extensions with mainly a nodular pattern of growth. We noted increase number of mitoses with increased mitotic rate (ki67: >50 %) and dispersed multinuclear giant cells. The cells reacted against the CD21, CD23 and focally for EMA.
Conclusion: The findings were consistent with a Follicular DCN. The patient after 6 months had a recurrence in the intraparotid lymph nodes

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PS-03-021
Cushing's syndrome due to medullary thyroid carcinoma: Case report
Y. Manel*, A. Besma, M. Issam, K. Aida, H. Imen, M. Nada, B. Fethi, B. Ammar
*Military Hospital Tunis, Dept. of Pathology, Tunisia

Objective: We propose to highlights the value of using immunostaining to localize both the ACTH and calcitonin within the same cells in medullary carcinoma of the thyroid.
Method: A case of medullary carcinoma of the thyroid gland that secreted adrenocorticotropin (ACTH) is reported.

Results: The patient was a 54-year-old man who consulted for Cushing's syndrome and chest pain. Radiologic stain showed cervical and intrathoracic masses. Serum levels of calcitonin and ACTH were elevated. The thoracic and cervical masses were resected. The histologic findings were typical of medullary carcinoma of the thyroid. The neoplasm had a predominantly solid pattern, and the neoplastic cells were either round or spindled, many with cytologic atypia. Immunohistochemical analysis showed chromogranin, calcitonin, and ACTH in the neoplastic cells. The immunostaining for chromogranin was intense in all of the cells, whereas weaker staining for calcitonin and ACTH was present in scattered cells. Thus, the medullary carcinoma of the thyroid in this patient was the source of ectopic ACTH secretion causing Cushing's syndrome.
Conclusion: Medullary thyroid carcinoma rarely causes paraneoplastic Cushing's syndrome. Immunostaining is important for the diagnosis.

PS-03-022
Extramedullary plasmacytoma of the larynx: A case report
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Objective: The clinical, imaging, and pathologic features of this neoplasm are discussed, with potential treatment options.
Method: We report a case of extramedullary plasmocytoma of the larynx in patient with long-standing Ig D myeloma.
Results: A 55-year-old man with long standing Ig D myeloma presented with dry cough and breathlessness for last 6 months. Direct laryngoscopic examination showed a gray-white submucosal mass in the subglottic region. Histopathological examination showed presence of pseudostratified columnar epithelium with underlying stroma having mature and immature plasma cells. The cells were mono to bi-nucleated having eccentric nuclei and condensed spoke like chromatin. Few cells had centrally placed nuclei with small but conspicuous nucleoli. These cells were positive to CD138. The patient was successfully treated with primary radical radiotherapy and showed no signs of local recurrence after 4 years follow-up.
Conclusion: Extramedullary plasmacytoma of the larynx is a rare disease, highly curable when radiotherapy is used.

PS-03-023
Angioleiomyoma of the nasal cavity
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Abstract: Background: Nasal angioleiomyoma is a very rare entity which occurs only in less than 1 % of all leiomyoma cases. It has been postulated that they orginate from either undifferentiated mesenchyme or muscular layer of vessels or both. They grow slowly and may persist for a long time. Patients present most commonly with nasal obstruction, epistaxis, facial pain or headache. Treatment of choice is generally local resection. Recurrence is not common. Case: A 62 year-old male complaining of frequent epistaxis presented with a polypoid mass of 2 cm diameter in his right nasal cavity. MRI revealed the vascular nature of the lesion. Pathological examination showed polypoid fragments of nasal mucosa covering a tumour composed of numerous thickened vessels with an iner coat of circumferentially arranged spindle cells. The tumour cells had plump to elongated nuclei and eosinophillic fibrillary cytoplasm. They were immunopositive for smooth muscle actin(SMA) and demsin. Via these features, it was reported as angioleiomyoma. Conclusion: Angioleiomyoma is a rare diagnosis in the nasal cavity, but it should be kept in mind in patients with recurrent and insistent epistaxis.

PS-03-024
Angiolipoma of anterior plica of palatine tonsil: A case report
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Abstract: Benign tumours of the tonsils are rare. Only a few cases of tonsillar lipoma have been previously reported. Although lipomas are discovered incidentally they can present as cough, foreign body sensation, voice change, airway obstruction, even angina and positional sleep apnea. A case of polypoid lipoma of anterior plica of the palatine tonsil in a 23-year-old male is presented. The polyp was excised. Histological examination showed lobulated adipose tissue with very rich vascular channels in the collagenous septa around the lobules. The vascular channels are immunopositive for CD34 and Factor 8. According to the morphological findings and immunohistochemical staining, it was diagnosed as angiolipoma. We may therefore conclude that angiolipoma of tonsil is a very rare neo¬plasm that must be considered in the differential diagnosis of tonsillary tumours.

PS-03-025
Granular cell tumour on vocal cord
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Abstract: In this article a 50 year-old male patient complaining of postnasal drip and nasal obstruction for 10 years is presented. Granular cell tumours are benign relatively rare lesions that can occur in any organ in the body. The most common sites of origin are the head and neck, while the vocal cord is a relatively uncommon location. The most common symptoms are hoarseness and airway obstruction. Histopathologically, it is a non-encapsulated tumour with poorly defined margins and is composed of sheets, cords, or nests of cells. Tumour cells are large and polygonal with abundant pale eosinophilic cytoplasm and small vesicular nuclei. The cytoplasmic granules stain positive for periodic acid Schiff. The tumour cells show positivity with S-100, neuron-specific enolase, CD68 and negativity with CK, HMB45. Eosinophilic granules are also strongly positive for the PAS reaction. Eventually it was diagnosed as the granular cell tumour located on the vocal cords. Granular cell tumours are resistant to radiotherapy in contrast to surgical excision which is very successful for the treatment. We may therefore conclude that granular cell tumours are rare neo-plasms that must be considered in the differential diagnosis of laryngeal tumours.

PS-03-026
Hemangiopericytoma of the nasal cavity: A case report
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Objective: Hemangiopericytomas are unusual vascular tumours that rarely occur in the paranasal sinuses and nasal cavity. They are thought to arise from pericytes that surround capillaries, however, there is no proven etiology of these tumours. A 59 year-old-female complaining of nasal obstruction and postnasal discharge for 6 months presented with a mass in the nasal cavity located to the left middle concha. MRI confirmed the anterior rhinoscopy findings and indicated a polypoid image. Histologically, the tumour was submucosal, unencapsulated, and showed fascicular pattern. The tumour cells were uniform, spindle-shaped with oval nuclei, accompanied by an inflammatory cell infiltrate including eosinophils. "Stag horn" vessels, as typical for hemangiopericytoma, were identified as well as focal nuclear atypia. Immunohistochemistry revealed a strong staining pattern to vimentin but no reaction with actin.

The cells were immunoreactive for CD 34, slightly for Bcl2 and CD99 but negative for S-100 and epithelial membrane antigen (EMA). The Ki67-proliferation index was <2 %.
Conclusion: Hemangiopericytomas are unusual vascular tumours that rarely occur in the paranasal sinuses and nasal cavity. The pathologist should consider the diagnosis in cases with nasal polypoid masses.

PS-03-027
Angioma-like lesions in benign thyroid nodules
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Objective: Vascular, angioma-like lesions in thyroid nodules may occur although rarely. Their congenital or acquired nature is matter of debate.
Method: We aimed to report characteristics of 6 cases of thyroid benign nodules with angioma-like lesions.
Results: Angioma-like lesions in thyroid nodules were detected in 6 cases. The gender ratio was 2:4 (man:woman), the age ranged 61–82 years. The clinical diagnoses were thyroid nodular goiter and thyroid nodule. FNAC was performed in 2 cases. Contrast substance injection for thyroid imaging was performed in 4 cases. Prothrombin-time and cephalin-activated ratio were abnormal in 2 cases. Treatment consisted in total thyroidectomy (4) and right lobe resection (2). Microscopic analysis revealed sporadic nodular goiter (5, out of 236 thyroidectomies for goiter) and adenoma (1). The patients' history showed chemotherapy (for surgically resected lung adenocarcinoma) and sandostatin treatment (pancreatic neuroendocrine carcinoma) (one case each); arterial hypertension, dyslipidemia, diabetes and cardiac stent procedure (5,3,1 and 1 case respectively). Thyroid angioma-like lesions/aggregates (1–12/thyroid specimen) were intranodular (hyperplastic adenoma-type nodule in goiter and adenoma) and, measured 1–10 mm, (quasi-entire thyroid specimen analyzed microscopically). Vascular parietal, non-obliterating foam-cell-dots were seen in these lesions, along with rare 2–5 macrophage thick sheets (6 and 2 cases, respectively).
Conclusion: The results of our study suggest that thyroid angioma-like lesions may occur in thyroid adenoma or adenoma-like hyperplastic nodules in goiter, independently from FNAC procedures. Foam-cell-dots may be seen in the vascular wall suggesting a relationship to patients' history (dyslipidemia, contrast substance injection, clotting disorder).

PS-03-028
Cerebral edema as a secondary impact and involvement in forensic evaluation
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Objective: We studied the occurrence of primary brain trauma and secondary cerebral oedema and each of them intervention to produce death.
Method: We reviewed the cases with cranio-cerebral trauma (total 262 autopsied between 2012 and 2014) with cranio-cerebral trauma, with secondary cerebral edema that occurred.
Results: We met skull fractures in 84 % of cases, associated with meningeal lesions, cerebral trauma with other sites, which occurred after traumatic cerebral oedema. The time period between trauma and secondary cerebral edema aged from a few hours to 18 days. Locating brain trauma was at the time, front, parietal, basal occcipital and diffuse. In 23 % of cases we found fibrosis of intracerebral vessels. The most common circumstances were falls, traffic accidents, accidents at work, or risk sports.
Conclusion: Evolution to worsening of the posttraumatic secondary cerebral oedema or fatal complications due to pre-existing factors require caution in forensic assessment. In arguing contribution to death proces of secondary cerebral oedema has an essential role ruling out other causes of death.

PS-03-030
Lymphoepithelial carcinoma of the parotid gland: Report of a rare case
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Objective: Lymphoepithelial carcinoma (LEC) is an uncommon tumour accounting for 0,4 % of malignant salivary gland tumours. It is an undifferentiated carcinoma accompanied by a prominent non-neoplastic lymphoplasmacytic infiltrate. It displays identical histologic features to nonkeratinizing undifferentiated nasopharyngeal carcinoma.
Method: A 41 year old man presented with right parotid, slowly enlarging, painless, non-tender mass of 5 months duration. Physical examination of the right parotid gland revealed a firm, semi-mobile mass measuring 3 cm in maximum dimension. Ultrasound revealed a well defined homogenous mass measuring 3,3 × 1,6 cm in the superficial lobe of the right parotid gland and enlarged lymph nodes. Physical and radiologic examination of the nasal-oral cavity and nasopharynx were in normal limits.
Results: Fine needle aspiration cytology showed dispersed single atypical cells in a lymphoid background. Total parotidectomy and right neck disection was performed. Microscopically, solid carcinomatous sheets, trabeculae and isolated small groups of syncitial-appearing large tumour cells with scant amphophilic cytoplasm and vesicular haphazardly arranged nuclei intermingled with lymphoid tissue and surrounded by salivary gland were observed. A diagnosis of primary LEC of the parotid gland was made.
Conclusion: We herein present the clinicopathologic features of primary LEC of the parotid gland with review of the literarure.

PS-03-031
Clear-cell tumours of the thyroid: A challenging diagnosis
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Objective: Thyroid neoplasms consisting of clear cells are rare and prone to pose severe diagnostic challenges. The aim of this study was to differentiate between a primary nodule and a metastatic clear-cell tumour mainly a clear-cell renal carcinoma.
Method: We retrospectively reviewed two cases with pathologically diagnosed clear-cell tumour in 2014 at the pathology department of the Rabta hospital. The first case had a metastatic clear-cell renal carcinoma and the second case had a clear-cell adenoma.
Results: They were respectively a 80 year-old man and a 55-year-old woman who presented with a thyroid swelling. Macroscopic examination of the resected specimens revealed a solid well circumscribed nodule. Microscopic examination revealed solid areas composed of large polygonal cells with a pale cytoplasm and hyperchromic nuclei in the first case. In the second case, the tumour had a follicular growth but was cytologically similar. Immunohistochemical analysis revealed the clear cells to stain positive for CD10 and negative for thyroglobulin in the first case. Neoplastic cells were immunonegative for CD 10 and positive for TTF1 and Thyroglobulin in the second case.
Conclusion: The patient's history of kidney disorders as well as careful microscopic and immunohistochemical examinations are essential to diagnose clear-cell renal carcinoma.

PS-03-032
Recidivant mucosal melanoma in nasal cavity: Case report
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Objective: Female age 73 with ulcerative pigmented lesion at nasal floor suspected for haemangioma. Fragmented material contained invasive mucosal melanoma with ulceration in stage I of disease and positive margins. Three years after she went radical excision of recidive melanoma that infiltrate the inferior nasal concha and Melanoma in situ mucosae on the nasal floor and both middle nasal conchas and margine to the upper nasal wall. The nasal floor mucosa was negative from tumour so as the margin to the rest of the septum. Regional lymph nodes (19) at right cervical region were negative.
Method: To confirm melanocytic origine of tumour cells samples were screened for Melan A and HMWCK34βE12.
Results: Inadequate resection lead to 3 years disease-free period and local recidive after. Immunohistochemistry confirmed surface expression of melanoma cells and infiltrative growth into submucosa.
Conclusion: Despite the expectation that surgical excision should spare tissue in the head and neck region, it is important that intervention is sufficient and margines are negative from tumour. Careful and minute specialist examination are required in already inaccessible localization. Each incidence pigment change should be radically removed, knowing that 30 % of all melanomas in this region are unpigmented ones.

PS-03-033
Interest of immunohistochemistry in the diagnosis of thyroid carcinoma
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Objective: We aimed to investigate whether immunohistochemistry (HBME-1, cytokeratin-19/calcitonin and chromogranin in medullary carcinoma) provides additional information concerning the diagnosis of thyroid carcinoma.
Method: It was a retrospective study about 210 nodules of thyroid which were collected over 3 years (2010–2012) in our hospital. Twelve cases (5.71 %) were difficult to diagnose. We performed an immunohistochemical analysis on these 12 cases. Eleven follicular tumours were difficult to interpret. The antibodies used were HMBE-1 and cytokeratin 19. The last case was suspected to be a medullary carcinoma and we used chromgranin and calcitonin.
Results: In 11 follicular tumours, 10 cases expressed HMBE-1 and CK 19 so we retained the diagnostic of papillary carcinoma in its follicular variant. The stain was negative for CK19 and HMBE-1 in one case so we conclude in follicular carcinoma. The last case was stained with calcitonin and chromogranin which confirmed the diagnosis of medullary carcinoma. In all cases, immunohistochemistry has permitted the diagnosis and has specified the histologic subtype.
Conclusion: In our study, Immunohistochemistry has contributed in the diagnosis of thyroid carcinoma with difficult interpretation. But morphological features should always prime in the diagnostic decision.

PS-03-034
Mucosal large cell neuroendocrine carcinoma of the head and neck regions of the Japanese patients
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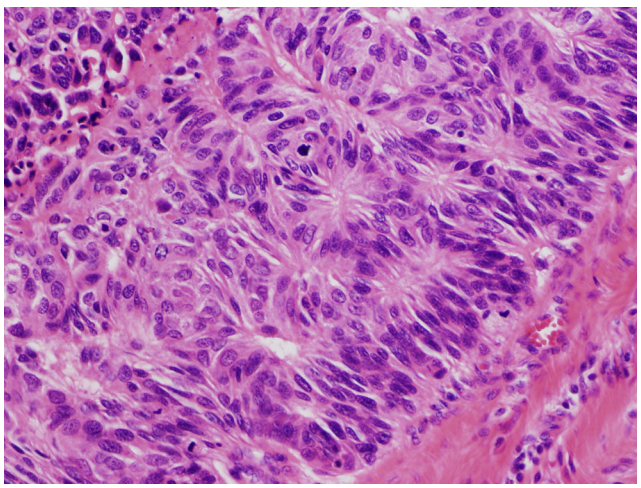
Objective: Our aim is to elucidate clinicopathological characteristics of mucosal large cell neuroendocrine carcinoma (M-LCNEC) of the head and neck regions.
Method: We selected 123 cases, which were diagnosed as "basaloid squamous cell carcinoma" and "poorly differentiated squamous cell carcinoma" from a pathological file of our hospital during 2002–2015, and we re-estimated these cases, according to the diagnostic criteria of pulmonary LCNEC. We examined them on neuroendocrine (NE) markers; CD56, chromogranin-A, and synaptophysin, immunohistochemically, and we re-diagnosed the cases, in which two or three NE markers are immunopositive, as M-LCNEC. We examined the clinicopathological characteristics of M-LCNEC.
Results: Twelve cases (9.8 %) were extracted. All cases are male and the mean age is 63.5 year-old (range 44–75 year-old). The primary sites are at the lingual root (3 cases), larynx (5 cases), maxillary sinus (2 cases), hypopharynx (1 case), and nasal cavity (1 case). Five cases are dead. Histologically, the tumour cells showed large nests formation with the central necrosis, rosette formation and/or nuclear palisading at the periphery of the nests. The immunestochemistry indicated that the tumour cells are frequently positive for NE markers. High Ki-67 labeling index (>78 %) was seen. A few of immunestivity for p63 were infrequently seen.
Conclusion: M-LCNEC of the head and neck regions is an extremely rare and established entity. Although M-LCNEC sometimes accompanies squamous differentiation, p63 imminopositive rate trends to reduce with prominent NE differentiation.

M-LCNEC:



PS-03-035
Salivary gland type carcinoma of the Larynx: Report of 5 cases
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Objective: Carcinomas originating from mucous glands of the larynx represent less than 1 % of all laryngeal cancers. Most of the minor salivary gland tumours arise in the subglottis; however, they can also occur in the supraglottis, in the false vocal cords, aryepiglottic folds and caudal portion of the epiglottis. It is commonly confined to the submucosa with no involvement of the surface epithelium.
Method: 5 cases the salivary gland type carcinoma of larynx were evaluated.
Results: All of the patients were males and their ages ranged between the 58–79 years old. The diagnosis of three cases were mucoepidermoid carcinoma (MEC) and the two others were adenoid cystic carcinoma (ACC). The tumour is localized to subglottic area in one case diagnosed as ACC. In the other ACC, tumour is limited to the left aryepiglottic fold.In two cases diagnosed as MEC tumour is spreaded from left cord vocale through the epiglottis. And the last one, tumour is localized to the anteriory commissure. Immunuhistochemically all cases shown positive for PanCK, p63 and four cases positive for Alcian Blue.

Conclusion: The prevelance of the salivary cancer of laryngeal was very rarely. There was a problem which differantiate in diagnosis from other laryngeal carcinoma.

PS-03-036

Benign lymphoepithelial cyst in lymph node: A rare case presentation

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Objective: Benign lymphoepithelial cyst is an infrequent lesion usually occurs in the parotid gland or the lateral cervical area including lymph nodes.
Method: An 18-year-old male patient, presented with a painful swelling in the cervical region. The clinical impression was malignancy. MRI was done and it revealed a hypo dense area with regular margin within the lymph node. The lesion was surgically excised and sent for histopathological examination. On gross examination the specimen was a 3.2 cm lymph node and a cystic area measuring 0.7 cm in diameter.
Results: Histopathology showed a lymph node containing a cyst lined by squamous epithelium with surrounding areas densely infiltrated with mostly lymphocytes. Immunohistochemical study with markers CD 20, CD 3, Bcl2, Bcl6, showed normal distribution of B and T cell lymphocytes. No evidence of malignancy was seen. The diagnosis was benign lymphoepithelial cyst.
Conclusion: According to literature 90 % of lymphoepithelial cysts were lined by squamous epithelium. However there were also reported cases where the cysts were lined by respiratory epithelium, columnar or cuboidal epithelium. The pathologist must differentiate it from Warthin tumour, metastatic squamous cell carcinoma, sialolithiasis and malignancies.

PS-03-037

Odontogenic tumours: Clinicopathological study of 12 cases

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Objective: Our aim is to review cases of odontogenic tumours in order to study their pathological features.
Method: Our retrospective study of 12 cases is based on the classification of the World Health Organization in 2005, over a 12 years period collected in the department of pathology of the Military Hospital of Tunis.
Results: The mean age of our patients was 36,9 years. The sex ratio was 2,2. Functional signs were dominated mainly by swelling. Four patients underwent a computed tomography scan which identified a hyperdense lesion in 2 cases and hypodense lesion in 1 case and a filling defect in 1 case. Microscopic examination showed 8 keratocysts, 1 dentigerous cyst, 1 ameloblastoma, 1 complex odontoma and 1 odontogenic fibroma. The treatment was surgical in all patients. Complete tumour resection was performed on 10 patients. The recurrence occurred in 2 patients.
Conclusion: Due to the diversity of ondontogenic tumours, the diagnosis is often difficult. The diagnosis approach of the pathologist must be based on clinical data to establish diagnostic hypotheses and morphological features.

PS-03-038

Influence of cobalt chloride (CoCl2)-induced hypoxia on the expression of CD44 and CD24 in salivary gland carcinoma cell line

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Objective: The objective of this study was correlate the tumoural CoCl2-induced hypoxia assessed by HIF-1, CAIX and GLUT1 with expression of adhesion molecules CD44 and CD24 in salivary gland carcinoma cell line.
Method: The effect of CoCl2-induced hypoxia on the expression of HIF-1α, GLUT1, CAIX, CD44 and CD24 was assessed in salivary gland carcinoma cell line (HTB-41) by reverse transcriptase-polymerase chain reaction and immunoblotting.
Results: The present data showed that CoCl2-induced hypoxia up-regulated the expression of HIF-1α and influenced pH regulation and glucose intake by up-regulating the expression of CA-IX and Glut-1. We observed that 50 uM or 150 uM of CoCl2 was capable to influences CD44 and CD24 mRNA enhancing, however, protein expression of CD44 and CD24 at 50 uM was unchanged and was drastically reduced at 150 uM CoCl2 concentration.
Conclusion: Together, present data suggested that hypoxic mimetic microenvironment could induce HIF-1α up-regulation, changes in pH regulation and glucose intake. In addition, a reduction on CD44 and CD24 expression in HTB-41 cell lineage with increased CoCl2 concentration was observed; it might be related with cellular decrease protein synthesis capability.

PS-03-039

Clear-Cell odontogenic carcinoma of the mandible: A case report, an immunohistochemical profile

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Objective: This study reports on the morphologic and immunophenotypic features of clear cell odontogenic carcinomas (CCOC) occuring in the mandible of young woman, showing extensive infiltration into adjacent tissues. CCOC is an extremely rare neoplasm and so far only 75 cases have been reported in the English-language literature.
Method: The tumour presented a monophasic pattern composed entirely of clear cell nests separated by cellular collagenous stroma. There was no evidence of ameloblastic differentiation. Most tumour cells contained PAS positive, diastase sensitive glycogen granules. The reports on immunohistochemical findings of CCOC have been inconsistent. This case was immunoreactive for known neuroectodermal markers- CD99(O13), NSE and CD56. Positivity for Vimentin, AE1/AE3, CK7 and EMA was also seen.
Results: To the authors' knowledge CD99(O13) has not been investigated previously in CCOC. Identification of the CD99 and other neuroectodermal markers positivity may prove to be useful in differentiating it from other odontogenic tumours, and salivary gland hyalinizing clear cell carcinoma(HCCC). Additionally, High labeling indices for the proliferation markers Kİ-67 and to p53 might predict a unfavorable prognosis for the case.
Conclusion: A surgical resection was performed, subsequently adjuvant radiotherapy was given. The patient was free of recurrence at 9 months follow-up.

PS-03-040

Non odontogenic tumours of the face bones: About 14 cases

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Objective: Tumours of the face bones include varied histological entities. It is often the radiological check up that suggests the diagnosis and histopathological examination provides the confirmation. Description of the clinical and pathological characteristics of non odontogenic tumours of the face bones.

Method: It is a retrospective study about 14 cases of non odontogenic facial bones tumours collected between 2000 and 2014.
Results: The mean age was 36.6 years. The sex ratio was 1.8. Functional signs were dominated by swelling. Our series included 9 benign and 5 malignant tumours. Histological study showed 5 chondrosarcoma, 4 osteoma, 1 fibrous dysplasia, 1 osteoide osteoma, 1 ossifying fibroma, 1 osteochondroma and 1 histiocytosis. The treatment was surgical in all patients. The recurrence occurred in 7 patients.
Conclusion: Due to the rareness and the diversity of facial bone tumours, their diagnosis is often difficult. The diagnostic approach of the pathologist must be based on clinical data to establish diagnostic hypotheses.

PS-03-041
Nasal Eosinophilic Angiocentric Fibrosis: A case report
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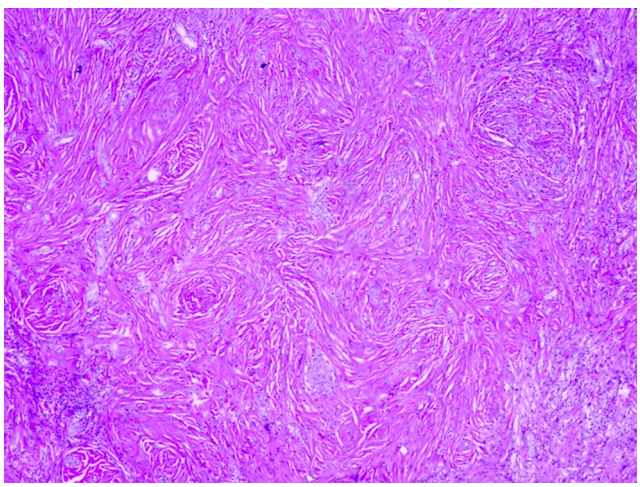
Objective: To present a case of female patient with a nasal eosinophilic angiocentric fibrosis (EAF) and discuss the relationship between this entity and IgG4-related disease (IgG4-RD).
Method: We prospectively identified one case from our University Hospital. Relevant medical history was reviewed. Histological and IgG4 stain were performed in the tissue.
Results: A 37-year old patient attended the otorhinolaryngology clinic because of nasal obstruction and deformity. She referred a history of allergic rhinitis and chronic sinusitis. Physical examination revealed a mass in the nasal septum at the osteocartilaginous union that obstructed and thickened the nasal pyramid. Magnetic resonance showed a round well defined lesion in the nasal cavity measuring 1.6 × 1.6 × 2.2 cm. The lesion was surgically excised and the tissue was sent to the pathology department. Histologically, the nasal mass tissue demonstrated abundant small vascular channels surrounded by concentric layers of fibrosis with a stroma infiltrated by abundant lymphocytes, eosinophils and plasma cells. IgG4 stain was positive in plasma cells surrounding the fibrotic stroma although the IgG4 to IgG ratio was less than 40 %.
Conclusion: EAF is an extremely rare and benign lesion of the upper respiratory tract. Present evidence suggests EAF to be part of the IgG4-RD spectrum.

Eosinophilic Angiocentric Fibrosis:



PS-03-042
Diffuse and strong cyclin-D1 and pancytokeratin positivity in peripheral Primitive Neuroectodermal Tumour (pPNET) of parotis: A case report
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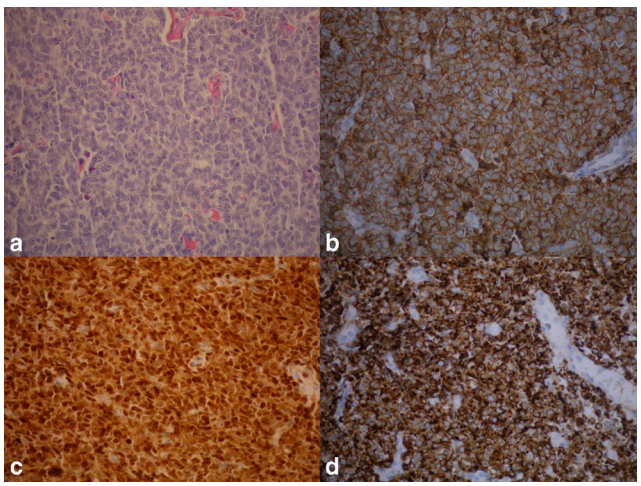
Objective: Peripheral primitive neuroectodermal tumour (pPNET) of head and neck is rare. CD99 positivity is considered sine qua non for diagnosis and other immunohistochemical markers show variable expression.
Method: Here, a case of pPNET of parotid gland showing diffuse cyclin-D1 and pancytokeratin positivity is presented.
Results: A 19-year-old female referred with swelling on the right side of her face. She did not have a chronic disease history. Physical examination did not reveal any other significant finding. Magnetic resonance imaging (MRI) of head and neck showed a well-defined solid mass located in parotis, 32 × 28 × 24 mm in size. An incisional biopsy was performed. In microscopic examination, tumour was composed of small round-to-oval cells with scant cytoplasm. Nucleoli were prominent in some cells. Immunohistochemically, tumour cells were stained positive for CD99, vimentin, cyclin-D1 and pancytokeratin. A high Ki-67 proliferation index was detected. Therefore, the patient was diagnosed as pPNET.
Conclusion: To our knowledge, there are less than 10 cases of pPNET of parotid gland reported in the literature. Lymphomas, neuroendocrine tumours, sarcomas and poorly differentiated tumours should be considered in differential diagnosis. Apart from the location, diffuse cyclin-D1 and pancytokeratin positivity was demonstrated in our case. The case is presented to be discussed in these aspects.

A) Hematoxylin-eosin (x400), B) CD99, immunohistochemistry, x400, C) Cyclin-D1, immunohistochemistry, x400, D) Pancytokeratin, Immunohistochemistry, x400:



PS-03-043
Polymorphous low-grade adenocarcinoma of soft palate in a male patient
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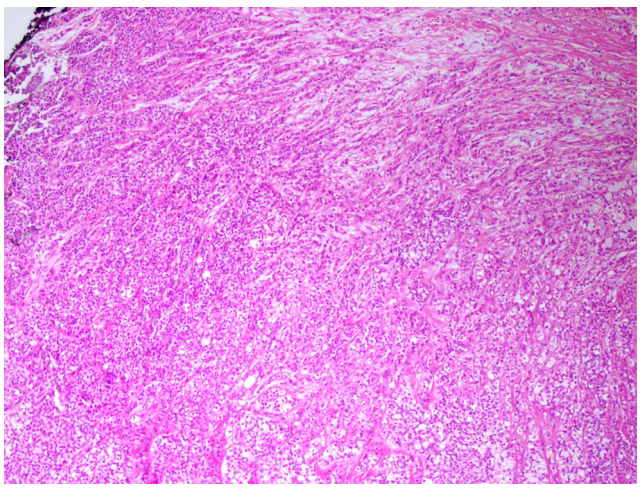
Objective: Polymorphous low-grade adenocarcinoma (PLGA) is a minor salivary gland tumour with a low malignant potential.
Method: We report a case of a male patient who was diagnosed as PLGA in soft palate.

Results: A 57-yers old-male patient presented with swelling in soft palate for 3–4 months. Local excision was performed. Macroscopically, the lesion was 1,4 × 1 × 0,9 cm and its surface was covered by mocosa. Histopathologically, the tumour was non-encapsulated and had infiltrating borders which were seen as solid nests with mucoid background in some areas. The tumour cells were small to medium size and uniform in shape and were surrounded by hyalinized eosinophilic stroma. Mitotic rate was 1-2/10 HPF and there was no necrosis. Immunohistochemically, tumour cells had positive staining with Vimentin, Pan CK, S-100, EMA, Bcl-2. Ki-67 proliferation indeks was 4–5 %. It was diagnosed as PLGA.
Conclusion: PLGA is twice more common in females, with a mean age of presentation at 59 years. Microscopically tumour cells are always regular and lacking in nuclear atypia. Mitotic figures are infrequent, and tumour necrosis is rarely seen. The differential diagnosis of PLGA includes pleomorphic adenoma, adenoid cystic carcinoma and monomorphic adenoma.

H&Ex100:



PS-03-044
Oncocytic papillary cystadenoma of nasopharynx: Case report
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Objective: Oncocytic cysts are rare benign, slow-growing lesions, lined predominantly by oncocytes, large polygonal cells with hyperchromatic nuclei and an eosinophilic granular cytoplasm. These cysts typically occur in the elderly and their incidence in upper respiratory tract biopsies is between 0.5 and 1 %.
Method: In this study, a 64-year-old male was presented. An endoscopic examination revealed well defined two small mass arising from right and left tonus tubarius with covered normal-looking mucosa.
Results: Lesions were removed totally. After a microscopic examination' oncocytic papillary cysadenoma' was diagnosed.
Conclusion: Management of these lesions is conservative and consists of local excision, the endoscopic approach being the treatment of choice. Although oncocytic cysts are benign lesions, follow-up is recommended, as recurrence is possible, especially in the case of patients with multiple involvement, since they may present a tendency to develop new cysts. In this report an unusual nasopharyngeal cystic lesion with multiple involvement occurring in a male patient was presented.

PS-03-047
FGFR1 expression in oral Squamous Cell Carcinoma (SCC) development
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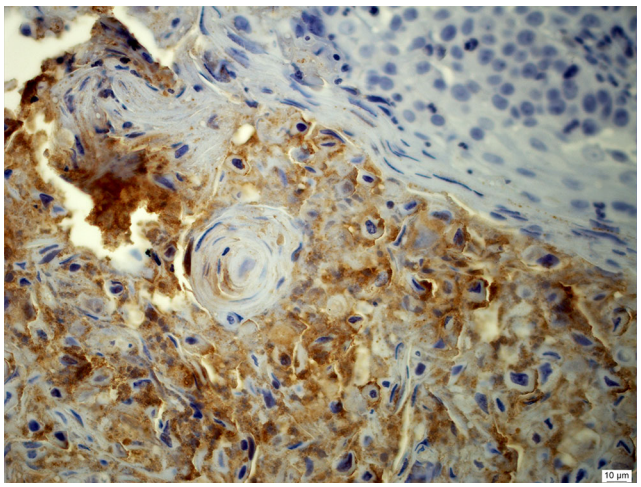
Objective: Signaling through the fibroblast growth factor receptor is complex pathway, reflecting the wide range of physiological functions controlled via FGF-FGFR. Amplifications of FGFR1 have been demonstrated in oral squamous cell carcinomas, but its significance still debatable. Thus, we examined FGFR1 expression in oral squamous cell carcinoma.
Method: Thirty-six OSCC samples were subjected to whole genome analysis through cDNA microarrays and expression profiles were obtained. Expression findings were validated in a different cohort using immunohistochemistry, and FGFR1 protein expression was analyzed according to clinicopathological parameters.
Results: Several FGFR1 pathway members were altered according to OSCC T stage, although FGFR1 mRNA expression itself was not. At a protein level, FGFR1 expression was observed in 33 cases (25.8 %), and its expression was related to p53 expression (p = 0.028) and was able to discriminate a worst prognosis in univariate analysis (p = 0.037).
Conclusion: Our study demonstrates that around 25 % of OSCC express FGFR1 at a protein level, and that FGFR pathway is important in terms of tumour development. Due to the recent targeted therapies based on FGFR1 status, we hope FGFR1 positive patients could be candidates to FGFR-targeted in future.

FGFR1 expression in OSCC case:



PS-03-048
Prognostic impact of Connexin 43 expression in oral Squamous Cell Carcinomas (SCC)
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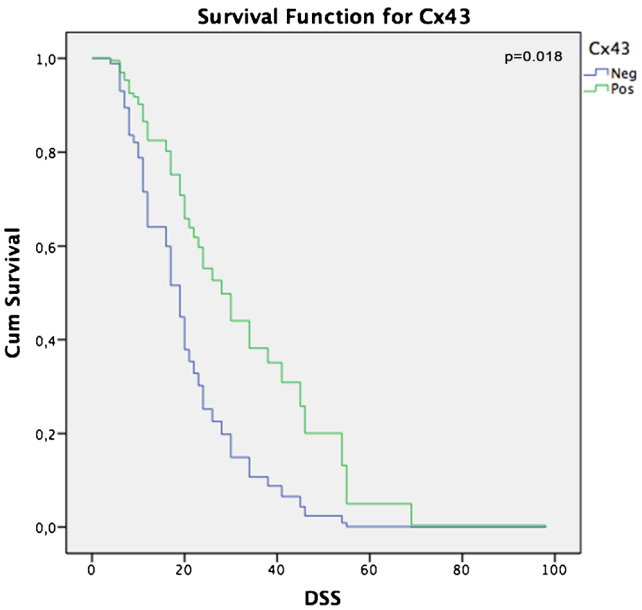
Objective: Connexins have been the targets of numerous studies due to their importance in cellular physiology, as one of the components of GAP junctions. Connexin 43 (Cx43) is one of the most common and most homologous connexin expressed in most epithelial tissues and it is possible that Cx43 play a different role during various stages of carcinogenesis. Thus, we examined Cx43 expression in oral squamous cell carcinoma.

Method: One hundred and thirty three OSCC samples were subjected to immunohistochemistry analysis for Cx43, and protein expression was analyzed and compared to clinicopathological information and survival data.
Results: Cx43 expression was observed in 65 cases (45.8 %), and the lack of Cx43 expression was related to histological classification ($p = 0.001$) and was able to discriminate prognosis as an independent prognostic factor in multivariate analysis ($p = 0.018$), together with know prognostic markers such as size ($p = 0.004$), histological grade ($p = 0.002$) and chemotherapy ($p = 0.025$).
Conclusion: Our study demonstrates that around 45 % of OSCC express Cx43, and that the lack of Cx43 expression is related to a higher histological grade, and to a worst disease-specific survival, although further studies could confirm its role as an important marker for OSCC survival.

Kaplan Meier analysis of Cx43 expression impact on disease-specific survival:



PS-03-049
Nested variant of urothelial carcinoma metastasis to the parotid gland
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Objective: We present a very rare example of a case of urothelial carcinoma metastasis to the parotid gland.
Results: A 54-year-old male, with a history of a nested variant urothelial carcinoma in the bladder, presented with a progressively enlarging parotidal swelling. US showed 4 × 3.6 × 2.5 cm hypoechoic mass. Fine needle aspiration (FNA) revealed highly cellular smears that were showed cohesive solid groups and irregularly branching cords as well as discohesive dispersed cells. The cells were uniform with oval bland nuclei showing finely granular chromatin. Scant eccentric cytoplasms were seen. Differential diagnosis included salivary gland tumours with basaloid morphology and metastatic urothelial carcinoma. Because no further definite diagnosis could be given, tru-cut biopsy was performed. Biopsy showed a tumoural infiltration with a nested pattern. Cellular morphology was similar to that of FNA. Immunohistochemical positivity for cytokeratin 20, uroplakin and GATA-3 supported a diagnosis of a metastatic urothelial carcinoma.
Conclusion: Parotid metastases from non-head-and-neck cancers are rare. Metastasis to the parotid gland from a bladder carcinoma is an unusual manifestation of disease. We could find only one case of parotid metastasis from bladder carcinoma in the literature. Our case is an example of a urothelial carcinoma metastasis to the parotid with well-documented cytomorphologic and histomorphologic features.

PS-03-054
Thyroid carcinoma: A retrospective study about 44 cases
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Objective: Incidence of thyroid carcinoma has been increasing in the world during the recent 3 decades. We believe that such increase is due to increased detection caused by widespread use of medical imaging, increase in thyroid surgery revealing occult cancer and more deliberate examination of surgical specimen. The aim of the study is the description of the clinical and pathological characteristics of thyroid carcinomas.
Method: We report a retrospective study about 210 nodules of the thyroid collected over 3 years (2010-2012), 44 thyroid carcinomas were diagnosed.
Results: Thyroid carcinoma represent 21 % of thyroid tumours. The mean age was 48.5 years. The sex ratio was 0.41(13/31). The most common location was the right lobe. The 44 thyroid carcinomas were divided into 41 papillary carcinomas, 1 follicular carcinoma and 2 medullary carcinomas. The stage of these tumours was T1 in 16 cases, T2 in 12 cases, T3 in 6 cases, T4 in 3 cases and 7 cases of micropapillary carcinoma. The survival rate was 100 % at 3 years.
Conclusion: This epidemiological study contribute to a better understanding and management of thyroid carcinoma. Further studies are mandatory to determine risk factors and elucidate pathogenetic mechanisms of thyroid carcinoma.

PS-03-056
Clinicopathologic implications of the heat shock-related 70 KDA protein 2 (HSPA2) and Cyclooxygenase 2 (COX-2) expression in Squamous Cell Carcinoma (SCC) of the larynx
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Objective: To investigate the expressions of COX-2 and Heat shock-related 70 kDa protein 2 in larynx carcinoma and their clinical significance.
Method: HSPA2, cox-2 EXPRESSION was immunohistochemistry in samples from 36 LSCC patients. The expression of HSPA2, cox-2 was analyzed by immunohistochemistry, and correlated with clinicopathological parameters.
Results: HSPA2, cox-2 were overexpressed in LSCC tissues compared to paired adjacent noncancerous tissues ($P < 0.001$). Clinicopathological analysis showed that HSPA2, cox-2 expression was significantly correlated with tumour size ($P = 0.001$), histological differentiation ($P = 0.03$), and tumour stage ($P = 0.0013$), lymph node metastases and recurrence, respectively (all, $P < 0.04$).
Conclusion: Our data indicate that HSPA2, cox-2 expression was increased in LSCC, which may be served as a prognostic marker.

PS-03-057
ANO1 and SHANK2 mRNA expression are associated with nodal metastases in oral cancer patients
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Objective: Cervical lymph node metastasis (CLNM) is a long established and still valid indicator of adverse prognosis for oral squamous cell carcinoma (OSCC). However, patients in early or even advanced OSCC may not always present clinically nodal disease. Consequently, predictive markers are much needed to guide treatment options, particularly elective neck dissection. This study aimed to find genes associated with metastasis using microarray methodology, in OSCC patients with a well-defined clinical profile.
Method: Tumour samples from patients over 40 years of age, smokers and drinkers, with tongue and/or floor of mouth squamous cell carcinoma were stratified in two groups: large, CLNM-negative (T2 or T3N0M0) and small CLNM-positive (T2 or T3N+M0). Cancer cells were laser capture microdissected from fresh tissue. cDNA was microarrayed using a GeneChip® Human Transcriptome Array and results were validated by qPCR in a larger cohort of patients.
Results: After microarray analysis, two overexpressed and three underexpressed genes were selected for validation by qPCR. ANO1 and SHANK2 were validated and showed a significant association with nodal metastasis ($p = 0.04$ and $p = 0.05$ respectively).
Conclusion: This study identified two genes relevant to nodal metastasis in a group of OSCC patients with controlled clinical features, a finding that may have important prognostic and therapeutic implications for this group of patients.

Acknowledgement:

Financial support and acknowledgment: This study was supported by Fundação de Amparo a Pesquisa do Estado de São Paulo/FAPESP (Grants 10/18581-1 and 10/18568-5) and Conselho Nacional de Desenvolvimento Científico e Tecnológico/CNPq (Grant 304977/2011-0). We acknowledge the GENCAPO (Head and Neck Genome Project) Consortium in the name of its members (listed in the Appendix) for sample collection and initial processing, clinical data collection, providing of histopathological analysis of tissue samples and informed consent acquisition of each patient.

PS-03-058
Podoplanin expression in laryngeal and hypopharyngeal carcinomas
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Objective: Podoplanin, a mucin-type transmembrane glycoprotein, is a lymphatic endothelial marker expressed in a variety of cancers. The objective of this study was to investigate podoplanin expression in the squamous cell carcinoma (SCC) of larynx/hypopharynx with adjacent squamous epithelium to assess the association between the podoplanin expression and the clinical-pathological characteristics.
Method: 50 primary laryngeal and hypopharyngeal SCCs were included to the study. Immunohistochemical staining for podoplanin expression was quantified by the Intensity Reactivity Score. The association between protein expression and clinicopathological parameters and survival was analyzed.
Results: 33 tumours were classified as podoplanin-low (66 %) and the remaining 17 tumours were considered as podoplanin-high (34 %). Thirty-one dysplastic epithelium exhibited podoplanin expression (62 %). There was no statistically significant correlation between podoplanin expression status and the tumour site, differentiation, stage of the disease, distant or regional metastases. Podoplanin expression level correlated significantly with adjacent dysplastic epithelium ($p = 0{,}046$) and alcohol usage ($p = 0.047$). The log rank test did not indicate any influence of podoplanin expression on survival ($p = 0.169$) or relapse rates ($p = 0.841$). Although not statistically significant, the majority of the study population were in advanced stage (68 %) and exhibited weak podoplanin expression. Most of the dysplastic epithelium foci were positive for podoplanin.
Conclusion: Although not statistically significant, the majority of the study population were in advanced stage (68 %) and exhibited weak podoplanin expression. Most of the dysplastic epithelium foci were positive for podoplanin.

PS-03-059
Tumour budding in laryngeal carcinoma
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Objective: Tumour budding has been defined as the presence of isolated single tumour cells or small cell clusters in the stroma at the invasive tumour margin. Tumour budding has been suggested to be a prognostic factor in various cancers. In this study, the relationship between tumor budding density and clinicopathological parameters is investigated.
Method: Fifty six patients with laryngeal carcinoma, all diagnosed as squamous cell carcinoma were evaluated. Patients were operated by partial or total laryngectomy and neck dissection. Isolated single tumor cells and clusters composed of fewer than five cells were defined as budding foci.
Results: The mean age of the patients was 59.7 (42–78) years of whom 54 were male and 2 female. The numbers of cases with absent, mild, moderate, and marked scores of budding were 15 (26.8 %), 18 (32.1 %), 11 (19.6. %), and 12 (21.4 %), respectively. Necrosis was present in 12 (21.4 %) and vascular invasion in 35 (62.5 %) cases. Six (7.3 %) cases were stage1, 14 (17.1 %) stage2, 21 (25.6 %) stage3, 15 (18.3 %) stage4. 11 (19.6 %) cases died of disease and 45 cases (80.4 %) survived. Statistical analysis, revealed that survival and budding were significantly associated ($p = 0.015$).
Conclusion: Tumor budding might be a valuable prognostic factor, particularly for survival in laryngeal carcinomas.

PS-03-060
EBV-positive mucocutaneous ulcer of the oral mucosa associated with HIV/AIDS
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Objective: To present two cases of Epstein-Barr virus-positive mucocutaneous ulcer of the oral mucosa in association with human immunodeficiency virus infection.
Method: The clinical, histomorphological and immunophenotypic features of two recently diagnosed cases of Epstein-Barr virus-positive mucocutaneous ulcer of the oral mucosa in HIV-positive patients were reviewed. Immunohistochemical staining for CD3, CD20, CD30, CD15, CD68 and Ki-67 was performed. EBER in situ hybridization was used for the detection of Epstein-Barr virus DNA within lesional cells.
Results: Both cases presented clinically as solitary well circumscribed ulcers which were characterized by dense superficial polymorphous inflammatory infiltrates. The infiltrates comprised cells with a predominant B-cell phenotype which ranged in size from small to intermediate with occasional large immunoblastic forms. Some of the larger B-cells had a Reed-Sternberg-like morphology. The B-cells co-expressed CD20, CD30 and CD15. EBER positivity was detected in most of the B-cells. Co-existent cytomegalovirus infection was coincidentally noted in the second case.
Conclusion: Epstein-Barr virus-positive mucocutaneous ulcer represents an unusual form of lymphoproliferative disorder associated with immune suppression and is documented here in the setting of human immunodeficiency virus infection. It should be distinguished from other forms of human immunodeficiency virus-associated oral ulceration due to its indolent nature and excellent prognosis following conservative therapeutic management.

PS-03-061
Melanoma of the oropharynx: A case report
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Objective: Report a rare localization of noncutaneous melanoma developed at the oropharynx.
Method: We report the case of a man of 54 years old who consulted for dysphagia in connection with a large unilateral swelling of the left tonsil lasting for 3 weeks. The biopsy brings back blackish fragments. A second examination was carried out after the first biopsy shows an extension to the right tonsil as well as hypo pharynx.
Results: A microscopic study shows a tonsillar parenchyma with a pigmented cell proliferation, matching a melanoma. The staging shows many visceral metastases.
Conclusion: The localization in the oropharynx of a melanoma is rare; the tonsillar seat is exceptional. Rare cases have been published in the literature.

PS-03-065
Epidermal Growth Factor Receptor (EGFR) and p53 co-expression in Head and Neck Squamous Cell Carcinomas (SCC)
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Objective: To evaluate the coexpression of EGFR and p53 in head and neck squamous cell carcinomas (HNSCC) and to identify possible correlations with histopatologic and TNM staging parameters.
Method: Fourty two cases of HNSCC were retrospectively selected. Double immunostain allowed the colocalization of EGFR and p53 on the same specimen. Microscopic evaluation highlighted cases with p53/EGFR co-expression and its possible prognostic value.
Results: 48 % of cases showed p53 positivity while EGFR was present in 85.7 % of cases. P53/EGFR co-expression was observed in 45 % of cases. Twenty five cases were laryngeal SCC (44 % of them co-expressing p53/EGFR) and 17 cases were pharyngeal SCC (70.5 % showing co-expression). For laryngeal SCC, a significant correlation was observed between tumor grade (G2), and p53/EGFR coexpression ($p = 0.017$). Most T3 and T4 cases showed no p53/EGFR coexpression ($p = -0.014$). All laryngeal SCC coexpressing p53/EGFR had M0 parameter ($p = -0.05$). For pharyngeal SCC, no significant impact of p53/EGFR coexpression on G or TNM parameters had been found. No significant correlation was observed for tumor grade or TNM staging parameters in pharyngeal SCC.
Conclusion: P53/EGFR colocalization defines a subclass of laryngeal SCC with less aggressive local invasiveness and low distant metastatic potential.

PS-03-066
Traumatic ulcerative granuloma with stromal eosinophilia in a young patient with liver encephalopathy
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Objective: Traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is a rare type of chronic traumatic ulceration of the oral cavity, clinically resembling squamous cell carcinoma. The pathogenesis is unknown. Most authors suggest that viral or other toxic agents may enter stroma through trauma, causing inflammation.
Method: We present a case of a 16-year-old boy who was admitted in ICU for liver encephalopathy caused by acute hepatitis A. A large ulcerative lesion, covered with thrombus, was observed on his tongue mimicking malignancy, although the possibility of an accidental tongue bite could not be excluded.
Results: On biopsy, ulceration of the mucosa, with exudate overlying an inflamed stroma, was shown. The inflammation was mixed with lymphocytes, plasma cells, histiocytes, eosinophils and large epitheliod cells, involving the underlying muscle. The epitheliod cells presented with voluminous nucleus and prominent nucleolus. Rare mitoses and occasional atypia were also noted. Findings as such are well consistent with malignancy. On the other hand, TUGSE is a rare entity of the oral cavity that should not be left out of the differential diagnosis.
Conclusion: TUGSE is a benign, chronic, self-healing lesion, not requiring surgical excision. Up to date evidence is not supportive that TUGSE may represent a CD30+ lymphoproliferative disorder.

PS-03-067
Unique presentation and histopathologic subtype of intramuscular hemangioma: Case report
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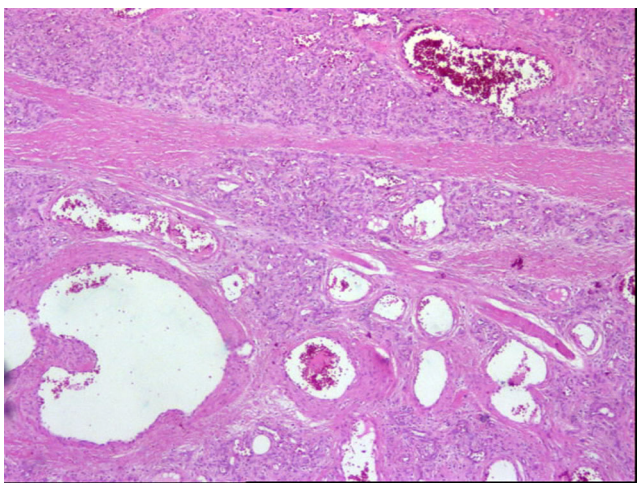
Objective: Hemangioma is the most common benign tumor of childhood, presentişng most commonly on cutanous and mucosal surfaces. On the other hand musculoskeletal presentation is extremely rare with the persentage of less than 1 %. Among musculoskeletal forms 15 % are detected in head and neck.
Method: Herein we present a intramuscular hemangioma of neck localized in sternocleidomastoid muscle (SCM) in childhood.
Results: A 10-year-old girl revealed to clinic with a mobile, 2 cm mass on medial side of right SCM. Magnetic resonance imaging revealed a well-defined mass with slightly increased signal intensity. Surgical resection was performed. Histopathologic examination showed multiple vascular spaces interspersed between the bundles of muscle fiber, confirmed the intramuscular hemangioma.
Conclusion: Intramuscular hemangiomas are benign and rare entity of infancy and childhood. A classification of three categories has been proposed according to vessel size: cavernous, capillary and mixed. The most common type is capillary type but our case is mixed type and more rare. The most common muscle involved in head and neck region is masseter muscle, but SCM involvement (as in our case) is really rare. According to localization and histopathologic type our case seems to be extremely rare. Spontaneously regression is generally absent because of this complete surgical resection is needed.

Figure 1:



PS-03-068

Papillary carcinoma arising in the thyroglossal duct cyst and synchronous occult papillary thyroid microcarcinoma: A case report

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Objective: Thyroglossal canal cyst is the most seen progressive abnormality of tyroid gland among congenital canal cyst. Papillary carcinoma is also a tumor mostly seen developing in this area of tyroid tissue on the wall of this cyst wall.
Method: In our case, 30 year-old woman having an operation because of a swelling on her neck got diagnosed of tyroid papillary carsinoma in thyroglossal canal cyst.In the total thyroidectomy material of this patient 3 papillary microcarsinoma pieces, 2 classical variants in right lobe sections and 1 follucular variant in left lobe sections, have been observed.
Conclusion: It has raised doubts whether it is primary or not as there are concurrently multifocal microcarcinoma in thyroid gland. However, if there is a synchronic papillary carcinoma in TTK and thyroid gland, the multifocal tumor development is also a matter of question. Because of this, as the cyst consistency with cyst epithellium is observed in our case, it is thought that there is a development of multifocal tumor in the cyst and thyroid.

PS-03-069

Plexiform neurofibroma of the larynx in a child: Case report

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Objective: Neurofibromatosis Type 1 (NF1) is an autosomal dominant disorder which is characterized by multiple cafe'-au-lait spots and neurofibromatosis with some somatic abnormalities. Laryngeal involvement in NF1 is rare and only few pediatric cases have been reported. Herein, we report a plexiform neurofibroma of the larynx in a pediatric case.
Method: A 9-year-old-girl was referred to hospital with laryngeal obstructive symptom, dyspnea which was increased during deep inspiration and in a supine position. The patient also fullfilled the criteria for NF1. On physical examination, mass was seen that originated from the vallecula and root of tongue. The mass was pale with smooth contours and covered by normal mucosa. The lesion was removed endoscopically for histopathologic examination.
Results: Microscopically, under the intact mucosa, the nodules which consist of uniform, spindle-shaped Schwann cell bundles and a loose stroma were detected. Immunohistochemically, Schwann cells were positive for S-100 protein and the presence of intratumoral axons in neurofibroma was detected by neurofilament positivity. By these findings, histopathological diagnosis was made as plexiform neurofibroma.
Conclusion: Plexiform neurofibroma of the larynx in children is rare, however if a patient with a positive NF1 family history presents with dyspnea and laryngeal mass, possibility of neurofibroma should be considered.

PS-03-070

Full-field OCT for fast diagnostic of Head and Neck cancer

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Objective: Full-Field OCT (FFOCT) produces optical slices of tissue using white light interferometry providing in-depth 2D images, with an isotropic resolution around 1 μm. These optical biopsy images are similar to those obtained with histology, but without tissue preparation and within few minutes. This technology could be useful when diagnosing a lesion or at the time of its surgical management.
Method: Here we evaluate the clinical value of FFOCT imaging in the management of patients with Head and Neck cancers by assessing the accuracy of the diagnosis done on FFOCT images from resected specimen. FFOCT images from Head and Neck samples were first compared to the gold standard (HES). An image atlas dedicated to the training of pathologists was built and diagnosis criteria were identified. Then, we performed a morphological correlative study: both healthy and cancerous samples from patients who undergo surgery of oral cavity, pharynx, and larynx were imaged. Images were interpreted in a random way by two pathologists and the FFOCT based diagnostics were compared with HES of the same samples.
Results: Here we present preliminary results showing that FFOCT provides a quick assessment of tissue architecture at microscopic level that could guide surgeons for tumor margin delineation during intraoperative procedure.

PS-03-071

Strong osteopontin expression in tumor-associated macrophages is predictor of better prognosis in oral Squamous Cell Carcinoma (SCC)

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Objective: Osteopontin (OPN) is a glycoprotein involved in progression of many carcinomas, including oral squamous cell carcinoma (OSCC). It is synthesized by a variety of epithelial and mesenchymal cell types, including macrophages. Recently, a distinct activities of OPN from stromal and parenchymal tumor cells has been proposed. The aim of this study was to evaluate the expression of osteopontin in tumor-associated macrophages (TAMs) from OSCC tissue and to determine its possible prognostic significance.
Method: The expression of OPN was immunohistochemicaly analyzed in TAMs from 86 OSCC and compared with clinicopathological variables. The staining intensity was semi-quantitatively assessed as high, moderate and low.
Results: Diffuse cytoplasmic positivity for OPN in infiltrating TAMs was classified as high in 21 patients, moderate in 47 patients, and low in 14 patients; OPN+ macrophages were absent in 4 patients. Strong OPN expression in TAMs was associated with low invasive front grade ($p < 0.006$), low level of inflammatory response ($p < 0.018$), and a better disease-specific survival ($p = 0.009$). Expression patterns were not associated with pT stage ($p = 0.28$), lymph node status ($p = 0.21$), nor with the WHO clinical stage ($p = 0.41$).
Conclusion: In OSCC macrophage-derived OPN probably has a different function compared with OPN secreted from tumor cells.

PS-03-072

Histologically benign carotid body paraganglioma with regional lymph node invasion: A case report

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Objective: Carotid body tumors are extremely rare, with an incidence of 0,03 % of all tumors. Extra-adrenal paragangliomas are uncommon tumors arising from neuroectodermal-derived paraganglion tissue. The carotid body tumor is the most common of the extra-adrenal paragangliomas but only a few malignant cases have been reported in the literature.
Method: We describe a case of malignant paraganglioma of the carotid body, emphasizing the value of immunohistochemical stains for differential diagnosis.
Results: A 57 year old woman presented with a left, painless neck mass. The MRI demonstrated a solid, encapsulated lesion on the left carotid

bifurcation, which was surgically excised. Macroscopic examination showed a well-defined, red to brown mass measuring 5,4 cm in maximum dimension. On microscopic examination, the tumor was composed of round epithelioid cells arranged in small and large nests around an elaborate vasculature, with involvement of a local lymph node. Focal nuclear pleomorphism and very rare mitotic figures were observed. The tumor cells were positive for chromogranin, synaptophysin, neuron specific enolase, but negative for panCK, TTF1, calcitonin. S-100 stained the sustentacular cells in the tumor.
Conclusion: This is a rare case of malignant carotid body tumor with histologically benign aspects and local lymph node metastasis, highlighting the aggressive phenotype.

PS-03-073
Evaluation of tumor microenvironment in salivary gland neoplasms
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Objective: In an attempt to better understand the tumor microenvironment, the aim of present study was to evaluate the vascular density, extracellular matrix destruction with release of angiogenic factors, and antitumor defense mechanisms in Pleomorphic Adenoma (PA) and Mucoepidermoid Carcinoma (MEC) of salivary glands.
Method: Immunohistochemical staining with anti-CD34, anti-mast cells and anti-CD8-T cells was performed on 23 salivary gland neoplasia specimens from PA and 21 specimens from MEC obtained from Araujo Jorge Hospital in Goiania-GO, Brazil. Immunopositivity areas were estimated by image analysis software.
Results: Female predominance was observed in both PA (68 %) and MEC (67 %). In PA cases the age ranged from 9 to 64 years, while in MEC cases age ranged from 13 to 75 years. Histologically, out of 21 cases, 6 (28 %) were classified as grade I, 12 (57 %) as grade II and 3 (14 %) as grade III. Immunohistochemical expression of CD34, mast cells and CD8 in MEC were greater than in PA tumours.
Conclusion: In malignant neoplasm was observed an enhanced vascular density that could lead to better nutrition and oxygen delivery to tumour, enabling tumoural growth and spread. Additionally, increased vascular bed in malignant neoplasm could allow the arrival of larger amounts of mast cells and CD8 cells.

PS-03-078
Tumour-to-Tumour Metastasis: Warthin Tumour as a recipient of cutaneous Squamous Cell Carcinoma (SCC)
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Objective: Warthin's tumour is a well-defined benign salivary gland neoplasm consisting of both epithelial and lymphoid components. Metastasis of an epidermoid carcinoma to Warthin's tumour is extremely rare and the differential diagnosis of malignant transformation is important. We present a case with squamous cell carcinoma (SCC) metastatic to the Warthin's tumour of parotid gland in a 71- year-old male patient.
Method: Excisional biopsy was performed because of wounds on his head. Left temporal area biopsy was diagnosed as BCC+SCC, right ear and nasal dorsum biopsy were diagnosed as SCC.In terms of investigating metastasis and local spread, the left parotid nodule larger than 1 cm was detected. A fine needle aspiration of parotid lesion was performed and a diagnosis of Warthin tumour was made. The patient underwent superficial parotidectomy as he was not suspected of having SCC in Warthin's tumour preoperatively.
Results: Islands of malignant squamous epithelial cells were found to invade the Warthin's stroma (many dilated cysts filled with secretion and lined by double layered cuboidal oxyphilic epithelial cells arranged in a papillary growth pattern, the papillae projecting into cystic spaces). A histological diagnosis of Warthin's tumour with SCC metastasis was made and metastasis was observed in periparotid lymph node.
Conclusion: SCC and BCC of cutaneous are very common neoplasms. Locally aggressive behavior is much more common than metastatic spread. The presence of transitional zones right from the benign oncocytic component to the frank malignant epithelium is important to be distinguished from the metastasis of primary carcinoma at another site.

PS-03-081
Aspergillus otomycosis: Two case reports
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Objective: Our aim is to study the clinico-pathological features of two cases of Aspergillus otomycosis.
Method: We report the case of a 50 years old man and of a 60 years old woman, complaining of intermittent otalgia lasting for months, despite repeated treatment with local antibiotics and antiseptic irrigation. Otoscopy showed a whitish, cotton wool like growth of the ear, measuring respectively 2 and 3 cm in diameter, associated with Case report: a hyperaemic tympanic membrane. A biopsy was made. Histopathological examination identified straight septate hyphal forms with acute angle branching. Grocott stain was positive. The diagnosis of aspergillus otomycosis was retained, confirmed by mycological examination.
Results: The diagnosis of aspergillus otomycosis was retained, confirmed by mycological examination.
Conclusion: Otomycosis also known as fungal otitis externa, is rare. Aspergillus, an opportunistic filamentous fungus, can rarely cause otitis externa. Histologic differential diagnosis includes candidiasis and mucormycosis. Antifungal treatment must be prompt and vigorous, to minimize the likelihood of hearing loss and invasive temporal bone infection.

PS-03-082
Oral proliferative verrucous leukoplakia: A case report of an elusive entity
N. Abdelhedi*, O. Adouni, A. Goucha, F. Tekari, I. Bettaieb, O. El-Amine, S. Miladi, S. Gritli, A. Gamoudi, A. El-May
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Objective: Proliferative verrucous leucoplakia (PVL) is a distinct, particularly aggressive form oforal leucoplakia. Our focus is to discuss morphological features, histogenesis andevolution characteristics of this elusive entity.
Method: A 77 year-old man, 50 packages per year, consulted for a lesion of the right lipcommissure. On examination, he had lesions of leukoplakia at the inner surfaces ofthe right and left cheeks, respectively measuring 2.5 and 3 cm. A biopsy on the rightshowed a verrucous carcinoma. A bilateral surgical removal of both labialcommissures was performed.
Results: On histology, it is a proliferating tumour in the epidermis having a papillomatousappearance with acanthosis. This proliferation has endophytic and exophyticdevelopment repressing to the depth an inflammatory chorion. This tumour is made oflarge cells, pale, with hyperkeratosis and parakeratosis, without cytonuclear atypia. On either side of this lesion, the mucosal lining is slightly papillomatous and hyperkeratotic without disruption or cytonuclear atypia.
Conclusion: PVL is a rare form of oral leukoplakia characterized by a significant propensity for processing with a high rate of progression to oral squamous cell carcinoma, verrucous carcinoma and difficulty of an early detection of problems. The most appropriate definition remains a combination of both clinically and histologically.

PS-03-083

Fascin and diaphanous 3 in Squamous Cell Carcinoma (SCC) of oral cavity

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Objective: Fascin-1 is an actin-bundling protein absent in most normal epithelia but expressed in many human carcinomas, where is associated with increased invasive and metastatic potential. Diaphanous-related formin-3 belongs to a family of formin orthologs, whose deficiency promotes motility, invasion and experimental metastasis and significantly correlates with aggressive disease in human tumours. The aim of this study is to assess the expression of Fascin-1 and Diaphanous-related formin-3 in 22 cases of Squamous Cell Carcinomas (SCC) of the oral cavity, in order to identify new biological prognostic markers.
Method: Fascin-1 and Diaphanous-related formin-3 expression was assessed with immunohistochemistry (IHC) in 22 formalin-fixed and paraffin-embedded SCC of the oral cavity and in 12 non neoplastic samples from normal mucosa obtained during dental procedures.
Results: At IHC, Fascin-1 was highly expressed in SCCs, whereas it was negative in non-neoplastic samples, while Diaphanous-related formin-3 expression was lower in SCC than in non-neoplastic samples.
Conclusion: These data demonstrate the different expression of Fascin-1 and Diaphanous-related formin-3 in SCC of oral cavity. Further studies should assess if Fascin and Diaphanous play a role in the adhesion disrupture during oral cavity cancer progression.

PS-03-084

Malignant transformation of nasal inverted papilloma into sarcomatoid carcinoma: Case report

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Objective: Nasal inverted papilloma is a benign epithelial tumour that develops from schneiderian mucosa lining the nasal cavity. It typically corresponds to an endophytic proliferation of transitional cells. Its evolution is marked by the risk of malignant transformation which is possible in 5–15 % of cases into an infiltrating squamous cell carcinoma, or more rarely a transitional cell carcinoma. We report an exceptionnel case of a sarcomatoid carcinoma developed on nasal inverted papilloma.
Method: A 57 years old, male, consulting for a chronic unilateral nasal obstruction with epistaxis. Intranasal endoscopy found multiple polypoid lesions that were resected. Frozen section found a benign inverted papilloma.
Results: The definitive microscopic examination revealed malignant areas. This areas were composed by large infiltrative sheets of spindle shaped cells with markedly atypical nuclei and numerous mitotic figures. Focally, are seen a squamous differentiation and undifferentiated component.
Conclusion: Besides their propensity to be associated with malignancy, inverted papilloma are characterized by their tendency to recur. So the treatment is based on a complete endoscopic resection that can be followed by a raditherapie.

PS-03-085

Analyses of the expression of TLR1, 2 and 6 in HPV- associated oropharyngeal Squamous Cell Carcinoma (SCC)

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Objective: To analyze the gene and protein expression of TLR1, 2 and 6 in HPV- oropharyngeal squamous cell carcinoma (OPSCC) cell lines and to assess the function of TLR2/TLR1 and TLR2/TLR6.
Method: Four different cell lines were used: two OPSCC HPV16+ (SCC2 and SCC90) and two OPSCC HPV- (SCC72, SCC89). qPCR was performed to analyze the expression of TLR1,2 and 6, IL-6 and IL-8 with and without the stimulation with peptidoglycan from Staphylococcus aureus.
Results: There were significant differences in the gene expression of TLR1 and TLR6 in HPV- associated OPSCC cell lines (SCC2 and SCC90) compared to OPSCC HPV negative cell lines (SCC72 and SCC89).
Conclusion: HPV- associated OPSCC shows downregulation of TLR1 and TLR6, which may be influencing in the activation of TLR2/TLR1 and TLR2/TLR6.

PS-03-086

Comparison of p16ink4a immunostaining in benign and malignant HPV-related oral lesions

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Objective: We aimed to analyze the difference between p16inka immunostaining in normal epithelium, two benign HPV-related lesions (papilloma and condyloma acuminatum) and one malignant HPV-related lesion (oropharyngeal squamous cell carcinoma (OSCC)).
Method: Five normal oral mucosa specimens, 15 papilloma, 15 condyloma acuminatum and 15 HPV-positive OSCC were included in the present study. Histological sections were immunostained for anti-p16ink4a (1:1000; Abcam 54210, clone2D9A12, Cambridge, MA, USA) using the streptavidin-biotin method. For the positive staining, score was based on a scale of 0 to 3+, as follows: 0- negative stain; 1+ less than 25 % of positivity and focal distribution; 2+ 26–50 % positivity and focal distribution; and 3+ 50–75 % of positive cells and diffuse distribution. The evaluation of the intensity score was based on: 0- negative; 1- low intensity; 2- moderate intensity; 3- intensive.
Results: The results showed no significant differences between the scores (positive x intensity) of p16ink4a in normal epithelium, papilloma and condyloma acuminatum. All the three lesions showed significant differences when compared to the OSCC. Table. Statistical analysis of p16ink4a immunohistochemistry stain for p16ink4a (Kuskal-Wallis pos hoc Dunn) Significant P value Normal vs. Papilloma No NS Normal vs. Condyloma No NS Normal vs. OSCC Yes **** Papiloma vs. Condyloma No NS Papiloma vs. OSCC Yes **** Condyloma vs OSCC Yes * NS= not significant; *$p < 0.05$; ****$p < 0.0001$
Conclusion: There are differences in the expression of p16ink4a between benign HPV-lesions and malignant HPV-lesions. Also, the study suggests that it is not possible to assure the presence of HPV by the detection of p16ink4a in benign lesions as used for OSCC.

PS-03-087

Cytogenetic alterations in premalignant and malignant lesions of the oral cavity

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Objective: Oral squamous cell carcinoma (OSCC) usually develops from a preexisting premalignant lesion. The aim of the study is to characterize the cytogenetic alterations in a series of premalignant and malignant lesions of the oral cavity.

Method: Thirty samples from 11 patients with OSCC were studied using Affymetrix genomic arrays through Cytoscan HD array (25 samples) and OncoScan array (5 samples). The samples included normal mucosa, hyperplasia, low-grade dysplasia, high-grade dysplasia and infiltrating OSCC
Results: The most consistent alterations found in low-grade and high-grade dysplasia were deletions and loss of heterozigosity in loci 9p21, 3p14.2, 3p26.3 and 6p25.3, where tumour suppressor genes and adhesion molecules regulator genes are located. In OSCCs these changes persisted, and other several alterations were seen. Gains in 11q13.3, 8q24.21 and 3q26.32 where the oncogenes CCND1, MYC and PIK3CA respectively are located, were seen only in OSCCs.
Conclusion: The early cytogenetic changes in premalignant oral lesions are deletions and loss of heterozigosity, whereas genetic gains are mostly seen in already developed OSCCs

PS-03-088
Laryngeal undifferentiated pleomorphic sarcoma with giant cell: Case report
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Objective: To explore the histopathology, the diagnosis and the treatment of undifferentiated pleomorphic sarcoma of larynx, a very rare laryngeal tumour which has a mesenchymal origin.
Method: We report a case of a glottic UPS at a 68-year-old male, who has been smoking for 30 years, and was hospitalized in January 2015 at Emergency County Hospital "Sf. Apostol Andrei" Constanta.
Results: The tumour was originated in glottic area, upper a right vocal cord, with no paresis. The tumour determined hoarseness for 5 months and dysphonia. Patient underwent surgical excision of the tumour. The immunohistochemical techniques proved positivity for vimentin, smooth muscle actin, CD68, CD34, Ki67, and negative for CD117, NFT, chromogranin, c-erbB2, AE1/AE3, MNF116, desmin, myogenin and p53.
Conclusion: Undifferentiated pleomorphic sarcoma of larynx is a very rare mesenchymal neoplasm. The diagnosis of UPS of larynx was a diagnosis of exclusion and the immunohistochemistry could have been helpful.

PS-03-089
A variant of papillary thyroid carcinoma
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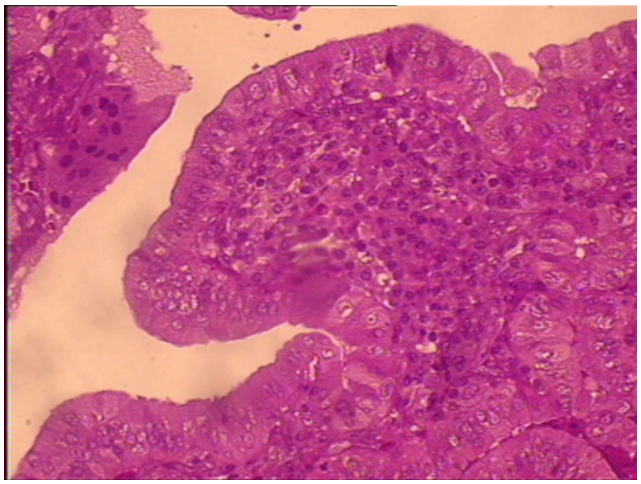
*Tunis, Tunisia

Objective: The Warthin-like tumour (TWL) of the thyroid gland is a rare variant of thyroid papillary cell carcinoma characterized by a lymphoid stroma.
Method: We report the case of a TWL of the thyroid in a 61-year-old woman presented with a cervical swelling evolving since 3 months without signs of neither compression nor dysthyroidie. Cervical palpation revealed a left isthmo-lobaire firm and mobile nodule measuring 2 cm in diameter. Thyroid ultrasonography showed a multinodular thyroid with a left supracentimetric hypoechoic nodule. Thyroid ponction was normal.
Results: The macroscopic exam showed a juxta-isthmic 2,5 cm in diameter nodule. On histology it was constituted essentially by papillary formations inside a cystic cavity mingled to some follicules. The stroma was often constituted of an abundant diffuse lymphoid cloth. Papillas and bladders were papered by oncocytic cells presenting the nuclear features of papillary carcinomas.
Conclusion: This observation provides on opportunity to recall clinical, histopathologic, differential diagnosis and prognosis aspects of this tumour.



PS-03-090
"Neoplastic" C-cell hyperplasia, medullary thyroid carcinoma and ret mutations: Report of two cases and review of literature
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Objective: Medullary Thyroid Carcinoma (MTC) accounts for 5–10 % of all thyroid cancers. Approximately 25 % of MTC is familial, caused by mutations in the RET proto-oncogene. We report 2 cases of MTC with histologic features suggesting hereditary form. Both cases presented in January 2015, so molecular RET-mutation testing results are not available by the date of the present abstract submission.
Method: Case 1 refers to a 24-year-old woman with elevated levels of circulating Calcitonin. Histologic examination of the thyroid showed 3 MTCs in both lobes (diameters 1–2 mm) and focal and nodular C-cell hyperplasia with histologic features of C-cell in situ carcinoma. Case 2 refers to a 44-year-old man with elevated levels of circulating Calcitonin. On histologic examination, diffuse C-cell hyperplasia was the main feature of the thyroid. Some nodules with "neoplastic" C-Cell hyperplasia features and a MTC of 2 mm were also present.
Results: Both cases showed strong Calcitonin and Chromogranin immunohistochemical expression whereas HBME-1 and CK19 were not expressed. To both patients was suggested molecular RET-mutation testing.
Conclusion: An early manifestation of all MEN2 syndromes, associated with germline and somatic RET mutations, is C-cell hyperplasia, which eventually progresses to multicentric neoplasia. Advances in genetic screening have enabled early detection of hereditary MTCs and prophylactic thyroidectomy for affected kindred. Histologic features of hereditary MCTs are of extreme importance

PS-03-092

Morphometric and ultrastructural analysis of pterygoid medial muscle after unilateral molar extraction: An experimental study

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Objective: To analyze morphometric and ultrastructural changes of pterygoid medial muscle (PTM), under occlusal defects, induced by unilateral left molar extraction, of Wistar rats.
Method: Thirty-six male rats: 24 for light microscopy (LM) and 12 for transmission electron microscopy (TEM), were divided into three groups (GI-15; GII-30; GIII-60 days), containing 5 animals/3 control each for LM and 3 animals/1 control for TEM. Morphometric studies were made measuring the area of PTM muscle fibers ipsi and contralateral to dental extraction. Qualitative analysis was performed to evaluate ultrastructural findings.
Results: There was a reduction of area of PTM of animals undergoing tooth extraction, both ipsi as contralateral. Both sides were similar when compared with each other, as assessed in the various evolutive periods. Differences were observed in fiber area, especially in first Group and these showed progressive increase, reaching their highest average in GIII. The ultrastructure showed asymmetry and disorganization of Z and I bands in PTM of GII.
Conclusion: Unilateral molar extraction can induce ipsi and contralateral morphometric changes of PTM with reduction of the fiber area. However, these fibers seem to adapt to these conditions throughout the experiment. Z and I bands are the most sensitive structures to this dysfunction, however these effects are transitory.

Sunday, 6 September 2015, 09.30 – 10.30, Restaurant
PS-04 Poster Session Infectious Diseases Pathology

PS-04-001

Langerhans cell histiocytosis of the thyroid gland: A report case

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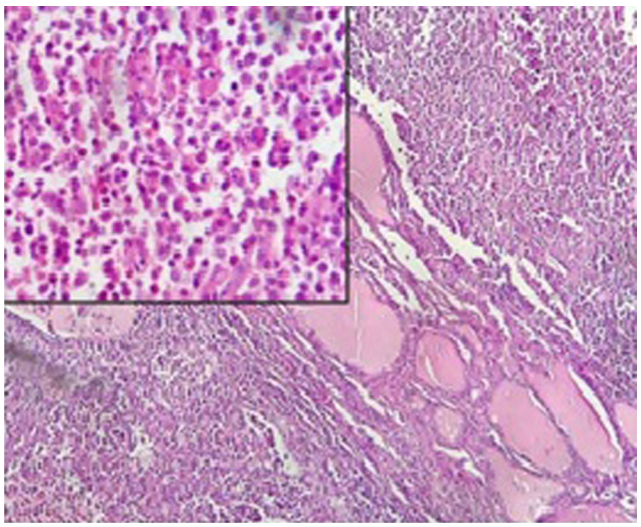
Objective: Langerhans cell histiocytosis has been called in several ways in medical history, depending on the anatomical location and also the name of (or) doctors who described this particular form of the disease. It is a neoplastic proliferation of Langerhans cells; the etiology is unknown. It occurs mostly in childhood. The bone is the first site of involvement (solitary eosinophilic granuloma) but many other organs can be involved (skin, lymph node, lung…). The thyroid is rarely affected; there are few cases reported.
Method: We report the case of a 26 years old man who undergoes a total thyroidectomy with lymph node dissection for suspicion of a process lymphomatous.
Results: Macroscopy: The thyroidectomy has two lobes mesuring respectively 6 × 4 × 3 and 5 × × 3 × 2 cm. When cut, we note the presence of grayish white fleshy in both lobes. Lymph node dissection reported 12 nodes. Histopathology: the thyroid gland and some lymph nodes are involved by nests of medium sized histiocytic cells with well defined cytoplasma, a folded or grooved nuclei that can be lobulated, the chromatin is finely dispersed and the nucleoli are inconspicuous, few mitosis are seen. The histiocytic cells are accompagnied with many eosinophils, small lymphocyts, and some neutrophils. Large focus of necrosis are identifined.The Langerhans cells express CD68, Ps100 and CD1a.
Conclusion: Langerhans cell histiocytosis of the thyroid gland are rare neoplasms; there are few cases reported in the literature. The histologic feature is characteristic and permits with the immunohistochimy to achieve a diagnosis even in the cases of unusual presentation.

Langerhans cell histiocytosis of the thyroid gland: He GX20:



PS-04-002

Pulmonal infection after the return from South America

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Objective: Histoplasmosis is a disease caused by fungus Histoplasma Capsulatum, which is found in soil or dust contaminated by bats' and birds' excrements. The occurrence is endemic as well as sporadic and humans are infected through the airway. Case Description: Two months after the return from tropical rain forests area in South America, a 24-year-old patient suffered from fever, headaches and haemoptysis for 2 weeks. The CT scan of the upper lobe of left lung showed a solitaire unconfined nodule of 13 mm and larger subhepatal lymphatic node. The patient's C-reactive protein was higher. There was a suspicion of atypical pneumonia and the patient started taking antibiotics. Bronchoscopia was negative. Mycoplasmosis and chlamydial infection were excluded. After 6 weeks the CT showed stationar nodule, subfebriles and haemorhagic sputum remained. There were TBC and tumour in the differencial diagnosis. TBC was excluded and the patient was indicated for the surgical revision of nodule. Peroperative biopsy showed a pulmonal process with central caseous necrosis similar to tuberculoma. Special methods detected microorganisms with Histoplasma capsulatum morphology.
Conclusion: Pulmonary histoplasmosis with morphology of granulomatous inflammation may occure in immunocompetent individuals as a solitary pulmonary nodule and may mimic the pulmonary cancer in radiologic findings.

PS-04-003

Subcutaneous dirofilariasis mimicking lipoma: case report of an emerging zoonosis

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Objective: Dirofilariasis is an emerging zoonotic infection caused by filarial nematodes transmitted to humans by mosquitoes. Human Dirofilariasis is rare and can be classified as pulmonary, subcutaneous, visceral and ophthalmic. We report a case of human Dirofilariasis from Greece with subcutaneous presentation.
Method: A 62-year-old male from the city of Patras presented with a palpable painless subcutaneous nodule in the anterior chest wall of 4 months' duration. An excision biopsy was performed.
Results: The gross examination revealed a gray-white 0.7 cm nodule. The pathological examination showed a central necrotic area surrounded by chronic inflammatory infiltrates. Necrotic tissue was found to contain multiple cross-sections of a nematode with a thick cuticle, surrounded by foreign-body giant cells, morphologically identified as Dirofilaria species.
Conclusion: Our case suggests that Dirofilariasis should be considered in the differential diagnosis of subcutaneous nodules in endemic countries and that the morphological features of the worm can facilitate the identification of the parasite.

PS-04-004

Primary tuberculosis of the penis in a young patient: A case report

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Objective: Although tuberculosis can affect any organ, penile tuberculosis is an extremely rare disease. It is occasionally associated with other entities, such as HIV infection, and reflects different modes of transmission.
Method: We report a case of an immunocompetent 17 year old male who presented with an ulcerated lesion of the penis.
Results: A 17 year old patient was admitted with history of a persistent, painful balanopreputial ulcer for the preceding 6 weeks. Bilateral inguinal lymph nodes were enlarged, firm and mobile. The biopsy of the lesion showed evidence of tuberculosis which was confirmed by a positive mantoux test. Gram, Ziehl-Neelsen, Giemsa and Grocott stains all yielded negative results. The HIV test was negative. The findings on a chest radiograph and abdominal ultrasound were normal. Successful treatment was achieved by combined tuberculostatic and surgical approach with circumcision.
Conclusion: Diagnosis of penile tuberculosis is often difficult because it can mimic numerous other diseases. This case emphasizes that the possibility of tuberculosis as the cause of a chronic ulcer on the penis should be kept in mind.

PS-04-005

Dying of tuberculosis in the 21st century: A case of intestinal tuberculosis

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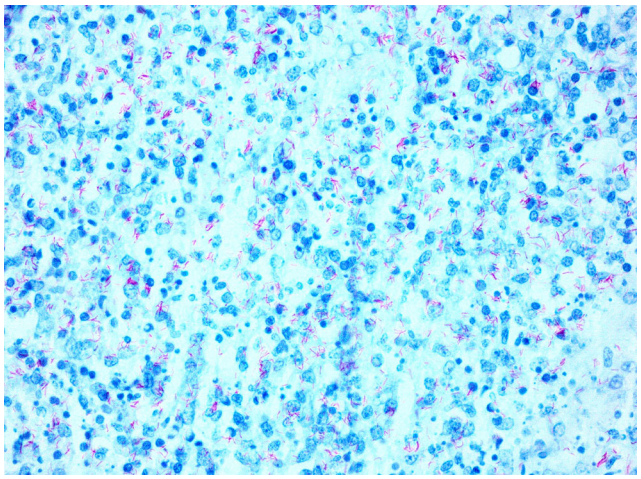
Objective: Tuberculosis (TB) is a disease caused by Mycobacterium tuberculosis and remains one of the world's deadliest infectious diseases. We will report a case.
Method: A 73 years old female presented to our hospital with abdominal pain and fever. She also had systemic mastocitosis, ulcerative colitis and minor thalassemia. After 16 days of hospitalization she was still unwell. An abdominal angiography was requested to identify a possible source of bleeding. Five days after she was submitted to a laparotomy with the hypothesis of ischemic enteritis. A parcial enterectomy was performed. The patient died the next day.
Results: We received a small bowel specimen (23 cm length) perforated and with fibrinopurulent exudate on serosa. Microscopic examination revealed few epithelioid cell granulomas with necrosis. Superficial ulcers were present and also thickening of the wall due to serosal fibrosis. Acid fast bacilli were identified. We also observed involvement of small mesenteric vasculature by inflammation. The diagnosis was intestinal tuberculosis. Peritoneal fluid culture and microbiological testing supported our diagnosis.
Conclusion: Intestinal TB represents the sixth most frequent form of extra-pulmonary tuberculosis. Given that most deaths from TB are preventable, the death toll from the disease is still unacceptably high and efforts to combat it must be accelerated.

Acid fast bacilli (Zhiel Neelson, 400x):



PS-04-006

Reporting fungal infections: Nodal Cryptococcosis in a patient with chronic liver disease

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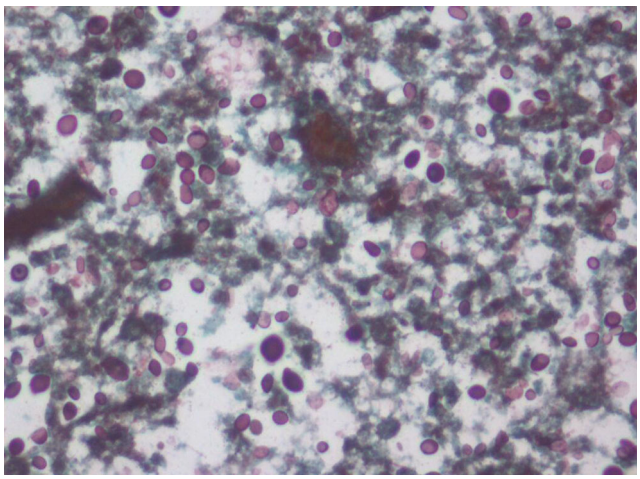
*Central Lisbon Hospital Centre, Dept. of Anatomic Pathology, Lisboa, Portugal

Objective: Cryptococcosis is a fungal disease caused by Cryptococcus. By inhalation and subsequent pulmonary infection, it may disseminate and cause meningitis or meningoencephalitis. Most cases occur in immunosuppressed hosts, including patients with HIV. We will report a case and highlight some clinical-pathologic considerations.
Method: We present the case of a 59 years old male with HIV and chronic liver disease caused by HCV. A CT revealed cervical lymphadenopathy.

A lymph node biopsy was performed and stained with special stains. Simultaneously, the patient started to decompensate from his liver disease.
Results: The microscopic examination revealed pleomorphic, round/oval yeasts with a mucinous capsule that stained bright red with mucicarmine; some were unencapsulated and had a narrow necked budding. The pathology report only said "Nodal Cryptococcosis". The research for Cryptococcus neoformans's antigen in blood was negative. These apparently no concordant results made infectologists carefully consider the introduction of antifungal medicines, that are hepatotoxic, so we asked for two external consultations, both corroborated our diagnosis.
Conclusion: Providing descriptions of the fungal elements in the tissue sections with a comment listing possible organisms that can show that morphology should help managing discrepancies between serology results and histopathology. After this case we started to report fungal infections differently.

Nodal cryptococcosis (Grocott, 400):



PS-04-008
Onchocerciasis in Serbia: Case report
M. Nikolic*, S. Milenkovic, Z. Vukasinovic Bokun, L. Prijic Plecevic, M. Lavrnic, M. Kiurski, N. Miladinovic
*KBC Zemun, Dept. of Pathology, Belgrade, Serbia

Objective: Onchocerciasis is a parasitic infection caused by nematode Onchocerca volvulus which is transmitted by the bite of black fly (genus Simulium). Onchocerciasis is a chronic multisystem disease with dermatologic, ocular and systemic manifestation.The adult worms elicit a strong granulomatous response known as onchocercoma.
Method: A 77 year old man was admitted to the Clinical Hospital Center Zemun because of the presence of a tumour on the left lateral side of the nose.
Results: Macroscopic examination showed the presence of an oval subcutaneous nodule, 14 mm in diameter, with normal overlying skin. Histological examination revealed a granulomatous inflammatory nodule in the reticular dermis, and on the border between the dermis and subcutaneous tissue. Adult worms of O. volvulus were identified within the center of the nodule, surrounded by numerous eosinophils and lymphocytes. The uteri of female adult O.volvulus worms contained eggs and microfilariae.
Conclusion: Onchocerciasis is known to be endemic in 37 countries throughout West and Central Africa, Central and South America, and parts of the Arabian Peninsula. It is estimated that 17–18 million persons worldwide are infected with O. volvulus, the vast majority of whom live in Africa (about 90 %). This case is noteworthy because the disease is uncommon outside endemic areas.

PS-04-010
Sex differences of experimentally induced systemic inflammatory response syndrome
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Objective: A study of morphological and immunological features of sex differences in experimentally induced systemic inflammatory response syndrome (SIRS).
Method: SIRS was induced by intraperitoneal LPS injection of O26:B6 E.coli strain at a dose of 1,5 mg/kg to mature males and females (in proestrus phase) Wistar rats. On the first day after LPS administration alterative changes of the liver, the degree of neutrophil infiltration in alveolar septa, structural changes of the thymus and spleen have been estimated. The levels of endotoxin, corticosterone, as well as AlAT and AsAT activity have been measured in the serum. The levels of IL2, IL4, IL6, IFNγ, TNFα produced by ConA activated splenic cell have been estimated in cultural fluid by ELISA.
Results: As compared with males in females SIRS was characterized by less pronounced inflammatory changes in the liver and the lung, accidental involution of the thymus, decrease of IL6 and rise of TNFα. In males SIRS was accompanied by increase of endotoxin and IL2 level, decrease of corticosterone, strongly pronounced inflammatory changes in the liver and the lung, accidental involution of the thymus.
Conclusion: In the experimentally induced SIRS morphological and immunological manifestations in males Wistar rats were more pronounced in comparison with females.

PS-04-011
Schistosoma in histopathological specimens in an European context: Series of 7 portuguese cases
R. Oliveira*, A. Costa Braga, R. Theias Manso, M. Ferreira
*Hospital Prof. Doutor Fernando, Lisboa, Portugal

Objective: Schistosomiasis is the second most common parasitic infection in humans. Although Europe is not endemic, considering globalization and some environmental factors, this is not an entity completely apart from the European reality.
Method: We searched in our database (SNOMED computer search) schistosomiasis cases between 2000 and 2015. We were able to identify 7.
Results: Mean age of diagnosis was 43,14. Sex ratio was 4:3. From the 7 cases: 6 were biopsies and 1 was a surgical specimen. 4 from gastrointestinal tract and 3 from genitourinary tract. Two of these cases had history of co-infection with HIV and 1 case with HBV. One of the cases, a urinary bladder biopsy, from one of the HIV+ patients was also diagnostic for squamous cell carcinoma; soon after the diagnosis the patient died. Histologically it was observed, in some, a granulomatous reaction that surrounded the schistosoma ova (with miracidium) and in others, a more calcified schistosoma ova within a fibrotic stroma.
Conclusion: All the reported cases were associated with migration (Portuguese-speaking African countries). In this population HIV and HBV infection is highly prevalent. Concerning HIV, dually infected patients with schistosomiasis and HIV may pose an additional risk of HIV transmition. Concerning HBV, the data is scarce and controversial.

Sunday, 6 September 2015, 09.30 - 10.30, Restaurant
PS-05 Poster Session Paediatric and Perinatal Pathology

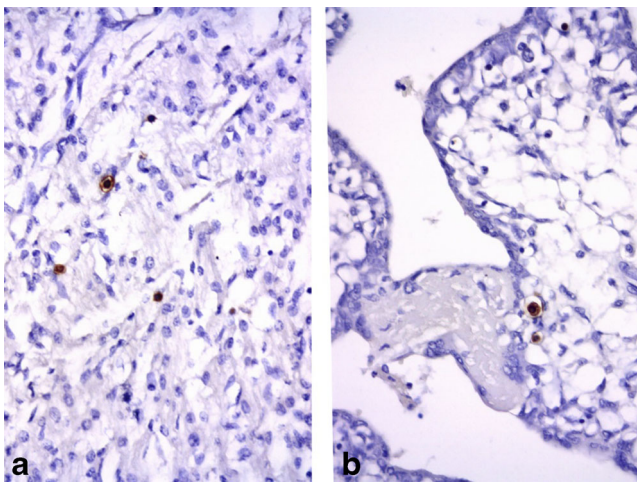
PS-05-001

A case of intrauterine parvovirus B19 infection

A. Kolobov*, V. Karev
*St. Petersburg State University, Dept. of Pathology, Russia

Objective: Human parvovirus B19 is a single-stranded DNA virus. During pregnancy, parvovirus B19 infection can be asymptomatic or cause a variety of signs of fetal damage, fetal anemia, nonimmune hydrops fetalis, spontaneous abortion and can result in fetal death. We report of the case of vertical parvovirus B19 infection.
Method: The case of intrauterine death at 22 weeks of gestation. B19-virus-specific immunostains (NCL-PARVO, Novocastra) were studied.
Results: Birth weight was 630 g. We find hydrops fetalis and congenital lung hypoplasia. Histology the presence of viral myocarditis with lymphocytic invasion and "lantern cells". Macroscopic placental examination shows slight and unspecific changes. The placenta's weight was 700 g. Histology may show villitis with lymphocytic invasion and "lantern cells". B19-virus-specific immunostains with brain, lung, liver, myocardium, and placenta were studied. Myocardium and placenta were positive.
Conclusion: Thus, this case demonstrates intrauterine parvovirus B19 infection with hydrops, myocarditis and specific villitis of placenta.

B19-virus positive cells in myocardium (A) and placenta (B), IHC, x200:



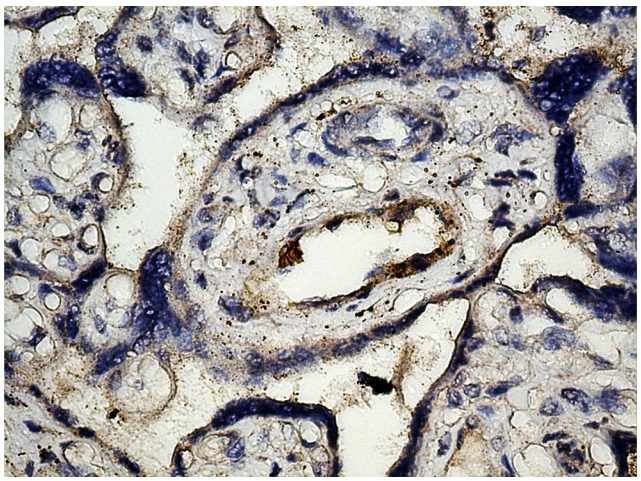
PS-05-002

Expression of the Nkx-2.2 in human placenta

A. Kolobov*, V. Melnikova, V. Karev, E. Gorbunov
*St. Petersburg State University, Dept. of Pathology, Russia

Objective: The development of the neural tube in the complex central nervous system results morphological, cellular and molecular changes, all of which are strictly regulated. Homeobox protein Nkx-2.2 contains a homeobox domain and may be involved in the morphogenesis of the central nervous system. Neural tube defects (anencephaly, cephalocele, spina bifida) are considered to be the most common and severe ones among congenital malformations. The purpose of the investigation was studying expression of the Nkx-2.2 in human placentas from stillborns with anencephaly.
Method: The placentas were collected from the two groups of patients: Group A - placentas from the stillborns with anencephaly ($n = 15$); Group B - placentas from the neonates without any congenital defects ($n = 20$). Nkx-2.2 expression was studied immunohistochemically using mouse monoclonal antibody to Nkx-2.2 (Anti-Nkx-2.2, Abcam). Further morphometric analyses were carried out with the Leica QWin Standard v2.8 program.
Results: The expression of Nkx-2.2 was found in Group B placentas. The expression area of Nkx-2.2 in endothelial cells of vessels of villi comprised 0,82 ± 0,08 %. Expression of Nkx-2.2 in Group A placentas (stillborns with anencephaly) was not found.
Conclusion: Thus, expression of the Nkx-2.2 in placentas from stillborns with anencephaly is absent.

Expression of Nkx-2.2 in endothelial cells of vessels of villi, IHC, x400:



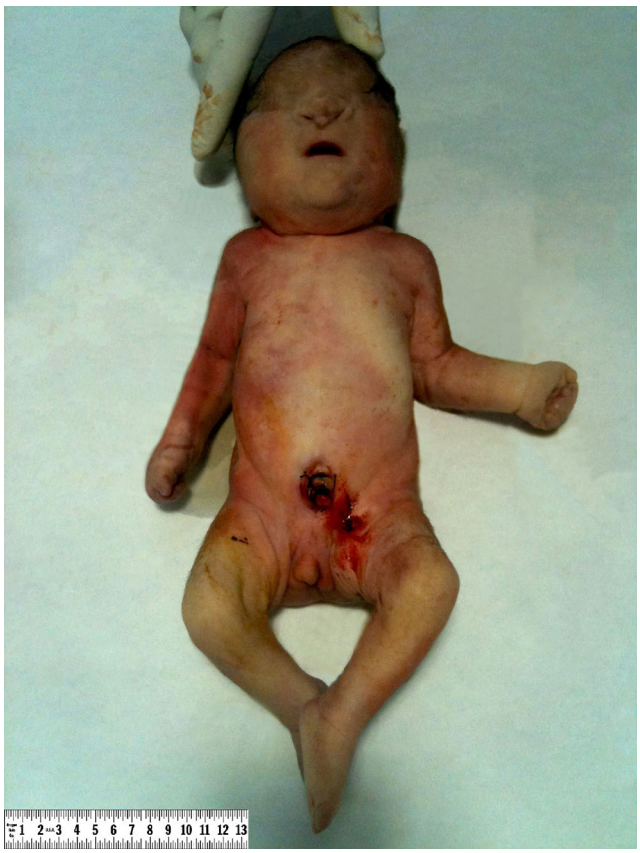
PS-05-004

Bilateral paraovarian ectopic adrenal tissue: A rare feature of Fraser syndrome

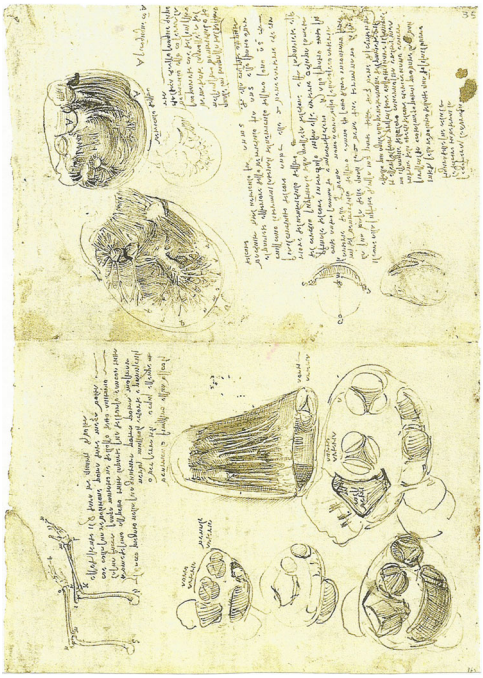
A. V. Dumitru*, G. Simion, A. Emanoil, M. Costache, M. Sajin, T. A. Georgescu, D. Secara
*Emergency University Hospital, Dept. of Pathology, Bucharest, Romania

Objective: Fraser syndrome is a very rare autosomal recessive disorder characterized by major features such as cryptophthalmos, syndactyly, malformations of the larynx and genitourinary tract, craniofacial dysmorphism, mental retardation, and musculoskeletal anomalies.
Method: An autopsy was performed on a female newborn with multiple congenital malformations to determine the cause of death.
Results: Gross examination revelead a severe facial dysmorphism with bilateral cryptophthalmos, low set ears, flat nasal bridge, micrognathia and incomplete ossification of the skull bones. We noticed bilateral complete syndactyly of both hands and feet. Also the newborn had an umbilical hernia, impersorate anus and ambiguous genitalia. Major internal organ anommalies were observed: hypoplastic lungs, bilateral renal agenesia with hypertophic adrenal glands, hypoplasic bladder. We also noticed two small paraovarian nodules which proved to be ectopic adrenal tissue on histopathological examination.
Conclusion: The diagnosis of Fraser syndrome can be made on clinical examination using the diagnostic criteria proposed by Thomas et al. As far as we know this is the first case diagnosed and reported in Romania.

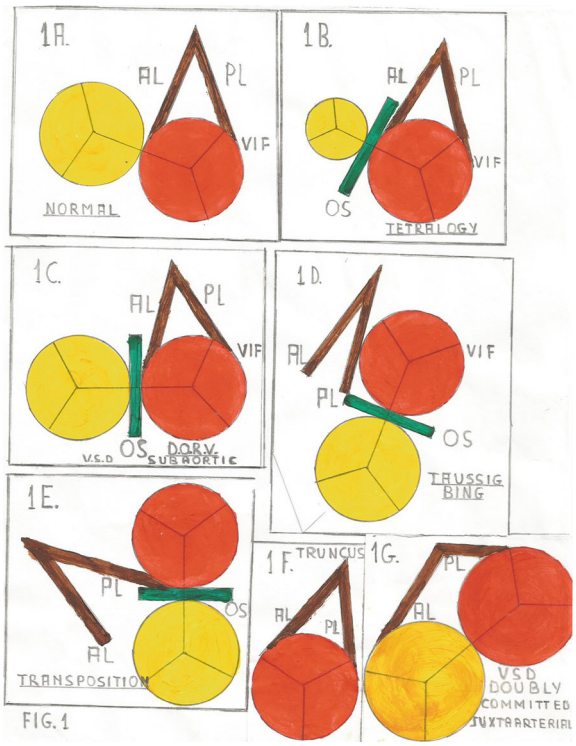
Phenotypic features of Fraser syndrome:



Leonardo's cord:



Leonardo's cord:



PS-05-005

Potential treatment of complex congenital heart malformations during cardiac morphogenesis.

A. Capuani*

*Private Practice, Cardiothoracic Surgery, Carrara, Italy

Objective: To investigate the mal- rotation of the trabecula septo-marginalis (TSM, Leonardo's cord) within cardiac looping in order to treat during cardiogenesis the ventriculo-arterial malformations.

Method: We observed the TSM in the most common cardiac phenotypes of ventriculo-arterial malformations (Tetralogy of Fallot, Double Outlet Ventricles, Transpositions of Great Arteries, Single Outlets) and we reviewed the up to date knowledge on genetic and epigenetic factors involved in cardiac looping.

Results: The anatomical observations support the hypothesis that the abnormal ventriculo-arterial connections are successive stages of the same TSM's malrotation process at ventricular level. We identified the counter-clockwise rotation of the outlet septum and the trabecula septomarginalis as anatomical landmarks to describe sequentially all these malformations which account the majority of the most complex congenital heart diseases.

Conclusion: The TSM follows the development of the right ventricle. The knowledge of the cardiac embryo-genetic factors determining the mal-rotation of the TSM will allow to interfere on the cardio-genesis modifying the ventricular development and finally reducing the incidence and the severity of the pathological phenotypes. With the recent developments of molecular biology we advocate protocols to investigate the sequential mal-rotation of the TSM in human cardiac tissues.

PS-05-007

Congenital cytomegalic inclusion disease with Disseminated Herpes Simplex Infection

J. Amidzic*, N. Vuckovic, I. Capo, M. Mocko Kacanski, A. Fejsa Levakov, J. Ilic Sabo
*Clinical Centre of Vojvodina, Centre for Pathology and Histology, Novi Sad, Serbia

Objective: Cytomegalovirus (CMV) and Herpes Simplex Virus (HSV) represent the major infectious causes of fetal and neonatal malformations in developed countries, as well as important pathogens that can lead to miscarriage.
Method: We report a case of fetal cytomegalic inclusion disease with disseminated Herpes Simplex Virus infection.
Results: Ultrasound examination performed routinely during pregnancy indicated the presence of fetal cerebral abnormalities (lissencephaly and ventriculomegaly). The pregnancy was electively terminated at 31st week gestation. The autopsy showed brain with smooth surface appearance without normal convolutions and absence of gyri and sulci in cerebral cortex, dilated lateral ventricles and occipitoparietal encephalomalatia. The histopathological examination of autopsy tissues taken from the brain, lung, kidneys and liver showed numerous enlarged cells containing prominent eosinophilic nuclear inclusions, that are pathognomonic for CMV infection. Multinucleated giant cells associated with HSV infection were found in all mentioned organs. Sections from the placenta showed features of mild chronic villitis and rare CMV inclusion-bearing cytotrophoblast cells.
Conclusion: Documentary evidence of histopathological detection of CMV inclusions in multiple organs are very sparse in literature. This case has been reviewed to highlight the causal relationship of viral infections in early pregnancy and abnormalities of the central nervous system.

PS-05-008

Distribution of the interstitial cells of cajal in the human choledochal cysts and gallbladders

G. Akturk*, O. Z. Karakus, O. Ates, E. Gurlek Olgun, M. Dalgic, E. Ozer, G. Hakguder, M. Olguner, F. M. Akgur
*Dokuz Eylul Universitesi, Tip Fakultesi Tibbi Patoloji AD, Izmir, Turkey

Objective: Interstitial cells of Cajal (ICC) are distributed with smooth muscle cells throughout the gastrointestinal tract and responsible for autonomous contractility. Existence of the ICC is still not shown in the choledochal cysts. Herein, we aimed to show whether the ICC are present in human choledochal cysts or not.
Method: The specimens consist of 14 common biliary duct from choledochal cysts, 35 gallbladders from cholecystectomies and 10 autopsy specimens for the control group. pCD117/c-kit immunhistochemical antibodies were used in the study. Comparable sections were stained with 1 % toluidin blue to identify from mast cells. Mean numbers of ICC in five randomly selected high-power fields (x40) were compared used Kruskall-Wallis tests.
Results: The number of ICC was determined as mean 12.2 ± 4.9 in the gallbladders, 3.4 ± 1.4 in the choledochal cysts and 9.8 ± 2.9 in the control choledochal group. There is no difference between gallbladders and control choledochal groups ($p = 0.056$). There is significant difference between choledochal cyst and control choledochal groups ($p = 0.001$).
Conclusion: This study demonstrates that ICC has been lesser found in the human choledochal cyst structures than the gallbladder. The low number of ICC may be responsible for appearance of the choledochal cyst to be based on a contractile impairment.

PS-05-009

Blood cysts of heart valves: A case report

N. Vuckovic*, V. Pilija, D. Vuckovic, I. Capo, A. Fejsa Levakov
*Clinical Centre of Vojvodina, Centre for Pathology, Novi Sad, Serbia

Objective: Blood cysts are exceptionally rare and could be diagnosed in various areas of the heart valves. Usually it is a solitary lesion on mitral valve in childhood.
Method: The female neonate, 27 days, 53 cm, 3450 g, was found dead in early morning hours. Previously, baby was healthy, well nourished, non neglected. Up to the day before, when she started to cough, and scheduled for next day regular pediatrician control. After the meal around midnight without problems she fell asleep, alone in the bed.
Results: The autopsy was performed with a spectrum of toxicological analyses. At the mitral cusps, on the tricuspidal cusps and on semilunar aortic cusps, on free valvular margin multiple blood cysts were diagnosed. Cysts were oval, up to 1 cm in diameter. The visceral pleural surface was with petechial hemorrhages, and on cut the lung tissue was slightly hyperaemic. Histology was consistent with mild viral pneumonia. Other organs and tests were within normal limits.
Conclusion: It is still unclear what the significance of heart blood cysts is, and if they could contribute to this neonatal death. The exact etiology and incidence is not yet estimated.

PS-05-010

Lymphangioma of the small bowel mesentery: A case report

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*Clinical Centre of Vojvodina, Centre for Pathology, Novi Sad, Serbia

Objective: Lymphangioma is a rather rare, benign condition characterized by proliferation of lymph vessels. Usually, it is located in the head and neck area and exceptionally in the small bowel mesentery.
Method: 3.5- year- old boy was admitted to hospital due to acute abdominal pain. The mass was diagnosed as tumour located in the small intestine. The resected part of small intestine 10 cm long with neighboring mesenterial tissue was submitted to Pathology. The termino-terminal anastomosis was performed. There were no complications during or after the surgery.
Results: On gross examination, the multiple cystic spaces were noticed on the mesenterial surface close to small bowel. The cysts were with milky white material or with serous yellow fluid, thin walled, smooth surface, from several mm to 3 cm. The small intestine mucosa, submucosa and muscle layers, blood vessels, ganglion cells and nerves were within normal limits. Cysts were covered with flattened endothelium, somewhere with smooth muscle and fibrous tissue in the wall. The diagnosis of cystic lymphangioma was made.
Conclusion: Although rare, lymphangioma can occur in the abdomen and can be the cause of acute abdominal pain or even ileus.

PS-05-011

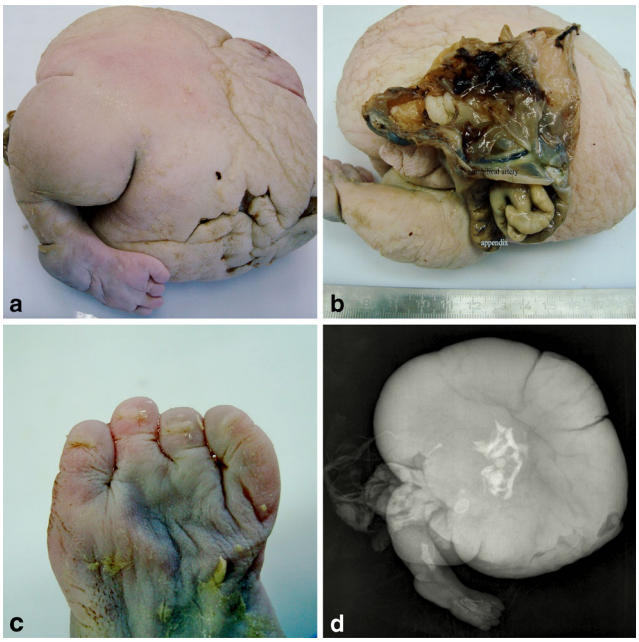
Acardius acephalus fetus - description of distinctive anomalies within TRAP sequence

P. Lewitowicz*, A. Wincewicz, D. Koziel, J. Matykiewicz, A. Horecka-Lewitowicz, M. Koda, L. Kanczuga-Koda, S. Gluszek, S. Sulkowski
*Jan Kochanowski University, Dept. of Pathology, Kielce, Poland

Objective: Acardiac fetuses are consequences of twin reversed arterial perfusion (TRAP). Here we present a case of maldeveloped fetus of 40-year-old gravida IX who in addition gave birth to a healthy, female child by a cesarean section.
Method: Twin placenta within intrauterine mass of maldeveloped fetus was fixed in formalin dissected and sampled for H&E slides.
Results: A diamnion monochorion type of twin placenta was recorded with incorrect single umbilical arteries (SUA) both in umbilical cord of

newborn and in atrophic second umbilical cord. A 1020 g malformed fetus consisted of rather well formed lower leg with four digital foot and amorphous body mass with omphalocoele and intestinal eventeration. X-ray showed discernible metatarsal and femur bone and undefined small bone cluster in the central part. In the centre of body mass a cavity contained intestines, which demonstrated a multifocal lumen atresia, blind terminal ends, persisting appendix, colon mucosa and scattered in between heterotopic pilosebaceus residues, remnants of adrenal glands, ganglia and neuroepithelium-covered nests. The macroscopic analysis of circulatory system implied that arterial supply of bones comprised anastomosing vascularity type originated from the end of umbilical artery.

Conclusion: The reported case was diagnosed as acardius acephalus with a peculiar pattern of organ malformations.



PS-05-012

On two rare hamartomatous lesions of the lungs in children

D. Mitkov*, T. Boshnakova, V. Mihailova
*5th Multiprofile Hospital, Dept. of Clinical Pathology, Sofia, Bulgaria

Objective: Two rare cases of congenital adenomatoid malformation (CAM) and multiple chondromatous hamartoma (MCHH) in the lungs of children are presented.

Results: The first case is CAM - hamartomatous lesion in which the main abnormality is an "adenomatoid" increase in the terminal respiratory structures (P.S. Hasleton, 1985). There are three subtypes of the disease, distinguished on the basis of the size of the formed cysts, extend of the lung involved and histologic features (Stocker et al, 1978). Our case is type III of CAM, which is a solid variant and affects an entire lobe. It is 17 days old girl born from second pregnancy after sectio Caesarea, after being 17 days on assistent ventilation and oxygen therapy, developed bronchopulmonary displasis and died. The postmortem histologic examination of the left lower lobe was consistent with immature canalicular stage lung - CAM type III. The second case is a rare multiple endobronchial CHH in 5 years old girl, born from a first uncomplicated pregnancy. The clinical symptoms started 6 months prior to hospital admission with cough, fever, and clinical and chest X Ray signs of atelectasis of the left lung. After left sided thoracotomy the gross specimen consisted of fully atelectatic dark blue parenchyma, with nodules of 1 to 3 cm in size, contained of islands of hyaline cartilage, glandular elements, smooth muscle fibers and cleft like spaces lined by cuboidal and ciliated epithelium. The preoperative diagnosis of the case presented a difficult problem.

PS-05-013

A case of craniolacunia associated with hydrocephaly and spina bifida aperta

I. Brainova-Michich*, L. Jelev, V. Ivanova, T. Dikov, A. Alexandrov, S. Hristov
*Medical University Sofia, Dept. of Forensic Medicine, Bulgaria

Objective: The first scientific publications describing the clinical and morphological complex of craniolacunia date back to 1941 and the discussion of its clinical significance continues.

Method: We present an autopsy case of 42-days old male child with multiple neural tube defects (NTDs). The gross examination of the cadaver revealed: hydrocephalus and open spina bifida at the level of 8th-9th thoracic vertebra with leakage of liquor, separated sutures between the skull bones and wide open fontanels, craniolacunia of the occipital bone and cranial basis, and occipital cleft.

Results: The histological examination showed widely spaced intertrabecular areas of the cranial bones, filled with normal appearing bone marrow; congenital bronchiectasias, lung and brain edema and venous congestion of the other internal organs.

Conclusion: NTDs still remain life-threatening conditions with high mortality rate in infants. They are one of the most frequent birth defects with complex and not fully understood etiology. Craniolacunia is usually associated with other NTDs. In cases of NTDs, X-ray examination might be useful as a part of the diagnostic algorithm for establishing presence of associated craniolacunia and identification of complicated anomalies.

PS-05-014

The relationship between apoptotic activity and prognostic factors in neuroblastomas

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Objective: The prognostic parameters established in determining risk groups of neuroblastoma for treatment are cellular differentiation, mitosis karyorrhexis index (MKI), the N-myc amplification and age. We aimed to study the prognostic significance of apoptotic activity in NBs.

Method: The study included 35 primary NB cases. The differentiation and MKI of neuroblasts were evaluated in H&E slides. Tumoural apoptotic activity was assessed by both immunohistochemical staining with bcl-2 and TUNEL method. The results were correlated with other prognostic factors and clinical outcome.

Results: Twenty-five(71.4 %) NBs were located in the adrenal. Sixteen(45.7 %) cases showed low and 19(%54.3) high MKI. Thirty-three(%94) NBs were immunopositive for bcl-2. The bcl-2 immunostaining scoring was <5% in 2(5.7 %) cases, 5–75 % in 6(17.1 %) and >75 % in 27(77.1 %). Of the remaining positive 33 cases, 14(40 %) NBs had the apoptotic index(AI) of ≤2 %, 11(31.4 %) of 2–4 % and 8(22.8 %) of ≥4 %. NB cases located in adrenal showed higher scores of bcl-2 positivity compared to extraadrenal tumours. AI was found to be significantly lower in girls. Statistically significant difference was observed between bcl-2 scoring and tumour localization.

Conclusion: Our results showed that apoptotic activity is unlikely to be a prognostic parameter in NB. We conclude that larger series and different methodologies are needed to evaluate the real prognostic value of apoptotic activity in NB.

PS-05-015

An immature cervical teratoma in a newborn: Report of a case

C. Pontinha*, C. Araujo, M. Ferraz-Oliveira, M. Mafra, M. Martins, A. Silva, V. Vital, P. Alves
*Central Lisbon Hospital Centre, Dept. of Anatomic Pathology, Lisboa, Portugal

Objective: Congenital teratomas tend to be extragonadal and histologically benign but carry a high mortality due to premature delivery of the baby. The usual site for congenital teratomas is sacrococcygeal region. These tumours are rare in neck region. Improvement in survival rates of these patients raises questions regarding the prognostic significance of immature germ cell elements. We will report a case and highlight some clinical-pathologic considerations.
Method: We present the case of a female newborn with 2 days of life, with a large cervical mass. Ultrasonography revealed a well circumscribed tumour, multilocular and with fluid density, suggesting cystic lymphangioma. Surgical specimen was sent for pathologic study.
Results: We received a 6 × 5 × 3 cm tumour, rubbery and partially cystic. Microscopic examination revealed an immature teratoma that demonstrated several mesodermal elements and immature neural tissue. The tumour was not completely removed.
Conclusion: Tumours affecting the fetus and newborn differ from those found in older children and adults, leading to diagnostic and therapeutic challenges. Clinical behavior of congenital teratomas is determined predominantly by whether or not the tumour can be completely resected. Histological tumour immaturity does not appear to correlate with malignancy. The long-term outcome with cervical teratoma is still to be elucidated.

PS-05-016

Prune belly syndrome - a report of a case associated with exceptional heart anomalies

M. Rassy*, M. Bosic, J. Vasiljevic, J. Markovic-Lipkovski
*Saint Joseph University, Faculty of Medicine, Dept. of Pathology, Beirut, Lebanon

Objective: Heart anomalies in Prune belly syndrome are rarely described in the literature. We hereby report a case of Prune belly syndrome with unique complex heart anomalies.
Method: The case concerns a 3-month old male deceased patient, with prior episodes of necrotizing entero-colitis, requiring several subsequent surgical small bowel resections. An autopsy was performed.
Results: On autopsy, generalized hypotrophy of skeletal muscles, urogenital and heart anomalies were most prominent. The abdomen was distended, with ascites and a thin wrinkled skin. At the urogenital level, cryptorchidism and bilateral hydroureteronephrosis were noted. Microscopic examination of the kidneys revealed preserved tissue architecture with rare dilated tubules. Heart anomalies were multiple and complex, consisting of a common atrium, a ventricular septal defect, a hypoplastic right ventricle and a hyperplastic left ventricle. Moreover, persistent left superior vena cava and patent ductus arteriosus were present. Other findings included bilateral hydrothorax and pulmonary hemorrhage and condensation. Lung sections revealed signs of diffuse alveolar damage, considered as the cause of death. The diagnosis of Prune belly syndrome associated with complex congenital heart anomalies was also made.
Conclusion: Heart anomalies in Prune belly syndrome should be carefully studied since their complexity can affect survival of such patients.

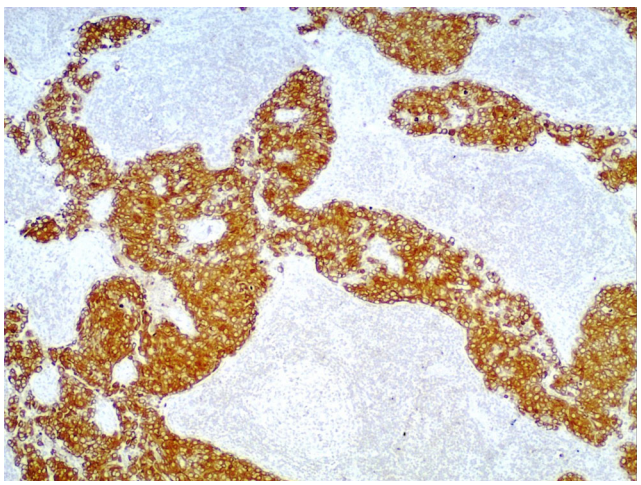
PS-05-017

Case report: Thymic carcinoma in a three-year-old child

D. Serteva*, E. Poriazova, V. Belovezhdov, M. Kamenova
*Medical University Plovdiv, General and Clinical Pathology, Bulgaria

Objective: The aim of this paper is to present a rare case of thymic nonkeratizing squamous cell carcinoma in a 3-year-old child.
Method: Clinical information, retrieved from medical records and computed tomography; routine pathohistological examination with hematoxilin/eosin staining, accompanied by a large immunohistochemical panel.
Results: We present a rare case of poorly differentiated nonkeratinizing squamous cell carcinoma of the thymus in a 3-year-old girl. According to the clinical data, there are two tumour formations located in the mediastinum and multiple bilateral lymph node metastases along the sternocleidomastoid muscles. The tumour was diagnosed on an excisional biopsy of a metastatic lymph node. It is composed of nests of malignant epithelial cells, which lack keratin production. The diagnosis is substantiated by an extensive immunohistochemical panel.
Conclusion: Thymomas, thymic neuroendocrine epithelial tumours and thymic carcinomas comprise the group of epithelial tumours of the thymus. They are rare and usually seen in the fourth and fifth decades of life. Thymic carcinomas constitute only 4–14 % of thymic epithelial neoplasms. Mediastinal tumours in children are heterogeneous and thymic neoplasms, in particular, are exceptionally rare, observed in only 1,5 %. Thymic carcinomas have aggressive behavior and are often diagnosed at inoperable stages, as in the reported case.

CK AE1/AE3, positive reaction in nests of squamous cell carcinoma. Metastasis in a lymph node:



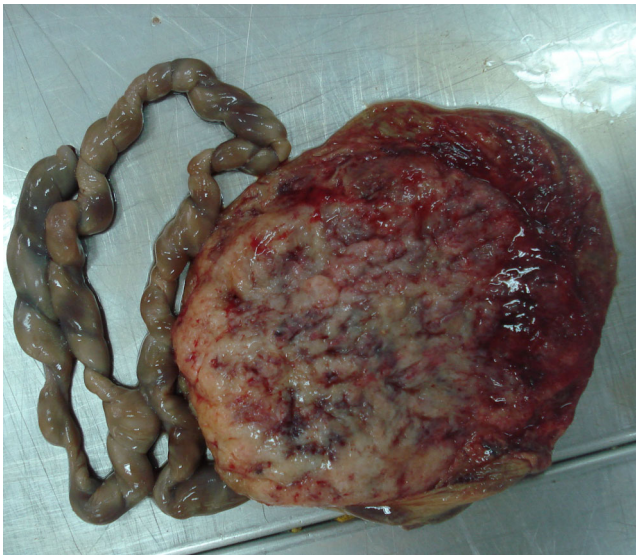
PS-05-018

Maternal floor infarction associated with umbilical cord hypercoiling

M. Taweevisit*, P. Thorner
*Chulalongkorn University, Dept. of Pathology, Bangkok, Thailand

Objective: To study maternal floor infarction (MFI) co-occurring with umbilical cord hypercoiling in a macerated fetus.
Method: The mother was a 28-year-old woman with initially unremarkable pregnancy. This was her 3rd pregnancy. The previous two pregnancies had been uneventful. During routine antenatal care, fetal ultrasound had shown discrepancy of fetal size and gestational age. At 34 weeks, she delivered a macerated male fetus, weighing 400 g without congenital anomaly.
Results: The placenta revealed confluent firm, stiff, convoluted yellow-white rind-like area on the maternal surface, extending into the placental substance as ramified yellow-white strands, accounting for approximately 40 % of the placental volume. Histology demonstrated eosinophilic fibrinoid material obliterating the intervillous space and separating chorionic villi. The villous capillaries had involuted, with persistence of villous stromal cells and villous outlines. The umbilical cord was hypercoiling, recognized as 0.8 coils/cm (>90 percentile; >0.3 coils/cm).
Conclusion: This is the first report of co-occurrence of MFI and umbilical cord hypercoiling. Such changes might cause the hydrostatic pressure gradient imbalance between villous stroma and intervillous space, involving in pathogenesis of MFI.

MFI co-occurring with umbilical cord hypercoiling:



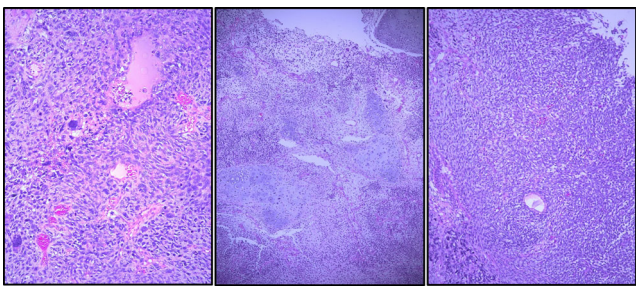
PS-05-019

Anaplastic sarcoma of the kidney: A rare unique renal neoplasm

M. H. Arabi*, H. Al-Maghraby, A. Yamani, Y. Yousef, H. Huwait
*King Abdul-Aziz Medical City, Dept. of Pathology, Jeddah, Saudi Arabia

Objective: Anaplastic sarcoma of the kidney (ASK) is an extremely rare pediatric tumour which usually presents as a large renal mass with less than 30 cases have been reported so far in the literature. Herein we present a case of this rare entity.
Method: A 3- year-old girl, presented with a large abdominal mass. Pelvic and abdominal CT-scan showed 17.3 × 11 × 15cm large right renal multi-loculated mass. The cut surface of the nephrectomy specimen showed a multiloculated cystic mass formed of variable-size cysts filled with clear serous fluid with adjacent solid areas showing focal hemorrhage and necrosis. Microscopically, the tumour is composed of pleomorphic mesenchymal spindle cells with marked atypia, associated with chondroid differentiation (benign and malignant) and focal round primitive mesenchymal (blastema-like) cells. Focal myxoid and rhabdoid differentiation is present. Tumour cells are positive for vimentin, CD56, desmin and negative for WT-1, CK AE1/3, CK7 and EMA.
Results: Based on the histomorphology, immunohistochemistry, and literature review, the present features were most consistent with the newly described entity Anaplastic sarcoma of the kidney (ASK).
Conclusion: ASK is an unusual renal neoplasm of unknown origin and pathogenesis. The treatment options are yet to be standardized.

Pleomorphic mesenchymal spindle cells with marked atypia associated with chondroid differentiation and focal round primitive mesenchymal cells:



PS-05-020

Bone sarcoma with BCOR/CCNB3 gene fusion: Report of two new pediatric cases

S. Boudjemaa*, J. M. Guinebretiere, L. Dainese, S. Hachemane, G. Leverger, A. Coulomb
*Hopital Armand Trousseau, Dept. de Pathologie, Paris, France

Objective: Ewing sarcoma family of tumours comprises heterogeneous osseous and extra-osseous small blue round cell tumours (SBRCT) with EWSR1-ETS translocation. In a subset of bone tumours with the same characteristics but lacking the canonical EWSR1-ETS translocation, a new BCOR-CCNB3 gene fusion has recently been identified, suggesting a distinct biological profile. BCOR encodes the BCL6 co-repressor and CCNB3 encodes the testis specific cyclin B3, on the X chromosome. We report two new pediatric cases.
Method: Two boys aged of 8 and 9 years respectively presented knee pain with limping and pathological fracture of the femur.
Results: Imaging showed osteolytic femoral lesions without soft tissue extension. Histologically, the bone was infiltrated by SBRCT with strong CD99 and CD56 expression, consistent with Ewing sarcoma family of tumours. Transcripts, particularly EWSR1-ETS were negative. Further screening focused on BCOR/CCNB3 gene fusion was positive and tumour cells strongly expressed cyclin B3 and CCNB3 markers.
Conclusion: Bone sarcoma with BCOR-CCNB3 gene fusion is a newly described entity that should be taken into account by pediatric pathologists in the evaluation of osseous SBRCT. The potential usefulness of cyclin B3 and CCNB3 as reliable markers is highlighted by immunohistochemical data. Such new knowledge will hopefully improve classification and treatment of these rare sarcomas.

PS-05-021

Yellow hyaline membrane disease: A glimpse from the past

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Objective: The first cases of Yellow Hyaline Membrane Disease (YHMD) were seen in USA in the beginning of 1965, coinciding with the start of an active intensive care unit for premature infants and the era of prolonged survival of severe cases of respiratory distress syndrome in newborns. We illustrate the clinico-morphological features of YHMD with the last case examined by us in 1998.
Method: We present a case of an infant born with body weight 1050 g. Life threatening complications of pregnancy for the mother imposed delivery in the 28th gestational week by Cesarean section. Because of the infant's severe respiratory distress, intermittent positive-pressure ventilation was performed. On the 12th day the child died.
Results: The autopsy findings included brain and pulmonary hemorrhages. The histological examination of H&E stained slides revealed presence of bright yellow pigment localized on the luminal side of the eosinophilic hyaline membranes in the lungs and development of broncho-pulmonary dysplasia.
Conclusion: The occurrence of YHMD was a result of poor economic conditions at that time and the surfactant shortage in the hospitals. Hopefully, YHMD would remain a condition that is not seen in the practice nowadays and would be discussed only as a phenomenon with historical significance.

PS-05-022

Unilateral pulmonary agenesis: Report of a challenging case

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Objective: Pulmonary agenesis is a rare malformation with an estimated frequency of 1/10000–15000 autopsies. It consists in a complete absence

of lung, bronchus and pulmonary vessels of one or both sides and it may present isolated or in association with other anomalies. It has also been described as a feature of Goldenhar syndrome and Mardini-Nyhan association. Its etiology remains unclear, but abnormal development of the aortic arches during embryogenesis is considered a possible cause.

Method: We report a case of right lung agenesis encountered at a fetal autopsy at 14 weeks of gestation.

Results: First pregnancy of a 29-year-old female without recognizable risk factors for fetal abnormalities or family history of congenital malformations. Prenatal diagnosis included ultrasonography showing fetal hydrops with cystic hygroma. Fetal karyotype obtained by amniocentesis was normal (46, XX). Autopsy confirmed fetal hydrops and right lung agenesis, occipital encephalocele, cleft palate and hemivertebrae were detected.

Conclusion: Unilateral lung agenesis was first described by De Pozze in 1673. Although this anomaly is compatible with normal life, it presents varying degrees of severity. Prenatal diagnosis by ultrasonography is difficult and most cases are identified at autopsy rendering challenging differential diagnosis.

PS-05-023

Placental CCR5, BAX, CD34 and Ki67 placental expression in HIV-associated pregnancy

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Objective: HIV-associated pregnancy is not an uncommon condition in the recent years. Feto-placental sys-tem is highly sensitive to viral injury with HIV-induced vascular and immunologic placental disturb-ances being a most important cause of perinatal morbidity and mortality.

Method: 110 cases of HIV-associated pregnancy (study grope) and 280 cases of uncomplicated pregnancy (control group) were studied. Placental tissue was collected and immunohistochemical study was performed with antibodies to CCR5, BAX, CD34 and Ki67. Immune reaction was measured semiquantitative (by optical density) within the placental capillary endothelial cells, placental stromal cells and syncytiotrophoblast.

Results: CCR5 placental stromal cells expression was significantly elevated in the study group in compare to control ($p < 0.01$). CD34 endothelial expression revealed significantly elevated placental villi vascularity in the HIV-associated pregnancy group with a strong positive correlation between vascularity and the degree of placental insufficiency. BAX placental expression was significantly elevated in the study group (both endothelial and syncytial, $p < 0.05$) whereas placental cells prolifera-tion index (Ki67 expression) within the study group was significantly reduced ($p < 0.01$).

Conclusion: Revealed disturbances of placental CCR5 expression, villi vascularity and placental apoptosis and proliferation reflect the basic pathways of the development of HIV-induced placental insufficiency.

PS-05-024

Child with an unusual sacrococcygeal mass

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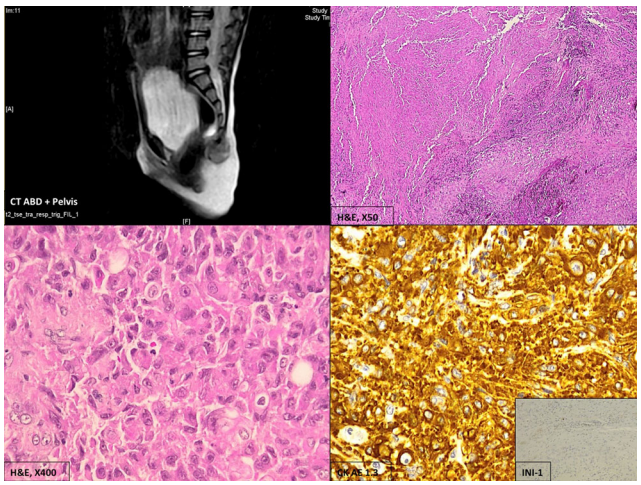
Objective: Epithelioid sarcoma is a rare malignant soft tissue tumour. Its occurrence in young children involving the sacrococcygeal region is even more rare. Herein, we present a rare case of an unusual saccrococcygeal mass in a child.

Method: A 3-year old girl presents with a sacrococcygeal mass. The mass is 3.3 × 3.5 cm and involves the coccygeal bones on imaging. On resection, the soft tissue tumour is nodular, white-tan, firm, and involves the coccygeal bones/cartilage. Sections show nodular infiltrative tumour, involving adjacent soft tissue. The tumour is composed of necrotizing granuloma-like areas, epithelioid and spindle cells. The tumour cells are large, markedly atypical with prominent nucleoli, abundant eosinophilic granular to vacuolated cytoplasm, and rare mitosis. There are extensive areas of tumour necrosis present (50–60 % of tumour). There is minimal to moderate extracellular matrix mostly collagnized stroma and few areas of myxoid changes. There is extensive lymphovascular invasion present. The tumour is positive for CK AE 1.3, EMA, CD34, CD99, and negative for INI-1.

Results: Based on above data, the tumour was diagnosed as epithelioid sarcoma.

Conclusion: The differential diagnosis of a child with sacrococcygeal mass should include rare tumours such as the epithelioid sarcoma.

Composite Epithelioid Sarcoma:



PS-05-025

Involvement of t lymphocytes in the placentae with villitis of unknown etiology from pregnancies complicated with preeclampsia

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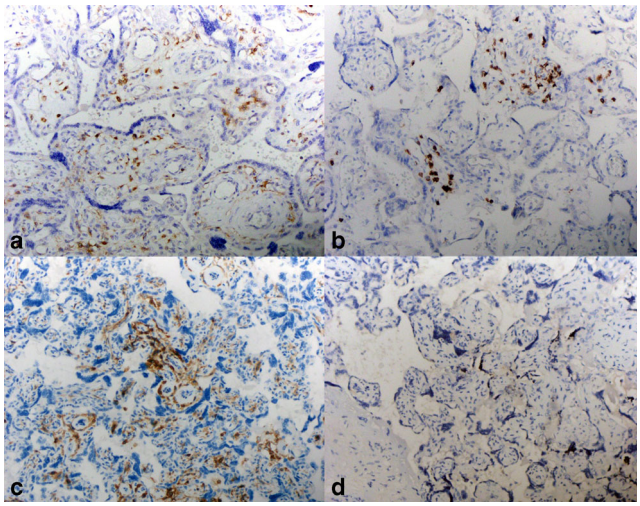
Objective: The aim of the study was to compare immunohistochemical expression of different T type lymphocytes in foci of villitis of placentae with villitis of unknown etiology (VUE) without and with preeclampsia (PE).

Method: Fiftyfour placentae were collected from women who had villitis of unknown etiology with ($N = 27$) and without ($N = 27$) preeclampsia. Immunohistochemistry for types of T lymfocytes was performed on formalin fixed and paraffin-embedded sections by use of the CD3, CD4, FOXP3, CD25, CD8 and CD68 antibodies. All data analysis was done by R Development Core Team.

Results: There was higher immunohistochemical CD4 positive T lymphocyte count and CD4 positive/CD8 positive ratio in placentae with villitis of unknown etiology complicated with preeclampsia compared to control group.

Conclusion: The higher immunohistochemical CD4 positive T lymphocyte count and CD4 positive/CD8 positive ratio in placentae with villitis of unknown etiology complicated with PE could point to their role in ethiopathogenesis of preeclampsia.

Immunohistochemical staining for CD4+ and CD8+ T lymphocytes in the focus of VUE in the placenta from pregnancy without PE [A-CD4+, B-CD8+], and in the focus of VUE in the placenta from pregnancy with PE [C-CD4+, D-CD8+]:



PS-05-026

Myxoïd liposarcomas: Report of two pediatric cases

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Objective: Liposarcomas represent <3 % of sarcomas under 20 years, the most common being Myxoid Liposarcomas (ML). A specific TLS-CHOP fusion gene resulting from the t(12;16) is present in 95 % of cases. The prognosis is excellent despite a possible progression to round cell liposarcomas with exception for those with a round cell component <5 %, still classified as high grade tumours, independently of age.
Method: We report 2 cases in 15 and 16 year-old patients with respectively 12 × 8 cm and 6.5 × 4.5 cm right thigh swellings. In patient 1, lymphangioma was suspected because of congenital lymphangiectasy with lower extremity lymphedema.
Results: Surgical biopsies both showed characteristic features of low grade MLs with positive TLS-CHOP fusion gene. Karyotype identified a t(12 ;16) (q13 ;p11) in patient 1. Specimen resections showed well circumscribed, partly cystic tumours, with myxoid areas. Histological examination confirmed ML without round cell component and free margins. Patients are closely followed up, disease free at 5 years follow-up.
Conclusion: ML may be observed in the pediatric age group. The prognosis is excellent except for tumours with a round cell component < 5 %. RT-PCR for TLS-CHOP fusion gene should systematically be performed to confirm diagnosis and exclude lipoblastoma in the youngest patients.

PS-05-027

First time isolated omental panniculitis in a child: Could surgery be avoided?

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Objective: Isolated omental panniculitis is a rare entity, which presents with the inflammation of the fatty tissue of the omentum.
Method: The symptoms may vary from local (e.g. abdominal tenderness or palpable mass) to systemic manifestation including abdominal pain, back pain, fever, weight loss, and bowel disturbances.
Results: We presented this case as a first awareness of omental panniculitis in a childhood.
Conclusion: It must be kept in mind at the differential diagnosis of ileus.

PS-05-028

Sirenomelia: Case report

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Objective: A case of sirenomelic baby of 18 weeks gestation is reported. In last 4 years this is the 3rd similar diagnosis in a population of 400,000 in our city.
Method: The mother has not any relationship with her husband, has not any important disease history, does not drink alcohol, smoke or take drugs and a 24-year-old housewife. Gravida: 3, abortus: 1, ectopic pregnancy: 1. In the18th weeks of pregnancy, because of the emergency, the ultrasound was done and oligohydramnios was seen, then medical evacuation performed and fetal material was examined.
Results: Crown- heel length was 16 cm, head circumference was 15 cm, with ambiguous genitalia and bottom of the fetus looked like the mermaid legs due to contiguity, it was 138 g. At radiography, there were 2 femurs and 2 tibias. The extra vertebrae, the median pelvic bone, the posterior tilt of the sacrum, the posterior fused fibula, and the fused feet are well shown. And urothelial and anal orifice could not be determined.
Conclusion: There was an artery and a vein in the umbilical cord. Kidneys and lungs were found atrophic in the autopsy. Sirenomelia dipus was diagnosed. Sirenomelia is a rare congenital anomaly with an incidence of one in 60,000 pregnancies.

PS-05-029

Placental angiogenesis and trophoblastic invasion in early- and late-onset preeclampsia

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Objective: Recent concept of early- (before 34 weeks) and late-onset (after 34 weeks) preeclampsia (PE) is based on the diverse pathogenic pathways of this entities. Trophoblasic invasion disturbances is the key event in early-onset PE development that mediated by several disregulatad mediators interactions. To study patterns of placental expression of certain mediators in early- and late-onset PE.
Method: Early-onset PE group included 15 cases, late-onset - 20 cases and control - 20 cases. All cases for study group were subdivided into moderate and severe PE subgroups. Immunohistochemical study was performed with KISS-1 and its receptor, GPR54, Notch1, Notch3, VEGF and VEGFR2 antibodies. Endothelial and syncytial expression of mediators was measured.
Results: KISS-1 syncytial and endothelial expression was significantly elevated in severe PE cases in compare to control. GPR54 syncytial expression in late-onset PE was significantly lower in compare to other groups. Both Notch1 and Notch3 placental expression was significantly elevat-ed in early-onset PE in compare to control, whereas its elevation in late-onset PE was insignifi-cant. VEGF and VEGFR2 expression was significantly decreased in early-onset PE.
Conclusion: The data confirm hypothesis of the role of placental angiogenesis disturbances in early-onset PE development. KISS-1 and GPR54 expression patterns confirm the role of abnormal trophoblastic invasion in early-onset PE.

PS-05-030

Flow cytometric evaluation of neutrophil CD64 as a reliable diagnostic marker for neonatal sepsis

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Objective: Bacterial sepsis in neonates is a clinical syndrome characterized by systemic signs of infection and accompanied by bacteremia in the

first month of life. The purpose of this study was to evaluate the diagnostic value of neutrophil CD64 in neonatal sepsis in a referral Children's hospital.
Method: The study included 68 neonates. 34 neonates with sepsis and 34 neonates for reasons other than sepsis were hospitalized at the hospital, were enrolled. For all infants studied, preliminary tests included CBC, CRP and blood cultures were requested. Simultaneous blood samples to assess neutrophil CD64 was prepared and sent to the laboratory.
Results: The mean levels of WBC in patients and control group were 12.49 ± 6.83 and 6.83 ± 3.47, respectively ($p = 0.01$). The mean levels of Neutrophil in patients and control group were 57 and 48 %, respectively. This difference was statistically significant ($p = 0.04$). The mean levels of CRP in patients and control group were 21.47 ± 24.15 and 9.25 ± 21.04, respectively and this difference was statistically significant ($p = 0.03$). The mean levels of Platelet in patients and control group were 245,000 and 299,000, respectively. The mean levels of CD64 in the patient group (74 %) was higher than the control group (61 %) ($p = 0.03$). Expression of CD64 at a cut-off value of 47 % had 94.44 % sensitivity, 76.36 % specificity, 95.22 % negative predictive value and 84.16 % positive predictive value. Very few patients had positive culture.
Conclusion: Neutrophil expression of CD64 is a useful diagnostic tool for early detection of neonatal sepsis. The assay is rapid, easy and reliable.

PS-05-031
Juvenile hyaline fibromatosis: A case report
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Objective: We report a rare case of juvenile hyaline fibromatosis. The patient is a 17-years-old girl who had presented in infancy with joint contractures, gingival hypertrophy and cutaneous lesions.Genetic examination confirmed the clinical diagnosis.During the period 2004–2012 the patient underwent excision of multiple papulonodular skin lesions located in head, trunk and extremities.
Method: Sections from all surgical specimens were embedded in paraffin and were stained with hematoxylin-eosin.
Results: Histological examination showed a homogeneous, hyalinized, eosinophilic matrix with cords of fibroblastic cells in the dermis and subcutis.
Conclusion: Juvenile hyaline fibromatosis is a very rare autosomal recessive disorder of the connective tissue caused by inactivating mutations in the ANTXR2 gene located on chromosome 4q21. In our case the parents are not consanguinous. The patient has not any visceral manifestations.

PS-05-032
Thanatophoric dysplasia: A case report and review of the literature
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Objective: Thanatophoric Dysplasia is a form of congenital skeletal dysplasia characterized by short limbs, small thorax, hypoplastic lungs, brain malformation and early neonatal death. The prenatal diagnosis of TD has been well established through sonographic visualization of skeletal malformations. TD is caused by mutations of the fibroblast growth factor (FGF) receptor 3 gene (FGFR3).
Method: Fetal ultrasonography at the 20th week of gestation led to prenatal diagnosis of skeletal malformation and the patient decided a voluntary interruption of the pregnancy. Radiological studies were performed and a tissue specimen was sent for molecular testing before the necropsy.
Results: Gross findings are short limbs with curved and short femurs, small thorax with hypoplastic lungs, and enlargement of temporal lobe of the brain without a cloverleaf skull morphology. The brain, body and lung weight ratios confirm macrocephaly and lung hypoplasia. Histopathologically, the longitudinal skeletal sections (femurs) show a disorderly and disturbed endochondral ossification. The epiphyseal growth plate is also severely disorganized. Temporal dysplasia is no clearly recognized. The radiological studies demonstrated the gross findings and support the diagnosis of DT type 1. The molecular test for mutation on FGFR3 is positive (p.Term807Trp).
Conclusion: We report a male case of Thanatophoric Dysplasia type 1 with the morphological findings and FGFR3 mutation. In most cases TD is a sporadic mutation. The FGFR3 mutation has been suggested in relationship with the abnormal brain development and the severely disturbed ossification. Most fetuses with TD are diagnosed correctly by ultrasonographic examination and the post-mortem studies confirm the morphological characteristics of TD.

PS-05-033
The importance of a fast and accurate diagnosis in neonatal onset hypotonia: A Merosin-deficient Congenital muscular dystrophy type 1A (MDC1A) case presentation
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Objective: To highlight the morphological aspects that enabled us to establish a fast and certain diagnosis and direct further confirmatory genetic tests.
Method: We performed a muscle biopsy in a 10 months old hypotonic boy, who had delayed motor milestones, was unable to sit, rise from supine, roll over or fully control his head, had achilean contractures, diminished active movements and creatine kinase level of 2700 U/l. The muscle cryosections served for histological, histochemical and histoenzimological stains. Immunohistochemical tests used antibodies against the three domains of dystrophin, alpha, beta and gamma sarcoglycans, dysferlin, utrophin, beta dystroglycan and merosin. Western blotting (WB) technique was used for calpain 3 and merosin.
Results: Muscle biopsy revealed a marked variability in fiber size, increased endomysial/ perimysial fibrosis, mononuclear endomysial inflammatory infiltrates, necrotic fibers, highly suggestive for a dystrophy. Absence of merosin immunostaining, confirmed by WB, and normal expression of all the other proteins diagnosed our little patient with MDC1A.
Conclusion: The pathological diagnosis, confirmed by the detection of a nonsense homozygous mutation in the LAMA2 gene: c.5221C>T, p.Arg1706*, is essential for clinical surveillance and genetic counseling as the boy's mother, pregnant again, can be properly monitored.

PS-05-034
Duplications of alimentary tract in children
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Objective: Duplications of alimentary tract (DAT) are uncommon congenital lesions. Our study will analyze this entity anatomical and histopathological characteristic.
Method: Fifteen-year documentation and paraffin embedded samples retrospective analysis at Pathology Department, Mother and Child Health Care Institute of Serbia.
Results: In the period from February 2000 to January 2015, 23 patients with 24 DAT were treated at Institute. Ages ranged from 3 days to 15 years (median 13 month) and 54.16 % were younger than 1 year. A size varies from 2 to 18 cm. The most frequent site involved in 29.17 % was ileum, than come jejunum and colon (16.66 %), esophagus (12.5 %), thorax (8.33 %), mouth, stomach, duodenum and rectum (4.17 % each). Predominantly males were affected (70.83 %). Most of the duplications were

spherical in shape (70.83 %). Common muscular wall between normal and duplicated segment was found in 7 (29.17 %). The luminal communication had 4 (16.67 %) duplications. One patient had two synchronous duplications of esophagus and jejunum. Presence of ectopic gastric mucosa was found in 29.17 % of duplications. Statistically significant association was found between gender and shape ($p = 0.04$).
Conclusion: DAT are rare condition that may occur anywhere from the mouth to the anus, diagnosis relies on histology and only treatment is surgery.

PS-05-035
Chorioamnionitis in pre-term pre-labor rupture of membranes is associated with increased expression of galectin-3
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Objective: Galectins are a family of animal lectins that recognize and bind glycoconjugates and are implicated in numerous processes including immunomodulation. Galectin-3, which can regulate immune responses upon infection and inflammation, was not studied so far in intrauterine infection leading to pre-term pre-labor rupture of the membranes (PPROM), though galectin-1 was recently reported to be implicated in the process. We determined galectin-3 protein expression in the chorioamniotic membranes and its changes during histological chorioamnionitis.
Method: Fetal membranes were obtained from women with PPROM with ($n = 15$) and without chorioamnionitis ($n = 15$) during second and third trimester. Tissue sections were immunostained using anti-galectin-3 antibody, avidin-biotin system, and DAB as chromogen. Immunoreactivity was evaluated semiquantitatively and statistically analyzed using ANOVA test.
Results: Galectin-3 protein was detected in the amnion epithelium, chorionic trophoblasts, mesenchymal cells, and decidual cells. Galectin-3 expression is increased in fetal membranes and in the amniotic epithelium ($p < 0.001$) in patients with chorionamnionitis.
Conclusion: Chorioamnionitis is associated with increased galectin-3 expression and strong immunoreactivity of the fetal membranes. Galectin-3 may participate in the regulation of the inflammatory responses to chorioamniotic infection.

PS-05-037
Placental biomarkers can be useful tests to determine gestational hypertension/preeclampsia requiring delivery in Fetal Growth Restriction (FGR) risk in asymptomatic woman: Case report of the placenta examination
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*University Hospital Wroclaw, Dept. of Pathology, Poland

Objective: To identify a potential role of placental biomarkers: PlGF, sFlt-1 and sFlt-1/PlGF index in determining gestational hypertension/preeclampsia requiring delivery in FGR risk asymptomatic woman.
Method: The first trimester combined test /NT, NB, DV PI, TR, UtA PI, beta-HCG, PAPPA (MoM 0,374) and MAP/ was performed in 27 years old primigravida. 1:62 risk of FGR was detected based on FMF Report. At 32 6/7 weeks AC 6,9 %, UmA PI 95 % and MCA PI 5 % were identified. PlGF, sFlt-1 and sFlt-1/PlGF index were performed immediately (the blood levels were respectively 48,8 pg/mL, 4590,0 pg/mL and 94,0). Unexpected high blood pressure 160/100 mmHg and UmA Pl above 95 % were detected 14 days later and gynecologist decided to immediate delivery by cesarean section. The newborn: 2050 g, Apgar score 9, good general condition. Placenta was referred to pathological examination.
Results: Decidual vasculopathy with atherosis in decidual arterioles, diagnosed in placentological examination, is associated with hypertensive disease, PE or other systemic disorder proceeding with vascular changes.
Conclusion: PlGF, sFlt-1 and sFlt-1/PlGF index can play an important role in early detection placental-depended pregnancy disorders and can help to indicate delivery at the optimal time for both maternal and fetal well-being. Placental examination confirm clinical findings.

Monday, 7 September 2015, 09.30–10.30, Restaurant
PS-06 Poster Session Cardiovascular Pathology

PS-06-001
Myocarditis and Cardiac Sarcoid as a cause of sudden cardiac death in UK based sudden cardiac death database
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Objective: The definition of myocarditis in post mortem tissue sampling is unclear and there is great variability in reported incidence. Histological diagnosis can be difficult when inflammatory cell infiltrates are focal and not diffuse with little myocyte damage. We review cases of sudden death attributed to myocarditis in a large UK based series.
Method: Our national SCD database contains information on 3,731 cases.
Results: Ninety-four cases (2.5 %) had myocarditis and 25 cases (0.7 %) had cardiac sarcoidosis making total 3.2 % of all SCD. In myocarditis cases, 55 % were male and 45 % were female. In cardiac sarcoidosis 72 % were male and 28 % female. The age distribution showed a younger mortality in myocarditis (30–49 years of age) compared to an older population with cardiac sarcoidosis (40–59 years of age). Most had no previous history of sarcoid. The most common cell type was lymphocytic (48 %), mixed cell type (19 %), neutrophil (14 %), eosinophilic (13 %), histiocytic (4 %) and giant cell (2 %).
Conclusion: Myocarditis causing SCD is low in this general population. Lymphocytic inflammation still predominates. Cardiac sarcoid can cause SCD in the absence of previous clinical diagnosis. We recommend a multidisciplinary approach with extensive sampling and the use of ancillary tests (viral polymerase chain reaction, genetic testing).

PS-06-002
The significance of individual histopathological changes in endomyocardial biosy in diagnosis and monitoring of Antibody-Mediated Rejection in patients after heart transplantation
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Objective: New International Society for Heart and Lung Transplantation (ISHLT) criteria for reporting pathologic antibody mediated rejection (pAMR) were recently proposed (2013).The aim of this study, was to assess the significance of histopathological changes in diagnosis and monitoring of AMR in Polish one center EMBs material.
Method: 1350 EMBs from 212 patients who underwent heart transplantation in years 2001 –2013, were initially diagnosed as AMR1and AMR0, according to ISHLT 2004 criteria (based on C4d positivity). In all EMBs histopathological features suggestive of AMR such as interstitial edema, endothelial swelling and intracapillary activated mononuclears, were specified. The frequency of each individual change was compared between groups.
Results: 121 EMBs from 16 patients with AMR1 (group 1), and 1229 EMBs from 196 patients with AMR0 (group 2), were analised. Endothelial swelling was observed in 47 (38,84 %) EMBs from group 1, in 195 (15,86 %) EMBs from group 2, $p < 0.001$; interstitial edema in 42 (34,71 %) EMBs from group 1; in 433 (35,23 %) EMBs from group 2,

$p = 0.988$, intracapillary activated mononuclears in 27 (22,31 %) EMBs from grup 1; in 83 (6,75 %) EMBs from group 2, $p < 0.001$. There was no significant difference in frequency of histopathological features when EMBs were analised according to time course after transplantation.
Conclusion: Intracapillary activated mononuclears and endothelial swelling are statistically more often found in EMBs of patients with C4d positive EMBs, therefore, presence of these two changes may be suggestive of AMR in patients with C4d negative stain. In our study, time after transplantation has no impact on presence of individual histopathological changes.

PS-06-003
Ultrastructural-morphometric findings of mitochondria of cardiomyocytes in the routine diagnostic setting of patients with dilated cardiomyopathy
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Objective: We analyzed the use of ultrastructural analysis in the routine diagnostic setting for diagnosis of dilated cardiomyopathy (DCM).
Method: We investigated consecutive right ventricular endomyocardial biopsies of 12 patients (female = 2, mean age 49 years) from a single referral center that were sent for additional ultrastructural analysis between 01/2012 and 02/2014. The main pathology was DCM ($n = 10$). Two patients served as controls ($n = 1$ ischemic cardiomyopathy, $n = 1$ sarcoidosis). Using a stereological cut point method, number, cut points and points of selected subcellular structures were counted as required. Secondary parameters were calculated. F-test and Student's t-test were used for statistical analysis.
Results: Significant differences ($p < 0.01$) were found between the two groups concerning the volume density of the mitochondria, with lower levels in the control group (0.023 vs 0.026). The opposite was true for relation of surface to volume density (mean values 10.24 vs 9.24 in DCM), indicative of a higher number of smaller mitochondria in DCM patients. The numerical density was also higher in DCM patients (0,90 controls vs.1,06).
Conclusion: The higher numerical density values in DCM patients and the above results are indicative of a higher capacity of oxydative phosphorylation along the christae and an elevated need for energy in DCM compared to other diseases.

PS-06-004
Lymphangiogenesis in heart valve endocarditis and degeneration
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Objective: Inflammation associated lymphangiogenesis has been identified during a few acute and chronic inflammatory diseases. Sparse data exist on lymphatic vessels presence in endocarditis.
Method: Total of 52 patients with surgically resected valves was included. Endocarditis was present in 18 aortic valves and 10 mitral valves. Control group consisted of 15 degenerative aortic valves and 9 degenerative mitral valves. There were 22 males in endocarditis group and 17 males in control group, respectively. Podoplanin antibody immunohistochemistry and morphometrical analysis was performed.
Results: The lymphatic density in endocarditis was 885,47 ± 648,71 vessels/mm2 in comparison to 51,73 ± 83,57 vessels/mm2 in degenerative valves. Lymphatic vessels mean size was 93,2 ± 249,2 μm2 and 60,6 ± 87,9 μm2 in endocarditis and degenerative valves, respectively.
Conclusion: Lymphangiogenesis is markedly more frequent during endocarditis as compared with valve degeneration. Aiming towards lymphangiogenesis may add to the future treatment of endocarditis.

PS-06-005
The isolated cardiac sarcoidosis diagnosed on Endomyocardial Biopsy (EMB) results: 2 case reports
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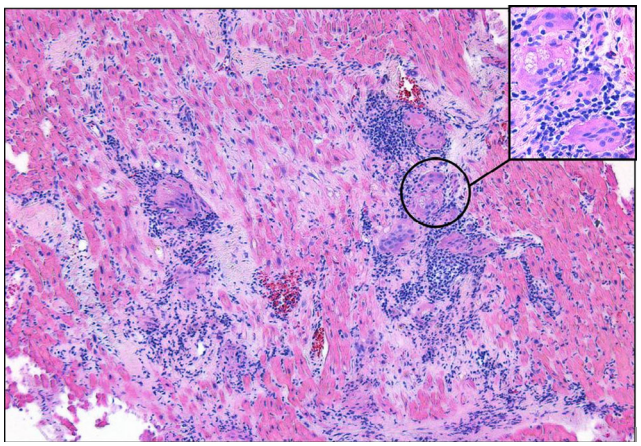
Objective: The frequency of isolated cardiac sarcoidosis diagnosed on the results of EMB biopsy is 0,2 %. We report two cases, which is 0,3 % of our EMB material for 15 years.
Method: A man of 47 years old and a woman of 50 years old presented with life-threatening ventricular arrhythmias (VA). Magnetic resonance imaging and positron emission tomography/computed tomography of heart detected active myocarditis. EMB was taken after radiofrequency ablation. Samples were stained with hematoxylin and eosin, Masson's trichrome, CD3, CD8, CD68, HLA-DR.
Results: The diagnosis was confirmed by histologic study of EMB which showed granulomas similar in size and morphology consisted of multinucleated giant cells with vacuoles and asteroid bodies, epithelioid cells, lymphocytes, histiocytes and a peripheral rim of fibrosis. Immunohistochemical analysis confirmed rimmed granulomas, detected the central distribution of CD68+ cells and the peripheral distribution of CD3+ and CD8+-ones. Chest computed tomography scan revealed no evidence of thoracic pathology.
Conclusion: In both cases the isolated cardiac sarcoidosis was diagnosed retrospectively after the results of EMB. The treatment with prednisolone at the initial dose of 1 mg/kg/day was prescribed in both cases. Reduction in prednisolone dosage resulted in rebound VA even 2 years after the disease onset.

EMB. Cardiac sarcoidosis, H&E, x 100:



PS-06-007
Role of the phosphoinositide-3-kinase/serin-treonin kinase (Pi3k/Akt) signaling in myocardial dystrophin expression in mice submitted to cecal ligation and puncture
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Objective: The cell signaling related to PI3K play a role in the pathogenesis of diseases with inflammatory component as sepsis. This pathway has also been reported as a regulator of cardiomyocyte contractility, which could be related to expression of the structural glycoproteins, mainly dystrophin, which confers stability to the myofiber and transmits force between sarcomeres and cell membrane to the extracellular matrix.

Method: Severe sepsis was induced by cecal ligation and puncture (CLP) in mice and the LY294002 (5 mg/kg) was used 1 h before surgery to inhibit the PI3K/Akt signaling. Histopathological, Akt and dystrophin expression were analyzed 24 h after CLP.
Results: The survival rate was higher in CLP plus LY294002 group as compared to only CLP and controls. Histopathologycal analysis showed foci of disorganized miofibrils and increased membrane permeability, more evident in CLP plus LY294002 as compared to CLP and controls. We observed decreased myocardial dystrophin expression in septic mice, but this dysthophin loss was more pronounced in myocardium from septic mice plus LY294002.
Conclusion: Evidences suggest that inhibition of PI3K/AKT may be involved in these myocardial structural changes and could be implicated in sepsis-induced cardiac depression and represents an innovative approach to study the intrinsic mechanism of cardiac abnormalities caused by sepsis.

PS-06-008
Short-term and long-term models of doxorubicin-induced cardiomyopathy in rats: Functional and histopathological comparison
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Objective: Doxorubicin (DOX), an antineoplasic agent, has been experimentally utilized to induce heart failure (HF) however, the best protocol remains unclear. This study described a critical comparison of a short and long-term DOX infusion protocols to induce HF in rats.
Method: Wistar rats were allocated in ST group (short-term), treated with cumulative dose of 15 mg/kg of DOX during 2 weeks and LT group (long-term) received cumulative dose of 18 mg/Kg of DOX during 9 weeks. Control groups received saline. Histopathological and echocardiography analysis at basal condition and 2 weeks after the end of the treatment was performed.
Results: Loss of myofibrils and vacuolar degeneration of cardiomyocytes in all DOX-treated hearts were observed. Interstitial collagen volume fraction was more significant in ST and LT group as compared to controls. No differences between ST and LT were observed. Echocardiographic study showed augmentation of left ventricular systolic and diastolic dimensions and reduction of ejection fraction in LT as compared to ST and controls.
Conclusion: Results indicated that LT infusion is more effective in inducing HF and cardiac changes when compared to ST-infusion. The unconformity between functional and structural changes could reflect a retard between the onset of myocardial changes and cardiac dysfunction.

PS-06-009
Congenital anomalies of the aortic arch: Autopsy study
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Objective: Congenital anomalies of the aortic arch, representing a wide range of relatively less known and rarely clinically diagnosed congenital heart diseases (CHD).
Method: Retrospective analysis of autopsy protocols during 52-year period (1961–2013) from Archive for congenital heart disease Institute of Pathology, University of Belgrade; Mother and Child Health Institute, and Clinic for the gynecology and obstetric, Clinical Center of Serbia, from 2000 to 2011. A total of 1.460 cases of CHD were reviewed, and only in 245/1460 cases, the anomaly of the aortic arch was found (16.8 %).
Results: Survival over 1 year of age was 18.8 %, and under 1 year was 81.2 % of the cases. This showed statistically significant difference ($p < 0.01$). Right aortic arch was found in 26.9 % of cases. Vascular ring was observed in 3.7 % of cases. Tubular hypoplasia was observed in 20.4 % of cases. Coarctation of aorta occurred in 21.6 % of cases. Interruption of the aortic arch was found in 12.6 % of cases, and aortic arch atresia occurred in 6.9 % of cases. Left aortic arch with aberrant left subclavian artery was found in remaining 7.7 % of cases.
Conclusion: Recognition of these anomalies are essential for a possible a surgical correction, which often allows complete recovery of patients.

PS-06-010
Congenital corrected transposition of the great arteries: Autopsy study
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Objective: Congenitally corrected transposition of the great arteries (C-TGA) is characterized by normal veno-atrial connections, but with discordant atrio-ventricular and ventriculo-arterial connections, allowing hemodynamic correction.
Method: We analyzed autopsy records of cases with congenital heart diseases (CHD) during 40 years period. C-TGA was found in 33 out of 2.593 autopsy cases (1.3 %). The sex incidence showed a slight male predominance (male 54.5 % ; females 45.5 %). Modified Rokitansky technique was used for all cases with CHD.
Results: Associated cardiac anomalies were present in all cases of C-TGA. The most commonly associated anomalies were: ventricular septal defect (48.5 %), atrial septal defect (45.5 %), valvular or subvalvular pulmonary stenosis (33.3 %). Other associated cardiac leasions were malformations of aortic arch (15.2 %), hypoplastic left heart syndrome (15.2 %), patent ductus arteriosus (15 %). The major cause of death was bronchopneumonia (45.5 %), and the most frequent extra-cardiac additional congenital defect was asplenia.
Conclusion: The existence of the C-TGA do not change the quality of life of these patients, because it does not disturb the normal hemodynamics of the heart. The problem may arise when it appears with a number of other cardiac anomalies, so they determine and influence the lives of these patients. Intra-cardiac shunts are the most common form of associated cardiac anomalies.

PS-06-011
Hypoplastic left heart syndrome: Analysis of autopsied cases
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Objective: Hypoplastic left heart syndrome (HLHS) is characterized by several cardiac abnormalities. Anomalies that are included in this syndrome are hypoplasia or underdevelopment of the left ventricle, atresia or hypoplasia of the mitral valve, and aortic atresia or hypoplasia.
Method: The data were obtained by retrospective analysis of 2.593 autopsy protocols from the Archive of congenital heart deseases, Institute of Pathology, School of Medicine, Belgrade, and the autopsy protocol from the Institute for Health Protection of Mother and Child, from 1990 to 2014. The analysis used descriptive and analytical methods statistically.
Results: From a total of 2.593 autopsied cases, HLHS was found in 59 cases, or 2.3 % of the total number of autopsies in the period from 1990 to 2014 year. HLHS is more common in males ($p < 0.01$). High statistical incidence was found in hypoplasia of the aorta, and the right aortic arch ($p < 0.01$). Heart failure was the most common immediate cause of death, demonstrated by highly significant difference ($p < 0.01$). Endocardial fibroelastosis was also more often present in children with HLHS ($p < 0.01$).
Conclusion: In our study was observed increased occurrence of malformations in male patients, the longer survival in female patients, and the most common immediate cause of death was a heart failure.

PS-06-012

Myocarditis: Clinical and morphological features of autopsy cases

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Objective: Myocarditis (MC) is an inflammatory disease of the cardiac muscle without any association with ischemic heart disease, or other entities.
Method: We analyzed 30 autopsied cases with MC. For the pathohistological (PH) diagnosis of MC we used a modification of Dallas's criteria. We investigated the correlation between the clinical data obtained from the request for clinical autopsy, and PH findings in the myocardium.
Results: From 30 investigated cases with PH diagnosis, the clinically suspected diagnosis of MC was made only in 1 case (3.3 %), which showed high statistical significance ($p < 0.001$). From all the morphological forms of MC, the most common findings were acute MC (76.7 %). MC as the cause of death was found in only 8 /30 (26.6 %) cases, what showed a statistically significant difference ($p = 0.016$). Rhythm disorders were observed in only 5/30 (16.6 %) patients, what showed also a statistically significant difference ($p = 0.001$).
Conclusion: In this study we confirmed that only in one case the clinical diagnosis of MC was suspected. This indicates that the clinical diagnose of MC is still very difficult, and that the number of diagnosed cases is far from real. Autopsies are the rule.

PS-06-013

The tetraspanins expression in cardiac myxomas with florid ancient degenerative changes: The study of partially calcified 14 cases highly suspected of atrial thrombosis

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Objective: In this study we have endeavored to an evaluation for the expression of tetraspanins in ancient, degenerated cardiac myxomas. Here, the question has been posed: can an imbalance of tetraspanins result in intratumoral thrombosis, necrosis, calcification and finally fragmentation of cardiac myxomas?
Method: The study included 14 cases of cardiac myxomas with advanced degenerative changes. Resected tumours were fixed in 10 % buffered formalin and were then processed with routine histopathological procedures. An immunohistochemical analysis using mouse monoclonal CD9 (EPR2949) and CD63 (ready for use; NKI/C3, Cell Marque) antibodies was performed.
Results: 7 tumours were right-sided atrial myxomas and 7 of them were left-sided measuring from 1.2 to 4.1 cm with medium size of 2.82 cm. The clinically higher suspicion of endocardial thrombosis was associated with sessile compared to polypoid myxomas, left sided tumours compared to right-sided ones. CD9 overexpression was recorded in every case with granular cytoplasmic pattern of staining. Weak granular cytoplasmic reactions were observed in case of CD63.
Conclusion: Observed here CD9 overexpression explains and confirms CD9 contribution in neovascularization and extracellular matrix modeling but the meaning of a weak expression of CD63 remains still unclear and needs further studies.

PS-06-014

Poly ADP ribose polymerase expression in the heart and nerve tissue in experimental diabetes model in rats

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Objective: Oxidative stress and inflammation has been implicated in the pathogenesis of diabetes mellitus. The present study investigated the role of DNA reparation enzyme-poly ADP ribose polymerase (PARP) in the pathogenesis of diabetic changes in the heart and nerve tissue.
Method: Diabetes mellitus (DM) was induced in rats by a single injection of streptozotocin (STZ) at a dose of 50 mg/kg. The PARP expression was studied by immunohistochemistry. The study was approved by a local ethical committee.
Results: Obtained results showed that induction of DM induced major histopathological changes in myocardial and nerve tissue, like the pericellular and perivascular oedema, focal necrosis and inflammatory changes. In addition, in diabetic animals number of PARP positive cardiomyocytes in myocardial tissue increased (32 ± 17 vs. 10 ± 3 cells/mm2 ; $p = 0.001$. Furthermore, in DM increased the numbers of PARP positive Schwann cells in nerve tissue compared to control group (23 ± 9 vs. 12 ± 4 cells/mm2; $p = 0.02$.
Conclusion: The present study suggests that increased PARP expression plays a pivotal role in the heart and nerve tissue damage in diabetes mellitus. Novel pharmacological strategies influencing on PARP expression could be beneficial in the treatment of diabetes mellitus. Funding acknowledgement. Supported by LCS grant Number 278/2012.

PS-06-015

A case from forensic practice with aortic dissection after aortic valve replacement: When you do not know the past

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Objective: Discussion of a case of aortic root dissection after aortic valve replacement (AVR) with reposition of right coronary artery (RCA).
Method: We present a case of an 88-years old deceased male who died in the outpatient settings and forensic autopsy was instituted. No past medical records were available.
Results: Gross internal examination revealed that the aortic valve had been replaced with a biological valve. The RCA was found to have been moved surgically 1.5 cm up in the aortic wall. There was dissection of the aortic root, forming a cavity adjacent to the aortic valve, in the area of native anatomical position of the RCA, underlying the stitches. The cavity was found filled with foul-smelling pulp-like whitish material with visible thick reddish-brown formation. Complicated atherosclerotic changes were seen away from the dissection, in the area of aortic arch. The histology from the wall defect showed cellular debris accompanied by mild lymphocytic infiltrates, compatible with atheromatous collection and passed thrombosis. Myocardial tissue exhibited chronic ischemic damage with disseminated foci of myocytolysis that were accredited cause of death.
Conclusion: The authors discuss the possibility of aortic dissection to be a postoperative complication, provoked by surgically compromised integrity of the aortic wall at the background of atherosclerosis.

PS-06-016

Primary cardiac sarcoma with SYT-SSX1 fusion gene

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Objective: Pointing out the need of combining morphology, immunohistochemistry and molecular studies for exact categorization of cardiac sarcomas due to their low frequency and heterogeneity.
Method: A 4.5 cm cardiac tumour was studied after surgical resection. The patient was a 41-year-old male with right auricular lesion, transmural affectation and intracavitary growth. Conventional histological sections were obtained and immunohistochemical stains. Molecular studies performed included FISH for EWS gene break-apart, RT-PCR for SYT/SSX fusion transcript, and single nucleotide polymorphism analysis.

Results: The tumour was a sarcomatous proliferation with spindle cells and elongated nuclei. Mitotic count per 10 high power fields had an average of 22. Immunohistochemisry showed strong vimentin expression and focal for keratin (AE1-AE3), enolase, CD99, and desmin (with dot-like pattern). S100, myogenin, and CD34 were negative. Dot-like desmin expression with enolase and keratin described in desmoplastic small round cell tumour wasn't confirmed after negativity for EWS gene rearrangement. However SYT/SSX1 gene transcript characteristic of synovial sarcoma was demonstrated with RT-PCR. Structural abnormalities of chromosome 3 and 12 were found.
Conclusion: Cardiac sarcomas are uncommon tumours. Synovial sarcomas are described around 1 % of them. Accurate diagnosis can be difficult without help of auxiliary techniques, but it's important to achieve the most effective treatment for patients.

PS-06-018
Amyloidosis of epicardial and intramural coronary arteries as an unusual cause of myocardial infarction: A case report
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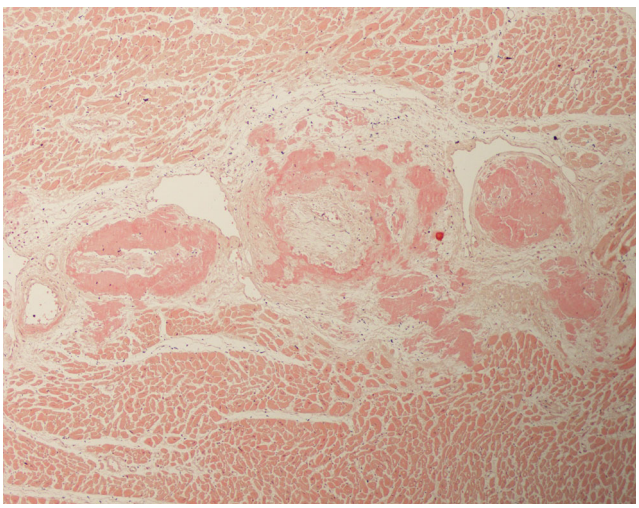
Objective: The systemic amyloidoses is a heterogeneous group of disease characterized by extracellular deposits of misfolded fibrillar protein - amyloid, causing multiple organ dysfunction. In amyloidosis, the greatest risk of death occurs in patients with cardiac involvement, who typically develop diastolic dysfunction and systolic heart failure then, with predisposition to arrhythmias and sudden death.
Method: We report a case of a woman (70 years) who died due to anteroseptal myocardial infarction and subsequent cardiogenic shock. Posmortal examination of a number of organs (heart, liver, spleen, kidneys, etc.) has discovered a senile systemic amyloidosis with deposition of transthyretin. Widespread amyloid deposits were found in extracellular spaces and in the wall of medium-sized and small blood vessels. The most pronounced changes were in the heart.
Results: Amyloid deposits in the epicardial and intramural blood vessels have significantly narrowed lumen and lead to myocardial infarction. Focal nodular deposits were found in the myocardioum. Atherosclerosis of the coronary artery was not significant.
Conclusion: Although the typical presentation of cardiac amyloidosis is an infiltrating restrictive cardiomyopathy, this case report illustrates that ischemic small vessel coronary disease caused by deposits of amyloid which can lead to fatal complications such as myocardial infarction.

Amyloidosis of intramural coronary arteries:



PS-06-019
A rare case of adenomatous struma in the right heart
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Objective: The existence of thyroid tissue in the heart is an exclusive rarity, even more rare if causing a histology such as Goiter disease. The objective of our work was to establish the frequency of thyroid tissue tumours in surgically removed heart tissue specimens between 2008 and 2015.
Method: A retrospective study was carried out in total 10 cases - tumours extirpated from the heart halves. We found such tumour in the right ventricle of a 57 years-old woman. Routine (HE), and histochemical (PAS and Hala El-Zimaity) were run for all tumours. The tumour of interest was additionally tested with immunohistochemistry.
Results: The thyroid tissue tumour in the heart represents 10 % of all extirpated tumours. This frequency is indeed lower, bearing in mind the small number of material available from the newly established Clinic of Cardiac Surgery.
Conclusion: Abnormalities of similar type (ectopic tumours), with a superimposed pathological process throws light on the tumourigenesis in an unusual place.

PS-06-020
Cardiac amyloidosis immunophenotype
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Objective: To investigate amyloid sites and types in endomyocardial biopsies from patients with diagnosed amyloidosis.
Method: Diagnostic immunohistochemistry of amyloid was performed using a panel of peptide antibodies against different types of amyloidosis. To detect ALκ amyloidosis an expanded kit of antibodies was used for the first time: commercially available antibody against ALκ amyloidosis and four new commercially unavailable antibodies directed against κ-light chain variable and constant regions.
Results: 49 biopsy samples from 49 patients (average age 70 years) - 30 males, 17 females and 2 of unknown gender were examined. The most common diagnosis was transthyretin amyloidosis (24 patients); ALκ amyloidosis was found in 13 patients and ALλ amyloidosis - in 11. Only one of 49 patients had AA-amyloidosis.
Conclusion: Transthyretin amyloidosis was the most common finding in endomyocardial biopsies mainly from male patients. Antibodies generated in our study against κ-amyloidosis were characterized by high specificity for detecting AL-κ-amyloidosis and had no specificity for other amyloidosis types.

PS-06-021
Desmin cardiomyopathy: Case report
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Objective: To reveal clinical and morphological features of desmin cardiomyopathy (CMP).
Method: Endomyocardial biopsy sample, taken from a man 26 years old with unspecified myopericarditis. At the age of 16 EchoCG showed symmetrical hypertrophy of left ventricular myocardium. Cardiac conduction disease, progressive diastolic dysfunction, hydropericardium, and increase in creatine phosphokinase and troponin levels appeared sequentially in the order listed. The sample was stained with H&E, picrofuchsin, congo red and periodic acid-Schiff. Expression of desmin, CD45, CD68, CD8 («Dako»), CD4 («Novocastra») was assessed by immunohistochemistry. Desmin gene was sequenced using ABI Prism 3130, (AppliedBioSystems) following phenol-chloroform DNA extraction from peripheral blood mononuclear cell fraction.

Results: Cardiomyocytes (CMC) appeared to be of different shapes and sizes, some of them - hypertrophic and with perinuclear halo. Cell nuclei had lumpy chromatin. Desmin was dispersed irregularly in the cytoplasm of CMC, with predominant location in distal parts of the cells. Sequencing of the desmin gene showed a splice-site mutation (IVS3+1G→A).
Conclusion: We report a case of transformation of hypotrophy phenotype to restrictive phenotype in desmin CMP. Histopathological characteristics of desmin CMP are: irregular desmin distribution in the CMC and indirect signs of idiopathic CMP (nuclear polymorphism, perinuclear halo).

PS-06-022
Postpartum spontaneous dissection of the coronary arteries in the absence of aortic dissection
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Objective: Spontaneous coronary artery dissection in the absence of aortic dissection is classically associated with sudden death during or within first year after pregnancy. The Left Anterior Descending artery (LAD) is the most frequent location of the dissection.
Method: We report the case of a 36 year old woman who suddenly collapsed 10 days following the uneventful delivery of her second child by cesarean section. She had complained of chest tightness and ear pain in the days prior to her collapse. She had no medical history and was not on any medication. At autopsy coronary artery dissection was found starting ~ 1 cm from the ostia of the LAD and extending at least 3 cm distally down both the LAD and left obtuse marginal branch. An extensive area of acute infarction was discovered, involving the lateral left ventricle wall extending towards the anterior and posterior surfaces. Histological findings confirmed acute myocardial infarction and coronary artery dissection, with no evidence of atherosclerosis.
Conclusion: Spontaneous coronary artery dissection should be suspected in those presenting with chest tightness in the peripartum period even in the absence of risk factors. It should be noted that ear pain can be a manifestation of cardiac pain.

PS-06-023
Left atrium bronchogenic cyst in a 10-year-old girl: A case report
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Objective: Bronchogenic cyst is a congenital anomaly, appearing mainly in the cervical and retroperitoneal soft tissue, and occasionally with intradiaphragmatic, intrapericardial, intraspinal localisation. The intracardiac presentation is very rare, diagnosed usually between the 2nd and 4th decade.
Method: A 10-year-old girl with common atrioventricular canal, mitral valve cleft and interatrial septal defect during a routine clinical control was diagnosed with a giant interatrial aneurysm protruding into the left atrium. Surgical resection of the aneurysm was performed in parallel to the basic defect correction.
Results: Intraoperative aspect of the interatrial lesion was a multilocular cyst with fluid collection, covered by a translucid membrane, mimicking a hydatid cyst. Microscopy revealed multiple cystic cavities, lined by PanCK and CK7 positive, but Inhibin, Calretinin, TTF1, WT1 and CD34-negative pseudostratified ciliated epithelium, disposed in a smooth muscle and fibrous conjunctive stroma, with focal calcifications, giant cell reaction and rich mononuclear inflammatory infiltrate with tendency to form lymphoid aggregates. Glandular structures with intraluminal mucin secretion were also present.
Conclusion: The reported case refers to a particular localization of bronchogenic cyst, the left atrium, discovered accidentally after a routine examination. As such, it should be considered for differential diagnosis whenever a cystic intracardiac lesion is suspected.

PS-06-024
Sitagliptin restores endothelial function in aorta in a T1DM animal model: Protective role of GLP-1R signaling
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Objective: The effect of dipeptidyl peptidase-IV inhibition on reversing/attenuating endothelial dysfunction was evaluated in an animal model of type 1 Diabetes Mellitus induced by streptozotocin.
Method: The animals were divided into four groups: controls, diabetics and controls and diabetics treated with sitagliptin 5 mg/kg/day during 2 weeks. Isolated aortic rings were used for functional studies and western blot analysis and histological sections were used for oxidative stress analysis and histochemical studies.
Results: Vasorrelaxation responses to acetylcholine were more potent in control rats treated with sitagliptin. Unexpectedly, in diabetic treated rats, sitagliptin seemed to compromise the acetylcholine maximum response. There were no statistically significant changes in the expression of active eNOS and active Akt in all groups, although a significant increase in the expression of GLP-1R in diabetic rats was observed compared to control animals, which tended to decrease with sitagliptin. A significant increase in DHE fluorescence intensity on diabetic rats aorta rings, compared to control animals, was significantly reduced after sitagliptin treatment. Finally, instead of a disruption of the aortic tissue, an increase in matrix density was observed on diabetic rats' aortas after sitagliptin.
Conclusion: In sum, the sitagliptin vascular beneficial effects, were compromised in the presence of T1DM, and were partially reversed by the drug in the 2 weeks treatment period.

PS-06-025
Intravascular bone formation in renal artery in an ectopic kidney: A case report
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Objective: Intravascular calcification of the renal artery is a common disorder especially in patients with chronic kidney disease. However, intravascular bone formation is exceptionally rare. We present a rare case of ossification of renal artery's wall in a patient with urothelial carcinoma of the renal pelvis.
Method: A 78 year-old man was referred to our hospital because of an infiltrating urothelial carcinoma of the renal pelvis in an ectopic kidney and underwent a total nephrectomy.
Results: Histological analysis demonstrated atherosclerotic plaques in the medial layer of the renal artery including a focus of bone formation with bone marrow presence.
Conclusion: In the vast majority of human atherosclerotic plaques calcium deposits are observed however osseous and bone marrow formation is exceptional. Evidence indicates that vascular ossification is a regulated process that resembles embryonic endochondral osteogenesis involving osteoblastic differentiation of vascular smooth muscle cells. However others investigators suggest that artery calcification is a non-endochondral ossification process, mainly observed in patients with diabetes as well as with end-stage renal disease. In these cases, mineralization resembles intramembranous calvarial bone formation, in which no cartilaginous precursor is formed.

PS-06-026

Morphological changes in the area of vascular anastomosis after reconstructive surgery

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Objective: Study morphological changes of vascular anastomosis.
Method: 12 samples of distal anastomosis of the femoropopliteal prosthesis was studied 2 years after reconstructive surgery. Material for the study received after amputation about irreversible ischemia and studied using light microscopy.
Results: 24 months after the operation in the anastomotic adventitia we observed focal and diffuse infiltration with polymorphocellular exudate, containing mainly lymphocytes, macrophages and single histiocytes. Hyperplastic neointima unevenly thickened, partially without epithelium, with portions of thrombotic masses. The boundary between intima and middle membrane is clear, with moderate diffuse focal of lymphohistiocytic infiltration. Twenty-four months after the operation inflammatory changes in the contact of prosthesis and artery remain, chronicity and resorption of prosthesis tissue take place. Resorption cells and macrophages surround the prosthesis, without penetrating its substance. Tunica media reactively modified by cells, producing cytokines and inflammatory mediators, contains foci of angiogenesis and destruction, internal elastic membrane is flattened or missing. Hyperplastic intima is dense, sometimes there are areas of destruction and expansion of both the neointima and endothelium covering it, which leads to thrombosis.
Conclusion: Despite the later stages, there is chronicity of the inflammatory process, which leads to intimal hyperplasia, destructive changes of the internal elastic membrane and the development of restenosis of the reconstructed area and thrombosis of prosthesis.

PS-06-027

MDM2, CDK4 and EGFR1 in intimal sarcomas of pulmonary artery

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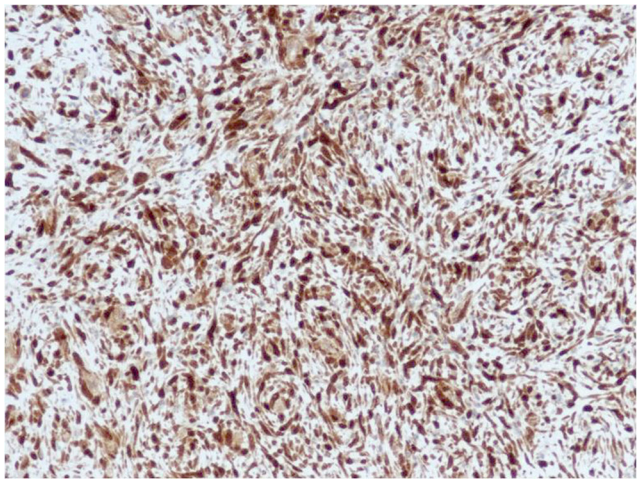
Objective: Intimal sarcoma is a strange and mesenquimal tumour that seats in large blood vessels, (mainly aortic and pulmonary arteries). It has a discussed miofibroblastic origin. It is a poorly differenciated tumour with atypia and a variable mitotic index. It is sometimes associated to MDM2, CDK4 and EGFR1 mutation. The MDM2 mutation is related to TP53 restriction, what can supose a terapeutic strategy. EGFR1is related to less differenciated tumours, less supervivence and quimioresistance and CDK4 delection has been demostrated in almost there sarcomas.
Method: We present two patients who were diagnosed by intimal sarcoma of pulmonary artery whose MDM2, CDK4 and EGFR1 were evaluated.
Results: In our patients, CDK4 was positive in both cases, however MDM2 was only positive in one of them. EGFR1 was negative in the two.Both cases were diagnosed after surgery and today they cotinue alive, after 27 months the first one and 5 months the second one. The first one has suffered from metastases that were resected and they two have no syntoms in this moment.
Conclusion: Currently, there is not a clear treatment strategy in chemotherapy. Overall immunohistochemical detection of overexpression of MDM2, EGFR1 or CDK4 means a molecular aberration that can benefit from targeted therapies.

CDK4 x200:



PS-06-028

Activation of calpain-1 and ubiquitin-proteasome system leads to dystrophin loss through inhibition of mTOR during septic cardiomyopathy

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Objective: Evidences from our laboratory demonstrated that cytosolic calcium overload caused increase activation of intracellular calcium-dependent proteases, such as calpain-1 resulting in dystrophin loss/disruption, which could be implicated in the genesis of myocardial depression. This study tested the hypothesis that increased amounts of calpain-1 and ubiquitin in experimental sepsis induced by CLP could be associated with dystrophin loss/disruption through the inhibition of cardiac mTOR expression.
Method: Male C57Bl/6 mice were subjected to sham or severe septic injury (SSI) induced by CLP.
Results: Twenty-four hours post-CLP, mice from SSI group presented increased levels of cardiac calpain-1 and ubiquitin that were associated with reduced amounts of myocardial dystrophin and mTOR expression as compared to sham group. These results show a relationship between sarcolemal dystrophin loss/disruption and mTOR expression that is possible caused by enhanced levels of cardiac calpain-1 and ubiquitin.
Conclusion: Our results reinforce the concept that calpain-1 activation represents a key target in dystrophin disruption behind cardiac dysfunction in severe sepsis/septic shock. Further studies are needed to elucidate this mechanism that may provide new interventional pathways to prevent septic cardiomyopathy.

PS-06-029

A comparison of clinical and histological diagnosis in heart transplant

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Objective: To assess the incidence of discrepancy between the pre-transplant diagnosis and the final histological diagnosis.

Method: Histological reports for the explanted hearts from 143 consecutive heart transplants performed between January 2006 and March 2014 were examined and the clinical data and final diagnosis recorded.
Results: 104 cases showed concordance and 36 significant disagreement. In 3 cases a definite diagnosis could not be made because the coronary arteries were not included. The commonest discrepancy was between a pre-transplant diagnosis of dilated cardiomyopathy (DCM) and a histological diagnosis of ischaemic heart disease (17 cases). Nine other cases thought to be DCM had varied final diagnoses which will be described and illustrated. Other pre-transplant diagnoses not confirmed histologically included valve disease, left ventricular non-compaction and viral myocarditis. Full details will be provided. In some of these cases steroid therapy or surgery might have been a more suitable treatment than transplantation.
Conclusion: 25 % (36/143) of the patients referred for heart transplant were not accurately diagnosed before the procedure and in a small but important minority of cases this could have affected management.

PS-06-030
Biatrial thromboembolus caught in transit through a patent foramen ovale: A case report
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Objective: An unexpected autopsy finding in a 53-year-old man with newly diagnosed disseminated coloncancer.
Method: A 53-year-old man who received chemotherapy for a T4 coloncancer was hospitalized with progressive dyspnea. Echocardiography showed an ejection fraction of 50 % and dominating right heart chambers. During subsequent CT scan the patient suffered cardiac arrest and all attempts at resuscitation failed.
Results: The pulmonary artery was blocked by a large thromboembolus and numerous peripheral emboli were found in both lungs. In the heart a vermicular thrombus (60 × 8 mm) was trapped in a patent foramen ovale.
Conclusion: Cancer is one of the most common acquired risk factors for venous thromboembolism (VTE). The prothrombotic state is exacerbated further by chemotherapy. Patients with active malignancy have a 4-fold to 7-fold higher incidence of symptomatic VTE than the general population. Foramen ovale remains patent in up to 27 % of the adult population. Among patients with pulmonary embolism (PE), the presence of a PFO is an independent predictor of death because of the risk of a paradoxical embolus (PDE). PFO is significant in the etiology of PDE if associated right-to-left shunt occurs - in our case increased right atrial pressure caused by high pulmonary vascular resistance. This case is a classical example of the association between cancer and venous thromboembolism, but with the additional unexpected finding of an impending paradoxical embolus across a patent foramen ovale.

PS-06-033
The impact of number and size of myocardial sample on Acute Cellular Rejection (ACR) diagnosis in endomyocardial biosy of transplanted heart
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Objective: ACR is focally distributed in transplanted heart, thus its diagnosis depends on number and size of myocardial samples. The aim of this study was to assess the impact of samples quality on diagnosis of ACR in EMBs of transplanted heart in Polish one center material.
Method: In 1350 EMBs from 212 patients who underwent heart transplantation between years 2001–2013, ACR was diagnosed according to ISHLT 2004 criteria. The size of specimens were categorized as follows: I -myocardial samples collectively >5 mm2 in size; II- myocardial samples 2–5 mm2 in size; III -myocardial sample/s <2 mm2 in size; IV-non-diagnostic EMB. The frequency of each ACR grade was assessed depending on myocardial sample quality.
Results: There were 24(1.74 %) completely undiagnostic EMBs.To category II 958 (70,96 %) EMBs belonged; 256 (18,96 %) EMBs to category I; 136 (10,07 %) EMBs to category III. Comparing sample quality to frequency of individual ACR grade we received following results: ACR 1R was diagnosed in 24,53 % EMBs from Ist category, 70,94 % EMBs from IInd category and 4,53 % EMBs from IIIrd category. ACR grade 2R was diagnosed in 35,00 % EMBs from Ist category, 58,33 % EMBs from IInd category and 6,67 % EMBs from IIIrd category. Minimal borderline ACR in 28,98 % EMBs from Ist category; 66,67 % EMBs from IInd category and 4,35 % EMBs from IIIrd category.
Conclusion: To diagnose ACR at least two myocardial samples of minimal surface 2 mm2 are needed.

PS-06-034
Papillary fibroelastoma: A medico-legal approach
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Objective: "Papillary Fibroelastoma (FE)" accounts for 7–10 % of benign primary heart tumours. Mainly found on valves [especially on the aortic (44.5 %), followed by mitral, tricuspid and finally pulmonary (8 %)]. It may be asymptomatic (incidentally detected by imaging techniques or during autopsy) or cause severe embolic complications. Authors present their medico-legal experience.
Method: The reports of 2954 forensic autopsies (performed between 2011 and 2013, territorial area = 29.206 Km2, inhabitants = 2.595.540) were reviewed.
Results: Two FE (0.07 %) were found. Both on males. One was aged 45 years-old; the tumour was on the pulmonary valve and he died of congestive heart failure (due to morbid obesity). The other was 53 years-old; the tumour was on the aortic valve and death was by hanging. Both FE were incidentally discovered during autopsy; had typical macro/microscopic features and measured <4 cm.
Conclusion: This series shows: 1) how rare FE is; 2) its possible location/origin on both sides of the heart (even on the least frequent valve); 3) and that Papillary Fibroelastoma must be searched for on natural and violent deaths, because although often an "innocent bystander", it certainly has medical relevance (embolic/ischaemic complications, sometimes dramatic or fatal) and legal importance (potential cause of falls, traffic or other accidents).

PS-06-035
Sudden adult death: Risk factors and causes of a medico-legal series
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Objective: Sudden Death remains an important Public Health problem, namely in what concerns diagnosis and control of risk factors. This study aims to obtain an insight in Sudden Death incidence, causes and underlying risk factors on Adults.

Method: The authors reviewed the files of autopsies performed, at a Medico-Legal Institute, to victims aged ≥ 18 years-old (n = 1053) and deceased during the year 2010 in a territorial area of 29.206 Km2 with a population of 2.595.540 inhabitants. Data was then submitted to statistical analysis.
Results: Sudden Death incidence in Adults was 45.3 % (n = 477). The main death causes were cardiovascular (76.7 %). Among the multiple risk factors disclosed, the most relevant were: male gender, old age, cardiovascular pathological personal antecedents (ischaemic).
Conclusion: Sudden Death incidence in Adults is high. Thus, the control of known risk factors, the search/diagnosis of new ones, the evaluation of risk factors' association (which may increase Sudden Death risk) - either by first or secondary prevention strategies - is vital in the attempt to reduce the number of unexpected fatal events.

PS-06-036
Autophagy activation in the cardiovascular system after two-hit sepsis model
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Objective: This study analyzed morphological, ultrastructural changes and autophagy activation through the LC3B and Lamp-1 protein expression on heart of mice undergoing sepsis induced by cecal ligation and puncture (CLP) followed by pneumonia (second-hit).
Method: Male C57/Bl6 mice were subjected to sham or moderated septic injury (MSI) induced by CLP. Three days post-CLP, surviving mice were subjected to a second-hit with Pseudomonas aeruginosa (Pa). Twenty-four hours after second-hit morphology, LC3B and Lamp-1protein expression were evaluated in septic/control hearts.
Results: Histopathological analysis showed scattered foci of myocytolysis with large amounts of autophagosomes; disrupted myofilamentar structure with intercalated disk alterations were more evident in CLP+Pa group than CLP. Increased myocardial LC3B and Lamp-1expression were more pronounced in septic than control groups. Additionally, was observed an increased mortality rate after second-hit when compared to mice submitted to CLP or pneumonia alone, suggesting that after second-hit sepsis is aggravated coinciding with increased mortality.
Conclusion: This is the first report analyzing autophagy activation in Two-Hit sepsis model (more closely mimics clinical sepsis). New studies are essential to understand the participation of structural proteins as possible targets to proteolytic pathways during septic cardiomyopathy given the continued impact of cardiovascular involvement and the risks of secondary infection on morbidity and mortality.

Monday, 7 September 2015, 09.30 – 10.30, Restaurant
PS-07 Poster Session Cytopathology

PS-07-001
Evaluation of coelomic fluids and its clinical correlation with cytologic diagnosis
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Objective: This study was undertaken to evaluate the coelomic fluids and its clinical correlation with cytologic diagnosis.
Method: This was a prospective study conducted on 70 patients of pleural, pericardial and peritoneal effusions, during the period between January 2012 to May 2013, presenting to the department of pathology, College of medical Sciences-Teaching hospital, Bharatpur.
Results: The present study include 70 cases of pleural fluid, pericardial fluid and peritoneal fluid and analysis was done. 34 cases are of peritoneal fluid, 31 cases are of pleural fluid and five cases are of pericardial fluid. 59 cases diagnosed as chronic effusion (84.28 %). Six cases are diagnosed as inflammatory effusion (8.57 %) and five cases are of malignant effusion (7.14 %) on cytological evaluation. Out of five cases of malignant effusion two cases are of malignant mesothelioma. Fifty percent were turbid, 47 % were clear and 2.9 % were hemorrhagic in appearance. 52.9 % of effusions were exudative and 47.1 % of effusion were transuadative. After comparison of results of cytology with clinical diagnosis overall sensitivity of cytology was found to be 60 %, specificity as 96.92 % and accuracy as 94.28 %, while positive predictive value (PPV) was 60 % and negative predictive value was 96.92 %. The study was statistically significant (p value = 0.003).
Conclusion: The most useful test in establishing the diagnosis of pleural, pericardial and peritoneal effusion is pleural, pericardial, and peritoneal fluids cytology and fluid cell count. Cytological study of the fluid is a complete diagnostic modality which aims at pointing out the etiology of effusion as well as, in certain cases, a means of prognostication of disease process.

PS-07-002
A case of epitheloid hemangienothelioma masquerading as inguinal lymph node metastasis
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Objective: To describe the cytologic findings in a case of epitheloid hemangioendothelioma (EHE) presenting as one-sided enlargement of inguinal lymph nodes.
Method: A palpable lymph node in the right groin, approximately 1.5 cm was aspirated both under ultrasound guidance and direct according to the palpation. Air dried smears were used for preliminary stains with Diff-Quick to evaluate cell content and amount of cell material. Additional smears were routinely stained with MGG. Cell material was also suspended in LBC and prepared as cell block for immunohistochemistry (IHC).
Results: Smears were bloody and had a moderate amount of single and small groups of epitheloid cells with discrete nuclear abnormalities. IHC revealed negativity for epithelial markers whereas endothelial markers were positive. CT revealed enlarged paraaortic lymph nodes that were not investigated further.
Conclusion: Excision biopsy revealed a vascular lesion whose morphology and immunophenotype were consistent with EHE. No other primary tumour was found.

PS-07-003
Human papillomavirus types in cervical infection and cervical intraepithelial neoplasia
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Objective: The study investigated the distribution of HPV in cervical infection, cervical intraepithelial neoplasia -CIN 1, CIN 2/3 and cervical cancer-CC in 124 HPV-positive women.
Method: The patients were tested for cervical smear, HPV infection and biopsy between may 2009-december 2014.
Results: The mean age of participants was 30.7 years (20–55). HR HPV was identified in 97/124 cases (78.2 %), LR HPV in 8/124 cases (6.5 %), both in 19/124 cases (15.3 %). The cytological analysis included 42 normal cytology, 40 ASCUS, 35 ASCH, 73 LSIL and 16 HSIL. The histological analysis included 37 negative for intraepithelial lesions, 75 CIN 1, 74 CIN 2/3 (CIN 2, CIN 3, CIS) and 2 CC. The overall prevalence of HPV was 82.2 % in cytological abnormalities, and 80.3 % in histological abnormalities. The 5 more frequent HR genotypes in order of decreasing frequency were 16,52,58,31,45 in NLIM; 16,52,31,51,53 in

ASCUS; 16,52,45,59,31 in ASCH;16,52,53,51,66 in LSIL and 16,73,18, 66,45 in HSIL, for cytological results, and 16,31,51,52, 58 in NLIM; 16, 52,51,66,39 in CIN 1; 16,52,31,59,73 in CIN 2/3 and 16,52 in CC, for histological results.
Conclusion: Our data shows that genotypes 16,52,31 are the most prevalent HR HPV in both cytological and histological abnormalities, comparable with other studies.

PS-07-005
Extra cell block material as a diagnostic surplus for biomarker analysis in pancreatic EUS-FNA: Comparison of different needles
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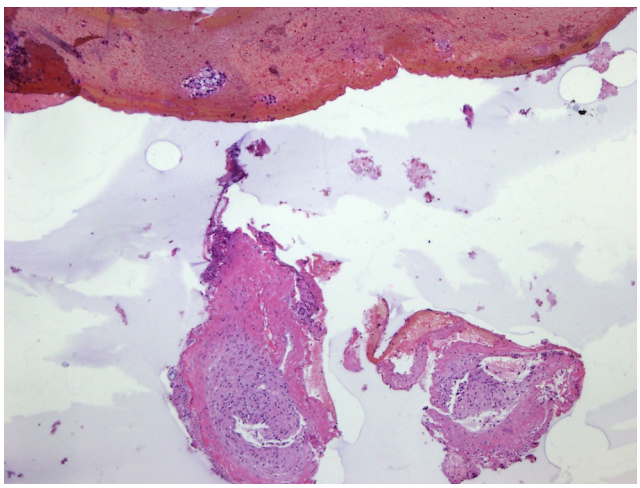
Objective: We aimed to assess the amount of material in cell blocks, obtained with different needles in pancreatic EUS-FNA.
Method: Diagnosis of primary pancreatic carcinoma was performed with EUS-FNA in 36 patients. We used one of the following needles: EchoTip 22G, EchoTip Procore 22G, EchoTip Procore 19G or Expect 19G Flexible. The material obtained was destined to make cell blocks using agar. Epithelium and stroma were separately quantified and divided in 0–1: absent-scanty, 2–3: moderate-abundant material.
Results: In 10 patients EUS-FNA was performed with a 22G needle; 9 with 22G Procore; in 11 with flexible 19G, and in 6 with 19G Procore. Cell blocks contained abundant epithelium in 63,3 % cases using flexible 19G needle; in 33 % with the 19G Procore; in 10 % with 22G and 0 % with 22G Procore. Abundant stroma was obtained with the 19G flexible in 54,54 % cases; in 30 % with 22G; in 16 % with 19G Procore and in 11, 1 % with 22G Procore.
Conclusion: Larger amount of material was obtained in the cell block of both epithelium and stroma by using the 19G needle. The acquisition of extra material can be used as a complementary diagnostic surplus in cytology for the performance of additional molecular techniques and biomarkers.

Cell block from pancreatic EUS-FNA:



PS-07-006
Malignant pancreatic pathology with fine-needle aspiration citology guided by endoscopic ultrasound: Experience of five years
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Objective: Expose experience and statistics obtained in this center during 5 years of use of this procedure, emphasizing malignant pancreatic pathology.
Method: All procedures performed routinely counted on physical presence of pathologist, quality and validity of material obtained was evaluated with Diff-Quick, part of it was fixed in alcohol to staining smear and needle wash was CytoRich. In those cases where material was obtained for cell block, this was fixed in formalin and/or CytoRich. Data analysis was carried out with a retrospective search from January 2008 to February 2015.
Results: In this period were performed 434 procedures, 195 (44.93 %) cases were positive for malignancy, 110 (25, 34 %) cases diagnosed as negative for malignancy, 66 (15.20 %) as benign cystic lesions, 47 (10.82 %) reported as inconclusive and 16 (3.68 %) diagnosed as papillary mucinous intraductal tumour. In the subsequent analysis contrasting results with clinical data, all positive case was confirmed (100 %), inconclusive results citology just 5 (10.63 %) were malignant disease and negative results only 1 (0.90 %) showed malignancy.
Conclusion: Concluding and because of good sensitivity and specificity of this technique, we consider in this center as the gold standard technique for diagnosis in malignant pancreatic pathology.

PS-07-007
Fine needle aspiration biopsy/cytology of epigastric tumours of unknown primary origin
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Objective: To compare sensitivity and specificity of fine needle aspiration (FNA) with or without core biopsy in the diagnosis of suspected epigastric neoplastic disease.
Method: In 4-year period a total of 194 ultrasound-guided FNA biopsies of pancreas, liver and upper retroperitoneum were performed (32 endoscopic and 162 percutaneous), obtaining direct smears and/or cell block preparations; or processed as larger core biopsies when possible. Sensitivity and specificity of cytological and histological results were determined following standard statistical methods.
Results: The most common were metastatic malignancies in liver (129 cases): 85 adenocarcinomas, 8 neuroendocrine tumours and 4 sarcomas and melanomas while 32 cases were hepatocellular carcinomas; followed by primary pancreatic adenocarcinomas (21 cases) and 2 neuroendocrine tumours. The retroperitoneal tumours comprised 4 sarcomas and 7 NHL and 1 metastatic squamocellular carcinoma. FNA cytology identified 54 of 63 malignant lesions (85.7 %) and FNA biopsy 133 of 151(88.1 %) when core sample was available. Cytologic evaluation showed high sensitivity (83.1 %) and 100 % specificity for malignant lesions while sensitivity was higher (88.1 %) when combined with core biopsies and they are similar to other studies (86 to 93.3 %).
Conclusion: FNA cytology is rapid and precise method with high sensitivity and specificity, while core biopsy provides specific tumour subtyping.

PS-07-008
Usefulness of Fine Needle Aspiration (FNA) in the diagnosis of pediatric salivary gland tumours: Review of our casuistry (2004–2014)
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Objective: Salivary gland tumours (SGT) occur in pediatric patients with lower incidence than in adults but with higher rate of malignancy(36 %). Frequently locations: parotid(83 %), submandibular(15 %) and sublingual(10 %). An accurate preoperative diagnosis is important for planning the correct therapeutic approach. The objective is to demonstrate the

utility of FNA of salivary gland tumours in pediatric and review our casuistry (2004–2014).
Method: 14 patients between 4 and18 years with SGT. In seven patients preoperative FNA was performed by cytopathologist (Papanicolaou, Diff-Quick and block cell). Assessment of the overall series and cyto-histological correlation (7 cases).
Results: Localization: parotid(10) submandibular(2), sublingual(1) and intraoral salivary glands(1). Histological diagnosis: 8 pleomorphic adenomas (PA) 2 mucoepidermoid carcinomas (MEC), 2 acinar cell carcinoma (ACC), 1 granulocytic sarcoma and 1 Hodgkin's lymphoma. Cyto-histological correlation of 7 cases: 100 %: 4(PA), 2(MEC), 1(ACC).
Conclusion: SGT, although uncommon, occur in the pediatric age. In our series benign tumours predominate (PA) and among malignant are more frequent the MEC and ACC (coinciding with the literature). The preoperative FNA is very useful in the diagnosis of these injuries, being a simple, safe, fast, Little aggressive tool and well tolerated by pediatric patients without sedation. In our experience, the sensitivity and specificity is 100 %.

PS-07-009
Automated detection of pre cancerous and cancerous cells using CellDetect® technology
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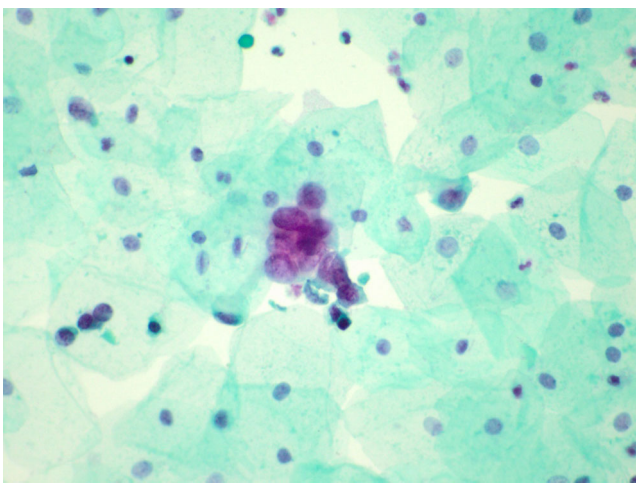
Objective: CellDetect® is unique histochemical-stain enabling color discrimination between normal cells and a variety of neoplastic cells/tissues, including cervix, bladder, colon and circulating tumour cells. Using this technology, normal cells are colored blue/green, while neoplastic cells are stained in red. This tinctorial difference coincides with clear morphological visualization properties. Computer aided detection (CAD) is a software that uses image-processing to estimate the likelihood that specific feature represents a disease process. In this study we tested whether CellDetect® can provide a basis for improved CAD.
Method: 17 cytological smears with biopsy-confirmed diagnosis were used. Cases included 9 LSIL/HSIL, 4 urothelial cancers and 4 NILM. Smears were stained with CellDetect® and showed a full agreement with biopsy results. Smears were photographed and the images were submitted to chromatic statistical analysis and then to local morphology analysis.
Results: Cells that showed positive red staining were analyzed based on pre-defined morphological parameters. The algorithm successfully identified all positive cells present on the image while excluding false signals resulting from cell clusters or inflammatory cells.
Conclusion: This study establishes definite feasibility that the color-morphology combination of CellDetect® can be utilized for CAD. Large-scale blinded study is required to validate these promising results.



PS-07-010
Minimally-Invasive Carcinosarcoma ex Pleomorphic Adenoma: A case report and literature review with cytohistological correlation
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Objective: Carcinosarcoma (CS) of salivary glands is a rare neoplasm, and the minimally-invasive form constitutes a subgroup with a more favorable prognosis. The cytomorphological features of this neoplasm can be appreciated on fine needle aspiration biopsy.
Method: We present a patient with a minimally invasive carcinosarcoma ex non-recurrent pleomorphic adenoma who underwent initial fine needle aspiration biopsy followed by surgical resection.
Results: The tumour was composed predominantly of a pleomorphic high-grade sarcoma exhibiting myoepithelial immunohistochemical features, with a minor component of in-situ and invasive salivary duct carcinoma (10 %). A limited area with features of a hyalinized pleomorphic adenoma was identified.
Conclusion: This is the third case report of the cytological features of carcinosarcoma ex pleomorphic adenoma of the salivary gland, with histologic correlation. It further illustrates the oncogenic relationship between epithelial and myoepithelial elements in the early stages of carcinosarcomatous transformation.

PS-07-011
Collagenous spherulosis on FNA: A case report
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Abstract: Collagenous spherulosis is a rare entity usually seen in association with benign breast lesions. It is often picked up incidentally with a reported incidence of about 0.2 % in cytological material. There are very few reports describing cytomorphological features of collagenous spherulosis. The presence of hyaline spherules surrounded by a single layer of benign myoepithelial cells is the hallmark of collagenous spherulosis on FNA. However, due to close cytological resemblance, it can be misdiagnosed as adenoid cystic carcinoma of the breast. A 63 year-old woman presented with a left breast lesion. Fine needle aspiration was performed. The smears showed scanty cellularity comprising of cohesive clusters and a few branching fragments of benign ductal epithelial cells closely intermingled with many spherical, acellular homogenous hyaline globules. Few bare bipolar nuclei were noted in the background. A diagnosis of collagenous spherulosis associated with benign proliferative breast disease was made. Cytopathologists need to be aware of this entity in order to differentiate it from adenoid cystic carcinoma of the breast which requires radical treatment.

PS-07-012
Persistent detection of psammoma bodies in cervical/vaginal smears revealed an ovarian psammocarcinoma
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Objective: The presence of psammoma bodies in cervical cytologic smears of asymptomatic women has been associated with benign and malignant gynecologic lesions. The aim of our study was to emphasize their role as a cytologic marker of a rare ovarian tumour.
Method: Case report: Pap smears were taken from a 54 -year old woman for routine screening. Microscopic examination showed cervical cells with no morphological abnormalities and a few psammoma bodies. Ultrasonography was recommended and it was normal. Six months later the Pap smears showed clusters of small atypical glandular cells, many psammoma bodies and foci of calcification. The diagnosis was serous papillary endometrial or ovarian adenocarcinoma. Clinical examination,

tansvaginal ultrasonography and uterine curettage revealed only an endometrial polyps, presence of psammoma bodies, calcifications and endometrial atrophy. Unexpectedly 6 months later there was cytologic evidence of persistent psammoma bodies and calcifications in the smears.
Results: A cervical cone biopsy was performed and histopathologic examination confirmed the cytologic diagnosis of malignancy. Metastatic invasive serous psammocarcinoma was observed with many psammoma bodies and calcifications. The ovary supposed to be the most possible primary site. Squamous cervical epithelium was normal. Surgical exploration was scheduled.
Conclusion: The presence of psammoma bodies in Pap smears is a rare finding (0,00047 %) and most frequently associated with benign conditions. However since there is the danger of a possible coexistence of malignant or borderline tumours, this finding should not be underestimated or ignored even in the absence of clinical findings or malignant cells. Ovarian serous adenocarcinoma is the most common neoplasm followed by the uterine malignancy.

PS-07-013
Eurocytology Project 2013-2015: The contribution of the Czech Republic
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Objective: To update the Leonardo - Eurocytology Project 2013-15 and the Czech Society for Clinical Cytology contribution.
Method: Description of activities undertaken - collaboratively and internationally.
Results: The Eurocytology website was originally developed with Leonardo funding in 2005–7. The Czech Society for Clinical Cytology became an official partner in the second phase 2013–2015 targeting on updated content with more languages including Czech and a new dynamic website/training platform. All current modules of the former website have been translated and incorporated into the curricula for cytotechnology and cytopathology education. Prague hosted in September 2014 the international working session. The Czech partners have reviewed the updated chapters of gynecology cytology by Amanda Herbert. The details of the platform are disseminated during national cytology and pathology congresses, workshops and seminars. The feedback from the website users proves increasing interest among the specialists. Due to lack of a language barrier the Czech language version may serve Slovak colleagues tutorials as well.
Conclusion: The updated website www.eurocytology.eu increases the level of cytopathology education in the Czech Republic.

PS-07-014
Extramedullary hematopoiesis as a liver mass lesion diagnosed by endoscopic ultrasound guided fine needle aspiration
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Objective: Extramedullary hematopoiesis (EMH) is the production of mature blood elements outside of the bone marrow. EMH can occur as a compensatory result of a marrow replacing process or from marrow space occupying lesions or marrow fibrosis. Clinically, it can present as a solid mass, and therefore malignant neoplasms or metastatic disease must be considered in the differential diagnosis. It most commonly occurs in the liver, spleen and lymph nodes.
Method: A 59-year-old man with jaundice was found to have a mass lesion with 7 cm in diameter in liver right lobe and peripancretic lymphadenopathies on abdomen ultrasonography (US). Endoscopic ultrasound guided fine-needle aspiration (EUS FNA) biopsy was performed. Cytologic examination and cell block sections displayed trilinear hematopoiesis, with the granulocytic, megakaryocytic and erythroid lineage precursors. A diagnosis of EMH was made.
Conclusion: EMH is an extremely rare and benign cause of liver mass and EUS FNA is an effective diagnostic method for abdomen masses.

PS-07-015
IgH assessment of non-Hodgkin lymphoma cells on FTA cards
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Objective: IgH status evaluation is a fundamental step in the diagnosis of B-cell non-Hodgkin lymphoma (NHL) but cells collection and storage by fine needle cytology (FNC) may be difficult. FTA cards are filter papers that immobilize and stabilize nucleic acids and can be stored at room temperature. This study evaluates whether IgH status may be assessed on FNC NHL cells stored on FTA cards.
Method: 45 NHL and 20 benign reactive lymph node (BRH) FNC cells were stored on FTA cards and DNA extraction were performed on two punched disks. Fifty nanograms of DNA were used to amplify exon 14 of Jak2 gene and to evaluated the IgH rearrangements by semi-nested PCR. Corresponding k/l light chain assessment was evaluated by flow cytometry (FC).
Results: The NHL and BRH extracted DNA means were 13,28 and 8, 19 ng/ul, respectively. IgH rearrangements were observed on 95 % (43 out of 45) and 90 % (40 out of45) of NHL cases from semi-nested PCR and FC, respectively.
Conclusion: IgH status of NHL can be successfully performed on FTA cards stored cells and the obtained data are comparable to those of FC.

PS-07-016
Age comparison of thyroid fine-needle aspiraton biopsies in Bedhesda system
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Objective: 381 thyroid fine needle aspiration biopsy materials we have applied Bethesda system in the last 2 years were handled.
Results: They were 322 females and 59 males. The results were: 69 nondiagnostic (17.6 %), 20 AUS (5.3 %), 270 benign (70 %), 10 suspected of follicular neoplasm (2.7 %), 3 malignant suspect (1 %) and 9 malignant (2.5 %). There wasn't any significant difference in terms of gender in these groups. According to age decades; 113 in decade IV (29.7 %), 101 in decade III (26.5 %), 85 in decade V (22 %), 46 in decade VI (12 %) and 36 in decade II (9.4 %). According to the groups, although there were 150 benign patients at 4th and 3rd decades, 17 AUS patients at 4th and 3rd decades, 42 nondiagnostic patients at 4th and 5th decades, 9 follicular neoplasm suspected patients at 4th and 6th decades, 3 malignant suspected patients at 4th and 3rd decades, 7 malignant patients at 3rd and 5th decades, there wasn't any significant difference in the statistical test. Only the number of the cytopathological examination of thyroid in the fourth decade was found meaningful ($p = 0.01$).
Conclusion: As a result, in our series there was no significant relationship between age and gender distribution and results of Bethesda.

PS-07-017
Distribution of the false negative outcomes of fine aspiration biopsies in thyroid nodules by age and sex
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Objective: In last 1 year in our hospital, of 402 thyroid fine needle aspiration biopsies (FNAB).
Method: 22 were considered benign and after thyroidectomy, malignancy was diagnosed.
Results: Of these, 20 were papillary carcinomas (17 female, 3 male), 2 were follicular carcinomas (both were female). According to current standards, 5 % false negative diagnosis is high, but in a detailed study, the 12 patients were microcarcinomas (diameters smaller than 1 cm), five of them were well located tumours about 2 cm, but there were multiple nodules, that might have taken samples from benign nodules. In re-examination of 22 patients, just like the first examination, in 17, malignancy was not considered. In review of the other 5 materials, malignant histological diagnosis was made. 19 patients were females and 3 were males. Mean age of papillary carcinoma was 44.5, and follicular carcinoma was 33.5. A total mean age was 43. As a result, false negative outcomes of FNAB results showed no significant relationship in terms of age and sex.
Conclusion: The failure in diagnosis of tumour material in five of 402 patients would be considered acceptable. Aspiration of multiple thyroid nodules may reduce the risk of false negatives.

PS-07-018
Distribution of the false positive outcomes of fine needle aspiration biopsies in thyroid nodules by age and sex
A. Kurt*, A. Arslan, I. Calik, S. A. Ozmen
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Objective: There are 3 categories related to risk of malignancy in Bethesda system; "Suspicious for a follicular neoplasm", "Suspicious for malignancy" and "malignant". When a cytologic material diagnosed as malignancy, but in the surgical pathologic examination it is benign, and in the re-examining of cytologic material if malignancy could not be find, it is false-positive diagnosis.
Method: In our hospital, 4 of 402 patients applied for Bethesda system after thyroid fine needle aspiration biopsy, malignancy was thought, but later in the thyroidectomy material there wasn't malignancy and all have received "nodular goiter" diagnosis.
Results: Cytopathology of the 3(2 female 1 male) false-positive patients were "suspected papillary carcinoma", and 1 was (female) "may be follicular carcinoma". These diagnosis do not take place in Bethesda, however they strongly indicatemalignancy, and seems to be cautious. So, it is more probable than "Suspicious for a follicular neoplasm" and "Suspicious for malignancy", but not just a diagnosis of malignancy. All of the patients were female, the average age was 46.
Conclusion: False positive cytology in thyroid surgery is considered riskier than false negative and 1 % false positive diagnoses can be considered higher than it should be.

PS-07-019
Cytological features of pleomorphic/necrotic lobular carcinoma in SITU of the breast detected by screening mammography
A. Sato*, T. Kawasaki, T. Yuminamochi, Y. Ishii, K. Nakazawa, S. Sato, N. Yamada, J.-i. Ambo, S. Moritani, S. Ichihara, T. Sugai
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Objective: Mammary pleomorphic lobular carcinoma in situ (PLCIS) is regarded as a pre-invasive counterpart of PLC. However, the cytologic features of this tumour have yet to be sufficiently analyzed and definitively determined.
Method: The patient was a 58-year-old postmenopausal Japanese woman. Screening mammography revealed pleomorphic micro-calcifications in a segmental distribution in the upper outer portion of the left breast. We performed ultrasound-guided, fine needle aspiration (FNA) of an irregularly-shaped hypoechoic mammary area with hyperechoic spots.
Results: The FNA specimen showed high cellularity in the necrotic background with calcifications. Singly dissociated tumour cells were prominent, whereas loosely-arranged tumour cell clusters were also observed. Large tumour cells were polygonal in shape and had eosinophilic, granular and/or foamy cytoplasm. The nuclear/cytoplasmic (N/C) ratio was intermediate, and some tumour cells contained intra-cytoplasmic lumina and/or mucin with a 'signet-ring' morphology. The nuclei had a fine chromatin pattern and irregular shapes with nuclear grooves, frequently with distinct nucleoli. Binucleated tumour cells were occasionally present. Mitotic figures were not uncommon. Histologically, the diagnosis of PLCIS, accompanied by comedo-like necroses with dystrophic calcification, was confirmed based on the mastectomy specimen. Immunohistochemically, cancer cells were negative for E-cadherin and positive for 34βE12 and GCDFP15.
Conclusion: Herein, we showed the characteristic cytopathological findings of mammographically-detected PLCIS.

PS-07-020
Endometrial serous carcinoma diagnosed by smear test
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Objective: A 58-year-old female patient with postmenopausal bleeding was admitted, endometrial thickening was seen by USG but she did not accept probe curettage so, only cervical smear could be taken.
Results: At cervical smear, atypical cells with prominent nucleoli containing irregular chromatin which formed three-dimensional groups and small papillary structures, nuclear hyperchromasia and coarsening on a dirty floor were seen and reported as "malignant cytology findings are consistent with glandular malignancy. Endometrial and endocervical curettage recommended". A week later macroscopically about 3 cc volume of hemorrhagic curettage material was histopathologically examined and atypical cells with prominent nucleoli and hyperchromatic nuclei were observed to create a papillary configuration. These papillary structures consisted of atypical hobnail cells. At immunohistochemical staining, positivity with Pan- CK, vimentin and P-16 were seen. There was a strong expression of P-53. It was reported as "Serous carsinoma". Serous papillary type of endometrial carcinoma is seen in 5–10 % and usually develops from atrophic epithelium.
Conclusion: Cervical smear test, is not for diagnosis, it is for screening. There is no method for screening and early diagnosis of endometrial cancer. At cervical smear material, the presence of cells falling from the endometrium may be a guide for further examination of endometrial cancer.

PS-07-021
New approach to sample preparation to cytology of voided urine in bladder carcinoma
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*Russian Oncology Scientific Center, St. Petersburg, Russia

Objective: Cytology diagnostic in bladder pathology is difficult. There is high specificity 62–97,4 %, and low sensitivity 20,8–84 %.
Method: We evaluate 300 patient with different bladder pathology. After collection whole voided urine sample was double centrifuged: first

time during 10 min by usual centrifuge 3000 r/min and secondly using Shandon Cytospin-3 («Thermo Shandon Limited», UK) 5 min by 2000 r/min.
Results: Using this approach cells were concentrate on glass up to 20 time more compared usual technique, but final cellularity depends on quantity of urine and presence of inflammation, cancer recurrence or other kind of pathology. Diagnostic value of cytological method grows from 45 to 92 %.
Conclusion: Using this approach we can evaluate urine cytology sample faster and accurately than conventional sample preparation.

PS-07-022
Epithelioid hemangioendothelioma in pleural fluid: Report of a case and review of the literature
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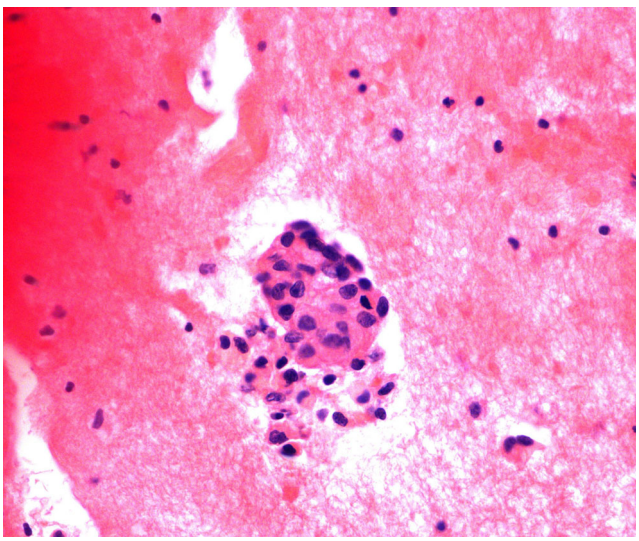
*Oslo University Hospital, Dept. of Pathology, Norway

Objective: Epithelioid hemangioendothelioma (EHE) is a rare vascular malignancy of intermediate grade that presents in a variety of sites, including soft tissue, bone, lung, liver, pleura and peritoneum, skin, lymph nodes, stomach, and brain. EHE can metastasize, with reported rates up to 30 % and mortality from 13 to 65 %.
Method: A 32 year old female presented with dyspnea and pain in the thoracic and abdominal region. Thoracic x-ray revealed "white lung" and pleural fluid. Cytology of pleural fluid with immunohistochemistry on cell blocks was performed.
Results: Morphological examination revealed scattered single cells and small groups with distinct nuclear atypia, suspicious of malignancy. Cell groups demonstrated intracytoplasmatic vacuoles or lumina. Cells were positive for vascular markers CD31 and CD34, cytokeratinAE1/AE3 and vimentin, and negative for all other markers, including calretinin, melanA, HCG, CD45 and BerEp4. The diagnosis was reported as suspicious of malignancy of unknown origin, possible sarcoma. Multidisciplinary discussion exposed patient had been suffering from pain in her ankle. Bone, and later pleural biopsy showed tumour compatible with EHE. The patient received chemotherapy but died few weeks later due to respiratory failure.
Conclusion: EHE is a rare, potentially serious, and diagnostically challenging disease. Hence awareness should be paid to this entity.

EHE cell block:



PS-07-023
Gonadal and extragonadal germ cell tumours: Cytologic features in Fine-needle Aspiration cytology (FNA)
R. Orellana Fernández*, R. Ballester Victoria, M. R. Escoda Giralt, R. Posada Caez, L. García Ortiz, A. Ferran Gibert, N. Combalia Soriano
*Parc Tauli Sabadell Hospital, Dept. of Pathology, Spain

Objective: To evaluate and describe cytologic features of germ cell tumours (GCTs), both primary and metastasis from gonadal sites, in FNA cytology.
Method: Aspirates from 9 GCTs (6 testicular and 3 extragonadal) with adequate cytologic material were analyzed with its clinical features and cytologic smears. The smears were assessed for background, cellularity, cell patterns, cytologic features and immunohistochemical staining. Cytohistologic correlation was done in all cases.
Results: We observed morphologic features that allow to identify each tumour in 6 cases: seminoma (2), embryonal carcinoma (1), choriocarcinoma (1) and mixed GCTs (2) -one with embryonal carcinoma, Yolk sac tumour and teratoma components and other with embryonal carcinoma and Yolk sac components-. Three cases were difficult to diagnose: Yolk sac tumour (2) and mixed GCTs with seminoma and Yolk sac tumour components (1).
Conclusion: Seminoma and embryonal carcinoma have cytologic features that allow its diagnostic in FNA cytology unlike Yolk sac tumour. The variant anaplastic seminoma may be indistinguishable from embryonal carcinoma. Organized clusters of epithelial and/or mesenchymal cells suggest teratoma. Mixed GCTs represent a diagnostic challenge in cytology because of sampling error on FNA. The cell bloc allows immunohistochemical study, helpful in the diagnosis of these tumours. Also, clinical data and blood test are relevant.

PS-07-024
The use of fine needle aspiration cytology as an additional tool for diagnosis of cherubism: A case report
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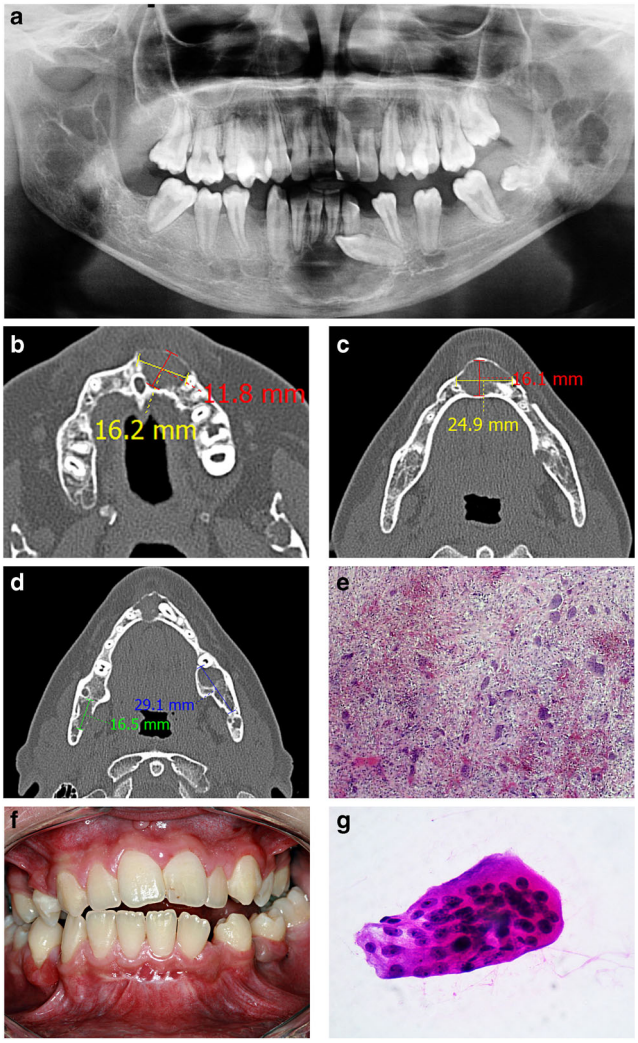
*Universade Federal Santa Maria, Dept. de Patologica, Brazil

Objective: The aim of the study was to demonstrate the use of fine needle aspiration cytology (FNAC) as an auxiliary tool in the diagnosis of cherubism through a case report.
Method: A 10-year-old girl presented bilateral symmetric mandibular increased. Image exams revealed well-defined bilateral multilocular radiolucent lesions in the angle and mandibular branches, as well as a large unilocular lesion in the mandibular symphysis. The results of laboratory tests (blood count, serum calcium, phosphorus, and alkaline phosphatase) were normal. On occasion, an incisional biopsy was performed in the symphysis, and the histopathology diagnosis was cherubism. Three years later, the patient returned with a new lesion in the anterior maxilla, with no defined edges and causing root resorption of incisors. FNAC was carried out with a 24-gauge needle attached to a 10 ml syringe.
Results: The exam showed typical multinucleated giant cells, besides some fibroblasts, with no evidence of cellular atypia. These features are not specific for the diagnosis of cherubism, but, if they are analyzed together with other data, it is possible to make the diagnosis.
Conclusion: FNAC, when combined with clinical and radiological data and laboratory tests, is a useful, safe and effective method that plays an important role in the diagnosis of cherubism.

Histopathological features and cytopathology of Cherubism:



Monday, 7 September 2015, 09.30–10.30, Restaurant
PS-08 Poster Session Digestive Diseases Pathology I: Upper gastrointestinal tract

PS-08-001
Primary gastric histiocytic sarcoma: Case report
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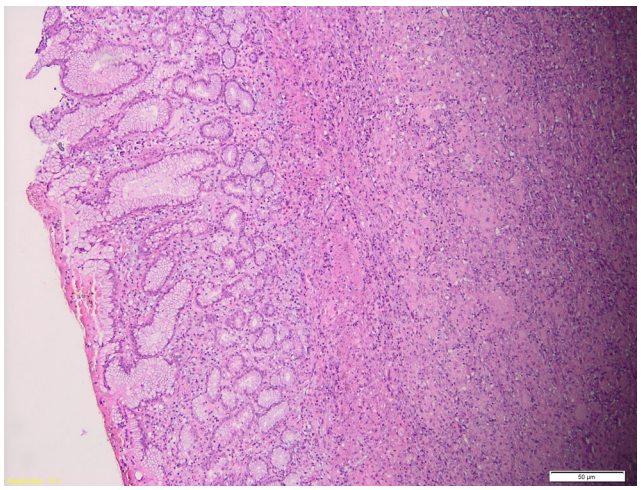
Objective: Histiocytic sarcoma is a rare malignant neoplasm with only a limited number of cases reported. The majority of cases occur in extranodal sites such as the intestinal tract, skin or soft tissues. However, regarding the intestinal tract, primary gastric involvement is exceptional.
Method: We report a 48 year-old male patient who was admitted for marked weight loss, night sweats, lethargy and cramp-like abdominal pain. Esophagogastroduodenoscopy revealed a 10 cm ulcero-fungating lesion located in the gastric fundus which extended both towards the cardia and the body region.
Results: Microscopically, tumour cells showed eosinophilic, abundant cytoplasm, convoluted, overlapping nuclei, vesicular chromatin and one or two visible nucleoli. Pleomorphic or multinucleated tumour giant cells were frequently observed. Immunohistochemical staining showed tumour cells were strongly reactive for CD68 and vimentin and focally positive for leukocyte common antigen (LCA) and S100. Tumour cells were negative for epithelial cell markers (CK7, EMA, CEA). Other negative markers included CD117, p63, HMB-45 and Ki67.
Conclusion: Histiocytic sarcoma is a rare, aggressive neoplasm that if present in an uncommon site can mimic other entities. Careful histopathological analysis and consideration of differential diagnosis are therefore imperative as this neoplasm has a poor outcome.

Primary gastric histiocytic sarcoma:



PS-08-002
Crohn's Disease of the stomach: Report of two cases
G. Halcu*, A. Evsei, M. Ionescu, C. Vasilescu, M. Calita, V. Herlea
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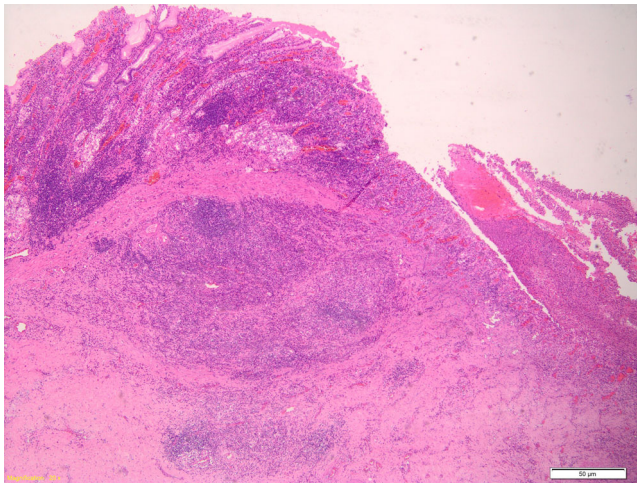
Objective: Crohn's disease (CD) is a chronic idiopathic inflammatory disease of the gastrointestinal tract. Ileocolonic and colonic/anorectal involvement is the most common, while stomach as a primary isolated site is very unusual.
Method: We report here two cases of gastric CD diagnosed in our institution. One is a 72-year-old male that presented epigastric pain and diffuse redness with small nodules on endoscopy. The other case, reports a 65-year-old female that presented nausea, vomiting, epigastric pain and multiple gastric ulcerations on endoscopy.
Results: Macroscopically, the first resection specimens had a thickened area of 2 cm diameter within the stomach wall with a slightly increased gray color, while the second case had multiple erosions and ulcerations of the mucosa. Histologically we found ulcerations of the mucosa with necrotic debris underlying non-caseating granulomas composed of epithelioid cells and multinucleated giant cells, and a polymorphous inflammatory infiltrate in both cases; in the second case, we report extensive intestinal metaplasia and focal areas of invasive carcinoma in the submucosa. The lymphatic nodules were free of tumour with reactive morphology.
Conclusion: Isolated gastric CD is a very rare entity. When diagnosis is a matter of great concern, the efforts should be diverted to confirm the diagnosis and specifically to search for dysplasia or neoplastic changes due to the higher risk of malignancy associated with Crohn's disease.

Ulcerated mucosa and non-necrotizing granuloma:



PS-08-003

Different patterns of MUC-1 expression in the gastric mucosa in premalignant conditions

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Objective: Mucin -1 (MUC-1) possesses a protective capacity which participates in composing the barrier of "mucus-bicarbonate". The aim of the study was to assess the expression of MUC-1 in patients with and without gastric premalignant conditions.
Method: 62 patients were prospectively enrolled in the study. Five biopsy samples were obtained from each of the patients according to the updated Sydney system. Slides were stained with hematoxylin and eosin, alcian blue, Giemsa and immunohistochemically with MUC-1.
Results: Loss of MUC-1, either patchy or complete, was noted in 52 % of the cases. Obtained results showed decreased MUC-1 expression in patients with atrophic gastritis compared to patients with superficial gastritis ($p < 0.001$). In addition, in patients with intestinal metaplasia, the MUC-1 was significantly downregulated ($p < 0.01$). In patients with H.pylori gastritis the MUC-1 expression was lower compared to patients without H.pylori infection ($p = 0.004$). Furthermore, the MUC-1 expression was significantly lower in the mucosa of lesser curvature compared to the greater curvature of both antrum and corpus.
Conclusion: MUC-1 expression was decreased in the gastric premalignant conditions, which is more prominent in the lesser compared to the greater curvature.

PS-08-004

Characterization of histopathologic lesions in gastroenteritis associated to norovirus in a model of study

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Objective: The aim of this study was to evaluate the histopathological lesions in gastroenteritis, associated to canine norovirus, suggesting the possibility of a novel model for human infection.
Method: Samples of small intestine were collected and fixed (10 % neutral buffered formalin) for a maximum of 48 h and 3 μm sections were stained for routine histopathological evaluation. Apoptosis studies combined the immunohistochemical detection of cytochrome c and the DNA fragmentation by TUNEL assay.
Results: The microscopic findings revealed severe epithelial detachment, mucosal loss and hypertrophy of all small intestinal layers. Also, an intense mononuclear inflammatory infiltrate within lamina propria of small intestine proximal segments were seen, very similar to IBD lesional pattern.
Conclusion: Canine inflammatory bowel disease (IBD) is a heterogeneous group of chronic gastrointestinal disorders with unknown etiology, immunologically-mediated, similar to human IBD. With this study it is tempting to hypothesize that canine norovirus could be significantly evolved in the complex aetiopathogenesis of IBD, identically in human Crohn disease - an example of human IBD, which could highlight the relevance of canine norovirus in the aetiopathogenesis of this chronic condition.

PS-08-005

Malabsorption and emaciation in a patient with Giardia Lamblia infection and underlying common variable immunodeficiency

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Objective: Severe small intestinal atrophy with subsequent malabsorption and emaciation due to Giardia Lamblia infection is uncommon.
Method: A 53 year old patient presented with severe weight loss and foul-smelling watery diarrhea. Colonoscopy revealed multiple polyps in cecum and ascending colon and biopsies were also taken from the duodenal mucosa.
Results: Histopathological examination of duodenum showed severe villous blunting with crypt hyperplasia and increased CD3 intraepithelial lymphocytes. Concurrent nodular lymphoid hyperplasia in lamina propria of the mucosa was observed. Several trophozoites of the parasite Giardia Lamblia were noticed on the surface of the mucosa. CD138 plasmatocytic marker did not detect any plasma cells in the lamina propria. Colon polyps were of regenerative nature with abundant eosinophilic leukocytes although the parasite was not detected in colon specimens. The patient was diagnosed with Giardia Lamblia infection, secondary malabsorption syndrome and common variable immunodeficiency. gamma-globulin substitution and antibiotic therapy resulted in gradual weight gain due to eradication of the parasite and restoration of small bowel villous architecture.
Conclusion: Parasitic infections with or without underlying immunodeficiency should always be taken in consideration in cases of malabsorption due to small bowel atrophy.

PS-08-007

Intestinal wall changers in experimental abdominal cavity high pressure

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Objective: Abdominal cavity high pressure in case of acute abdominal diseases occurs various complications and sometimes leads to patient's death. To prevent these complications curative intestinal stomas are used but it is not yet known whether intestinal wall is injured by abdominal cavity high pressure or not.

Method: Morphological study of intestinal wall has been performed in white laboratory rates in case of experimental abdominal cavity high pressure (18 animals). Specimens of intestinal wall were investigated with histochemistry in 10, 30 days, 3 and 6 month after experiment's beginning.
Results: It was carried out that intestine wall prominently injures with abdominal cavity high pressure. During the first month after beginning of the experiment acute and most often reversible changes are being spread: acute blood circulation abnormalities and intestinal wall oedema, secretion strengthening and alterative mucosa destructions. After 3 months intestine wall destructions become more resistant, level of secretion decreases. In 6 months atrophy and sclerosis of intestinal wall appear, that allows estimating these changes as irreversible.
Conclusion: Revealed data can become the base of issue for curative intestinal stoma closure time limits.

PS-08-009
Sarcomatoid carcinoma of the small intestine: Report of two cases and review of the literature
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*Hospital Universitario Basurto, Dept. de Anatomia Patologica, Bilbao, Spain

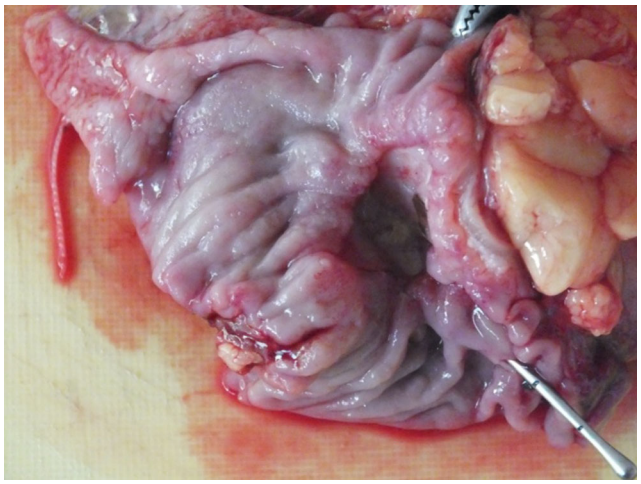
Objective: Sarcomatoid Carcinoma (SC), an aggressive and unusual tumour in the gastrointestinal tract, is rarely reported in the small intestine (30 cases to date). We report two cases, located in duodenum and ileum respectively.
Method: Case 1: A 50 years old male presented with dyspepsia. On CT: a hipogastric huge mass of 14 cm from duodenum and involving liver, galdbladder and colon. A diagnosis of SC was made from endoscopical samples. Post-quimiotherapy parcial resection was performed. Case 2: A 57 years old female with abdominal pain. On CT and surgery, an ileal mass of 8–9 cm is observed. Radiologically, GIST was suspected in both cases.
Results: Both, histopathologically are ulcerated with areas of necrosis and hemorrhage, and pleomorphic/discohesive tumour cells with a similar inmunohistochemical profile was detected (see table).
Conclusion: This rare variant of the small intestine carcinoma have poor prognosis, is highly aggressive and most patients present with an advanced disease. A wide range immunohistochemical panel should be performed for the differential diagnosis with the more frequent GIST.

	AE1/AE3	CK7	CK20	VIMENTINA	CD34	S100	ACTINA	DESMINA	C-KIT	DOG-1	Ki67
1	+++	+++	-	+++	-	-	-	-	-	-	80%
2	+++	+++	-	+++	-	-	-	-	-	-	70%

PS-08-010
Adenocarcinoma of minor duodenal papilla
O. Paklina*, G. Setdikova, E. Gordienko
*Moscow, Russia

Objective: The adenocarcinoma of minor duodenal papilla are most rare, with only a few cases described so far.
Method: Due to low MDP adenocarcinoma incidence, we offer our clinical observation as follows.
Results: A man, G., 51 with obstructive jaundice syndrome. EGD on admission: Large deep ulceration with underlying infiltrated edges around immediately after superior flexure on posteromedial wall. Ulceration size circa 3 cm, its floor covered with thrombosed vessels; contact petechiae. No bleeding on examination. Mucosal infiltration extends to MajDP enlarged longitudinal fold. MajDP itself is enlarged, oval-shape, 2 × 3 cm, swells in duodenal lumen, dense consistency, 2 mm opening, looks downward to complicate drastically cannulation. Abdominal CT: Liver size and parenchyma density normal. Intra-hepatic bile ducts dilatated, with up to 8 mm for lobar ducts. CBD dilatated up to 11 mm, coning at terminal section level. Gallbladder collapsed. Pancreas normal size. Wirsung's duct not dilatated. Parapancreatic mass not infiltrated. Gross: On duodenum opening through the anti-ampullar (crest, a 1.5 × 1.7 cm infiltrative ulcerous tumour was revealed with uneven dense boundary 1.5 cm proximally of MajDP. CBD opened into MajDP. No change in the ampullar zone. Micro: Moderately differentiated adenocarcinoma of MDP, PB type. Stage III (pT4, pN1, pM0).
Conclusion: Currently, prognosis for patients with MDP adenocarcinoma is unclear, yet reports are available on similar prognosis for ampullary carcinoma.

Gross:



PS-08-011
Comparing Helicobacter pylori detecting methods and their correlation with active chronic gastritis
Z. Kramer*, E. Kocsmár, I. Szirtes, A. Szijarto, L. Bene, G. Buzas, Z. Schaff, A. Kiss, G. Lotz
*2nd Institute of Pathology, Budapest, Hungary

Objective: Comparison of the diagnostic value of three H. pylori detecting methods (Giemsa, Immunohistochemistry (IHC), FISH); whether their sensitivity correlates with active chronic gastritis and with H. pylori infection associated structural mucosal changes.
Method: We examined 2981 gastric biopsies, defined the presence of active chronic gastritis and/or H. pylori infection associated structural mucosal changes. We evaluated the sensitivity and specificity of Giemsa, IHC and the H. pylori FISH test.
Results: Of the 2981 cases 687 (23 %) were positive with Giemsa, 795 (26,6 %) with IHC, 788 (26,4 %) with FISH. Their sensitivity and specificity were 83,3 and 98,9 % with Giemsa, 98,8 and 99,3 % with IHC and 98 and 99,6 % with FISH, respectively. We did not find any correlation between method sensitivity and the presence of structural mucosal alterations. Nevertheless the sensitivity of Giemsa showed positive correlation with active inflammation; 64 % of the IHC/FISH positive cases which did not show active inflammation were negative with Giemsa.

Conclusion: H. pylori diagnosis based on Giemsa stain has good specificity, but low sensitivity, therefore rutine IHC detection is recommended. FISH and IHC have similarly high sensitivity and specificity, moreover FISH method is capable to determine clarithromycin resistance.

PS-08-012

Endoscopy and histopathology in diagnostic of Barrett's esophagus

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Objective: Barrett's esophagus is a lesion of the lower portion of the esophagus that characterized by the replacement of the normal stratified squamous epithelium lining of the esophagus by simple columnar epithelium (intestinal metaplasia) with goblet cells and is considered to be a premalignant condition. Our purpose was to establish how often endoscopic diagnosis 'Barrett' actually corresponds to its morphology and is supported by histologic data.
Method: Endoscopic biopsies from 347 patients (M - 160, F-187), median age - 61 years old were taken and carefully evaluated by trained pathologists in order to find histopathological features of the Barrett's esophagus.
Results: Intestinal metaplasia in esophageal biopsies was found in 98 cases (28 %). In 72 (21 %) cases were 'non-informative' presenting only squamous epithelial layer without its base. Remained 177 (51 %) biopsies provided informative and representative data for BE exclusion - normal esophageal mucosa, gastric metaplasia, etc.
Conclusion: Complex approach including collaboration of endoscopist and pathologist, is necessary for correct diagnosis of Barrett's esophagus in order to determine the patients for further careful surveillance of this premalignant lesion.

PS-08-013

Monomorphic CD56+ intestinal T-cell lymphoma of the ileum with aberrant expression of CD20 and extensive extra-intestinal involvement: A case report

L. Santos*, H. Bettencourt, M. Jácome, I. Macedo-Pinto
*IPO Porto, Dept. de Anatomia Patológica, Portugal

Objective: Monomorphic CD56+ intestinal T-cell lymphoma(MTCL), also referred as type II enteropathy associated T-cell lymphoma, is an uncommon type of lymphoma of the intestinal intraepithelial T lymphocytes. The etiology of this disease is unknown and it appears to occur sporadically with no association to celiac disease.
Method: A 63 year-old male, with no relevant medical history, presented with intestinal perforation that underwent a segmental ileectomy. Postoperative clinical and imagiological examination revealed hepatic and lung nodules and a parotid mass. Partial parotidectomy was performed.
Results: Macroscopic examination of the ileum showed an ulcerative and infiltrative multifocal white lesion with perforation of the visceral peritoneum. The neoplastic cells were small to medium-size, monomorphic, with hyperchromatic nuclei and diffusely infiltrated the intestinal wall. Adjacent mucosa showed prominent intraepithelial lymphocytosis. The parotid evaluation revealed a poorly defined white lesion with similar microscopic findings. In both cases, the neoplastic cells expressed CD3, CD56 and focal CD20 and were negative for CD5, CD10 and EBER. A diagnosis of MTCL of the ileum with involvement of the parotid was rendered.
Conclusion: MTLC can occur without symptoms and present as an emergency associated with perforation. It can course with multifocal involvement of the intestine or extra-intestinal dissemination and the prognosis is poor.

Monomorphic CD56+ intestinal T-cell lymphoma:

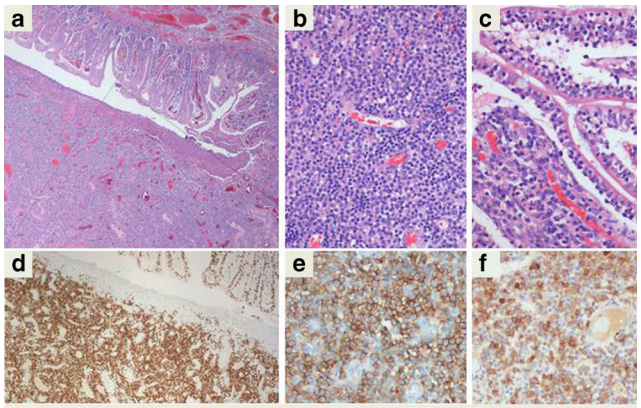

Fig.1: Cytomorphology and imunohistochemestry of MTLC of the ileum. Intraepithelial invasion (C); The neoplastic cells express CD3 (D), CD56 (E) and CD20 (F)

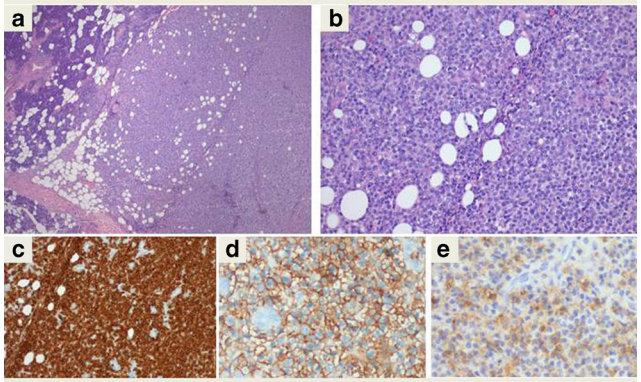

Fig.2: Involvement of the parotid by MTLC (A and B); The neoplastic cells are positive for CD3 (C), CD56 (D) and CD20 (E)

PS-08-014

Primary isolated extramedullary plasmacytoma of mesentery: A rare case report

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Objective: Plasmatocytomas are monoclonal plasma cell proliferations originating either in localized osseous tissue or in soft tissue (extramedullary plasmacytoma, EMP). The mean age of developing extramedullary plasmacytoma is 55 years, with a female predominance. Solitary EMP of the mesentery is extremely rare with only four cases reported in the literature so far.
Method: A 47-year-old man presented with severe epigastric pain and constant vomiting. On clinical examination he was tender in the epigastrium. Abdominal CT showed a large epigastric mass, completely replacing the pancreas and displacing the stomach anteriorly and to the left. Exploratory laparotomy revealed a mesenteric nodal mass obstructing the third part of the duodenum was revealed. Biopsies were taken.
Results: Histological examination showed morphological and immunohistochemical features of plasmatocytoma. This was followed by a full

staging for myeloma which was negative. Finally, a diagnosis of solitary EMP of the mesentery was set.
Conclusion: EMP is a plasma cell neoplasm without bone marrow involvement. In 17 to 33 % of plasmacytomas, the extramedullary disease will develop into multiple myeloma. More than 80 % of EMPs arise in the rich lymphatic tissue of the upper respiratory tract. Solitary EMPs are highly radiosensitive with a 10-year overall survival rate of 70 %.

PS-08-015
HER2 overexpression and correlation with clinicopathological factors in gastric carcinoma
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Objective: We aimed to find a correlation between human epidermal growth factor receptor 2 (HER2) gene amplification and clinicopathological factors in gastric cancer patients.
Method: We performed a retrospective study on surgical resection specimens from gastric cancer patients operated in Emergency County Hospital Timisoara, Romania, between 2010 and 2014. Clinicomorphological data and immunohistochemical HER2 expression were assessed.
Results: We identified 53 patients (36 male and 17 female, mean age 62, 98). HER2 was overexpressed (3+) in 6 cases (11,32 %), 10 (18.87 %) were equivocal (2+) and 37 (69.81 %) negative (0/1+). We observed HER2 overexpression in five patients with intestinal type adenocarcinoma (9,43 %) (p = 0,3252) and in 1 case (1,88 %) of diffuse type. All patients with HER2 positivity were men and in advanced stage disease (>pT2, p = 0,4463). HER2 positivity was identified especially in moderate histological grade (p = 0,2619). No significant differences were found in HER2 positivity regarding age and lymph node involvement. We observed a higher rate of HER2 overexpression in patients with lymphovascular invasion (83,3 %).
Conclusion: Although we did not notice any significant statistical correlation between the HER2 overexpression and clinicopathological factors, our results suggest that patients with advanced stage, moderately differentiated intestinal type adenocarcinoma are candidates for anti HER2 therapy.

PS-08-016
The diagnostic utility of DOG1 immunoexpression on gastrointestinal stromal tumour and the correlation between clinicopathological features
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Objective: DOG1 is a molecule proposed to be an alternative for CD117 in gastrointestinal stromal tumour (GIST) diagnosis. The aim of the study was to evaluate the diagnostic significance of DOG1 on GISTs, especially on CD117-negative GISTs.
Method: DOG1 was evaluated in 100 cases of GISTs immunohistochemically. The association between DOG1 expression and clinicopathological features, and immunoexpression of CD117, CD34, SMA, desmin, S100, and Ki-67 performed at the initial diagnosis were analyzed statistically.
Results: Ninety cases were positive for DOG1 and 89 cases were positive for CD117. DOG1 was directly correlated with CD117 (p = 0.001), and inversely correlated with SMA (p = 0.004). All CD117-negative GISTs (11 cases) were positive for DOG1. GISTs containing epithelioid cells were found to show higher tendency for DOG1 immunoreactivity (p = 0.017). No statistical significant association was detected between the immunopositivity of DOG1 and CD34, desmin, S100, Ki-67 proliferation index, age, gender, risk group, mitotic count, tumour size, growth pattern, cellularity, nuclear pleomorphism, ulceration, hemorrhage, and necrosis.
Conclusion: This study has showed that DOG1 is a reproducible marker for GIST diagnosis, particularly for CD117-negative GISTs. Higher expression of DOG1 may be found in GISTs composed of epithelioid cells. In GISTs with higher immunoreactivity of DOG1 might show lower expression of SMA.

PS-08-017
Molecular factors and dendritic cells in development of gastric cancer: New data in old Pathology
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Objective: Gastric cancer (GC) is still fourth most common malignancy in the world. Therefore, besides the clinicopathological factors known to be prognostic markers, new independent parameters like antigen presented cells, growth factors and some polymorphisms are being investigated. The aim of the study was to assess the expression and significance of HER2/neu, TGF-beta 1, his receptor -RII and mature CD83-positive dendritic cells (DCs), and Ile/Val single nucleotide polymorphism (SNP) of HER2 in GC specimens.
Method: Thirty six cases of GC were investigated immunohistochemically for HER2/neu, TGF-beta 1, TGF-betaRII and CD83 expression and with RFLP - PCR analysis for Ile/Val of HER2 SNP at codon 655 in 30 samples. The results were compared with clinical and pathological parameters of investigated patients.
Results: All patients were negative for HER2/neu expression. RFLP - PCR analysis showed that 66.7 % of the patients with metastases had AG genotype vs. 33.3 % were with AA genotype (χ = 4.76, p = 0.029). Also, 95.2 % of TGF-beta1 positive cases had low infiltration with CD83-positive DCs in tumour border while 47.6 % from TGF-beta1 negative samples had high infiltration (χ = 9.97, p = 0.002).
Conclusion: Our results suggest that SNP in HER2 codon 655 and investigation of DCs infiltration and some factor expression have important prognostic significance for the patients GC.

PS-08-018
Evaluation of relationship between ARID1A expression and clinicopathologic parameters in HER2 positive and negative gastric carcinomas
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Objective: Development of gastric carcinoma is regulated by many factors. AT-rich interactive domain 1A (ARID1A) is a tumour suppressor gene involved in chromatin remodeling and it encodes the ARID1A protein. Recent studies have shown the loss of ARID1A expression in gastric carcinomas may have a prognostic importance. In our study, we purposed to evaluate the interactions between ARID1A loss and HER2 status in gastric carcinomas.
Method: ARID1A expressions were studied in 113 formalin-fixed, paraffin-embedded gastric carcinoma specimens and its association with different pathological and clinical parameters was evaluated.
Results: Loss of ARID1A expression was detected in 54 (47.6 %) of 113 cases. ARID1A expressions were normal in most HER2 positive tumours (n = 20, %64,5), while defective expression of ARID1A was detected in HER2 negative tumours (n = 43, 52.4 %). Statistical significant association was not found between ARID1A expression and features of gastric tumours. Contrary, there was significant association between ARID1A expression and stage of HER2 negative tumours (p = 0.039).
Conclusion: Identification of specific biomarkers is very important for prediction of clinical outcome in gastric tumours. We demonstrated loss of ARID1A expression in HER2 negative gastric cancer negatively correlate with stage. These results suggest that ARID1A may play a role in the biology of HER2 negative gastric cancers.

PS-08-019

Morphological and immunohistochemical correlation in GISTs: A retrospective study of 21 cases

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Objective: Gastrointestinal stromal tumours (GISTs) are the most common primary mesenchymal neoplasms of the gastrointestinal tract, typically expressing CD117, CD34 and DOG1, composed of spindle, epithelioid or mixed cellularity.
Method: We performed a retrospective study on 21 cases of confirmed GISTs from our archive, aiming to establish morphological and immunohistochemical correlations. The samples were stained for CD117, CD34, DOG1 and Ki67.
Results: The cases showed spindle cell morphology in 66,66 % of cases, epithelioid in 14,28 % and mixed pattern in 19 %. CD117 was positive in 90.47 % of GISTs, CD34 in 95,23 %, DOG1 in 12 of 13 cases tested and Ki67 was >5 % in tumour cells in 28,57 % cases. Two GIST were C-kit negative, one CD34 and DOG1 and the other only CD34 positive. Both showed spindle cellularity. One had over 5 mitoses/50 HPF. Ki67 correlated with mitotic index in 61,9 % of cases. The pediatric GIST had a mixed pattern, intermediate risk of progression, and expressed both CD117 and CD34.
Conclusion: CD117 is the most reliable marker for diagnosis of GIST. In negative cases, DOG1 may support the diagnosis. The mitotic index was poorly correlated with Ki67 expression, confirming the former as a better parameter in evaluating tumour risk progression.

PS-08-020

Expression analysis of "Site" - specific immunohistochemical markers in Esophageal Adenocarcinoma

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Objective: Esophageal adenocarcinomas (EAC) do not show a specific immunohistochemical expression profile that may correlate with aggressiveness or aid in differential diagnosis. We characterized the immunophenotype of EAC by analyzing a range of markers of gastro-intestinal and other "site" specific differentiation.
Method: 117 primary resected EACs were included. A next-generation tissue microarray was stained with antibodies against CDX2, CK7, CK20, ER, MUC2, MUC5AC, MUC6, NapsinA, PAX8, PSA, Synaptophysine, and TTF1.
Results: Tumours could be categorized according to the expression of CK7 and CK20. Ninety-eight cases (84 %) were CK7 positive, 84 cases (72 %) were CK20 positive, and 73 cases (63 %) expressed both markers. Positivity for CK20 was linked to the expression the "intestinal" differentiation markers MUC2 ($p = 0.037$) and CDX2 ($p = 0.021$). Tumours expressing CK7 showed a trend towards unfavorable clinical outcome ($p = 0.095$). A minority of tumours expressed markers unrelated to the anatomical site (e.g. TTF-1, NapsinA, PSA).
Conclusion: EACs do not feature a distinct expression profile. The majority of tumours express CK7 and/or CK20, with a strong correlation between the expression of the "intestinal" markers CK20, MUC2 and CDX2. Expression of CK7 may be associated with a more aggressive growth. The expression of unrelated "site"-specific markers in EAC warrants caution when analyzing metastases of unknown origin.

PS-08-021

Gastric carcinoma with lymphoid stroma (gastric medullary carcinoma)

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Objective: Gastric carcinoma with lymphoid stroma (GCLS), also known as medullary carcinoma is a rare gastric neoplasia charaterized by poorly developed tubular structures with a prominent stromal lymphocytic infiltration. More than 80 % of GCLS are associated with Epstein-Barr virus (EBV) infection. We present a 76-year-old male patient with GCLS.
Method: A 76 year old man applied to hospital with weight loss in a 3 months. Gastroscopy revealed an ulcerated mass at the cardia and the biopsy revealed undifferentiated adenocarcinoma. He underwent a total gastrectomy.
Results: An ulcerated tumour with pushing border limited to the subserosa and dense lymphocytic infiltrate was detected microscopically. Sheets of polygonal cells with vesicular nuclei and prominent infiltrating lymphocyt were observed. Tumour cells were positive with cytokeratin, negative with synaptophysin, choromogranin, CD56. In-situ hybridization analysis of EBV latency associated RNA (EBER) was positive in lymphoid and tumour cells. The disease stage was T3N0M0. He had no relapse until now within 6 months of follow-up with systemic treatment.
Conclusion: GCLS forms 5 % of all gastric carcinomas and is rare tumour with an appearance similar to poorly differentiated carcinoma but its clinical behavior is similar to well differentiated gastric carcinoma. GCLS with lymphocytic infiltration is associated with two conditions: EBV infection and microsatellite instability (MSI). Our case GCLS showed positivity with EBER.

PS-08-022

Early cancer of the stomach. Modern approaches to morphological diagnosis

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Objective: Development of algorithm of morphological diagnosis of early gastric cancer, remote endoscopic mucosal resection and / or endoscopic submucosal dissection (EMR/ESD).
Method: Gastric tissue researched fully in step of 2 mm. Histological sections were stained with hematoxylin and eosin, PAS-reaction combined with Alcian blue, immunohistochemistry (IHC).
Results: Algorithm for the morphological study: 1. Determination of gastric pathologic process in accordance with the histological classification of gastric epithelial tumours (WHO, 2010). 2. Determination of the integrity of muscularis mucosa of the gastric (MMG) histologically and IHC (Desmin). 3. Evaluation of the depth of tumour invasion (from MMG to the deepest point of tumour invasion). The fundamental point is to reveal the depth of invasion more than 500 microns. 4. Determination of tumour emboli in the blood and lymph vessels histologically and IHC (CD34, D2-40). 5. Determination of the expression p53, muc-1 and muc-5AC, SK8 / 18 SK7. 6. Evaluation of the horizontal edge of resection. 7. Evaluation of the vertical edge of resection. 8. Formulation morphological conclusion with the TNM.
Conclusion: Proposes to develop algorithm morphological diagnosis of early gastric cancer, removed EMR/ESD. This approach allows us to objectively judge the effectiveness of endoscopic surgery.

PS-08-023

Neuroendocrine tumours involving the gastrointestinal tract: A clinicopathological evaluation of 26 cases

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Objective: Gastrointestinal tumours are rare and represent 2 % of malignant tumours. They arise in many organs and share common pathological features. In 2010, the World Health Organization (WHO) published a new classification based on their mitotic rate and the Ki-67 index. AIMS:

Description of the clinical and pathological characteristics of neuroendocrine tumours of the gastrointestinal tract.
Method: We report a retrospective study of 26 gastrointestinal neuroendocrine tumour cases identified over a period of 14 years (2000–2013). They were graded according to the new 2010 WHO classification.
Results: The average age was 49.64 years. There were a higher number in male. The most common location was stomach. According to 2000 WHO classification, the cases were devided into well-differentiated endocrine tumour (42.31 %), well differentiated neuroendocrine carcinoma (50 %), poorly differentiated neuroendocrine carcinoma (7.69 %). According to the new classification (2010), these tumours are reclassified in 16 neuroendocrine tumours G1, 6 neuroendocrine tumours G2 and 4 neuroendocrine carcinoma. Distant metastasis were presnt in 38 % of patients. Survival rate was 100 % at 12 months.
Conclusion: Those tumours have different prognosis. It is important to distinguish well-differentiated endocrine tumours whose grows slowly and poorly differentiated endocrine tumours characterized by aggressiveness and speed evolution.

PS-08-024
Thyroid transcription factor-1-positive neuroendocrine tumour of the ampullary region with multiple hepatic metastases: A case report
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Objective: Neuroendocrine tumours (NETs) (carcinoids) of the gastrointestinal and pancreatic region are considered negative for thyroid transcription factor-1 (TTF-1), some studies demonstrating even the specificity of TTF-1 for pulmonary origin in NETs.
Method: We present the case of a 47 years old male with a 14 mm diameter ampullary tumour, multiple hepatic metastases and no pulmonary lesions on CT scan. Hepatic metastases were present in both lobes with intrahepatic and extrahepatic bile ducts dilatation.
Results: We analyzed two biopsies, from the ampullary tumour and from a hepatic metastasis. Microscopic aspects revealed a predominant nested and trabecular proliferation, with some gland-like features. The tumour cells had moderate amount of cytoplasm, round monomorphic nuclei with "salt and pepper" chromatin and low mitotic rate (1/10HPF in ampullary tumour; 3/10HPF in metastasis). Tumour cells were chromograninA, synaptophysin, CD56, CK8/18 and CK7 positive, CDX2 focally positive, CK20 negative and 15 % Ki67 index. TTF-1 had a strong nuclear positivity in 90 % of tumour cells. In clinical context, the final diagnosis was grade 2 primary ampullary NET with hepatic metastases.
Conclusion: The positivity for TTF-1 in an ampullary NET with hepatic metastases may represent a pitfall in establishing a correct histopathological diagnosis without clinical correlations.

PS-08-025
Gastric neuroendocrine tumours with manifestations of Zollinger: Ellison Syndrome
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Objective: To carry on screening of ZES under gastric NET and to study it's clinical and morphological features.
Method: The gastric mucosal biopsies and surgical specimens from 21 patients with NETs of the stomach were investigated. The usual methods and the IHC study were used.
Results: From 2 to 6 biopsies of the gastric mucosa were needed for diagnostic in 62 % of considered cases. Hyperplastic epithelial, muscle and endocrine cells changes were revealed. Eighteen tumours were considered as G1 NET and 3 G 2-3, with invasion in the stomach muscular layer. The average age of patients was 50,2. 4 patients (19 %) demonstrated different ZES manifestations. Manifestations of aggressive peptic ulcers course in the form of complications (i.e. bleeding, stomach obstruction, diarrhea) seemed to be key clinic symptoms. Among them were three men. The average age of patients was 25. Tumours had small size (0,1–1,0 cm) and were detected either during surgery (25 %) or after gastrectomy (50 %). NET diagnosis was raised histologically, verified and corrected by IHC studies (gastrinoma).
Conclusion: Gastric NET accompanied with ZES can be very small and multiple. This demands to make multiple parallel sections of the resected stomach and thorough tumours search.

PS-08-026
Dieulafoy's Disease: Clinicopathologic features, morphological diagnosis
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Objective: Observation of clinicopathologic manifestations and complications of Dieulafoy's disease(DD).
Method: In our study we had 24 cases of DD - 16 males and 8 females aging from 19 to 79. All patients entered the clinic with a gastrointestinal bleeding.
Results: During endoscopical research an erosive artery was found in the affected region, which protruded the stormachs lumen, shaped like a papilla with light-colored central field among normaly colored mucous membrane. In morphological research these patients demonstrated typical morphological characters of disease's manifestation - stomach's mucous membrane atrophy with multiple hemorrhages in it's wall. In the submucosa — abnormal and malformed blood vessels with thickened walls and intraluminal organized thrombi. Also, tortuous artery with a preserved muscular tunic approximately 1,5 mm in diameter can be found. It goes through submucosa and closely sides with mucosa. aliber of the vessel does not match his placement. Severe dilated artery appers normal. There is no indication of inflammation process in mucosa, dystrophic calcification, deep ulceration of the vessel's wall, penetraton in it's own muscular tunic, vasculitis, indication of organizing aneurism and atherosclerosis. Thrombus commonly adjoins a defect in the vessel, protruding above mucosa. Ulcer in mucosa - without inflammatory reaction, typical for peptic ulcer. Fibrosis around defect is absent.
Conclusion: In immunohistochemical research in the pathologically formed vessel area we found a highly positive expression of vimentin, CD34, VEGF; mild expression of smooth muscular actine, ambiguous expression of TGFβ, FGFβ, CD105; negative reaction with PCNA; Ki 67 5–10 %.

PS-08-027
Differentiation markers in ampullary adenocarcinomas: Role of EGFR and beta-catenin in predicting histological subtype and biological behavior
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Objective: β-catenin acts as a transcription cofactor in the Wnt pathway, a structural adaptor protein linking cadherins to the actin cytoskeleton in cell-cell adhesion and also induces signal transduction through epidermal growth factor receptor (EGFR). This study aimed to demonstrate possible connections between β-catenin and EGFR with histological type and biological behavior in ampullary adenocarcinomas.
Method: We studied 47 consecutively resected ampullary adenocarcinomas immunohistochemically with antibodies against β-catenin and EGFR.
Results: Eighteen carcinomas were of intestinal and 29 of pancreatobiliary type. Disease stage (TNM) was 0 in two patients, I in two, II in 16 and III in

27. The differences in the expression of both β-catenin and EGFR between intestinal and pancreatobiliary type carcinomas were not statistically significant. Positive predictive value of β-catenin and EGFR for the intestinal type was 64 and 38 % respectively. β-catenin expression was associated with lower tumour grade ($p = 0.0527$) while EGFR was not. No significant connection was found between EGFR and β-catenin expression and disease stage.
Conclusion: Immunohistochemical expression of EGFR and β-catenin in ampullary carcinomas is not useful in differentiating intestinal from pancreatobiliary type. β-catenin expression is possibly associated with more favorable biological behavior.

PS-08-028
MDM2 and p53 expression in ampullary adenocarcinomas
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Objective: p53 is a tumour suppressor protein, negatively regulated by murine double minute 2 protein (MDM2). This study aimed to present their significance in ampullary adenocarcinomas and demonstrate possible connections with tumour grade, disease stage and histological type of differentiation.
Method: Forty-seven consecutively resected ampullary adenocarcinomas, 18 intestinal and 29 pancreatobiliary type, were immunohistochemically stained against p53 and MDM2.
Results: Differentiation was poor in six and well/moderate in 41. Stage (TNM) was 0 in two patients, I in two, II in 16 and III in 27. p53 was expressed in nine intestinal (50 %) and eight pancreatobiliary (27.6 %). Fifteen intestinal (83.3 %) and 20 pancreatobiliary (69 %) expressed MDM2. There were no statistically significant differences in the expression of p53 and MDM2 between intestinal and pancreatobiliary type. Sensitivity, specificity and positive predictive value of p53 in predicting intestinal type were 50, 72 and 53 % while these of MDM2 were 83, 31 and 43 %, respectively. Neither MDM2 nor p53 expression correlated with tumour grade and disease stage.
Conclusion: Immunohistochemical expression of MDM2 and p53 in ampullary carcinomas is not predictive of the histological type and is not associated with the biological behavior of the tumour.

PS-08-029
Clinicopathological features and prognostic factors of gastric cancer
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Objective: Gastric cancer (GC) remains the fourth most common type of cancer and the second most common cause of cancer-related death worldwide. The aim of the study was to compare the gastric cancer histopathological subtypes and evaluate the correlation between the histopathological and clinical parameters.
Method: 80 subjects undergoing gastric cancer surgical treatment carcinoma were enrolled in the study. The patients were treated in Riga East University Hospital in 2014. The surgical specimens were grossly and microscopically analyzed. The tumour classification was assessed according to WHO 2010 classification.
Results: Obtained results showed that the tubular adenocarcinoma was observed in 35 % of cases, signet ring cell carcinoma-in 30 %, undiferentiated carcinoma in 20 %, papillary adenocarcinoma in 10 % and mutinous carcinoma in 5 % of cases. The positive correlation between the tumour size and the numbers of metastatic lymph nodes, Bormann classification, gastric atrophy, lymphovascular invasion was observed. Furthermore, the negative correrlation between the Lauren classification and intestinal metaplasia, tumour vascular invasion was observed. In addition, the positive correlation between the Bormann classification and tumour vascular, perineural invasion and the numbers of metastatic lymph nodes was observed.
Conclusion: The tumour histopathological characteristics correlated with the clinical course and prognosis.

PS-08-030
Concordance of the results of detection of HER2 amplification in gastric adenocarcinoma using CISH and FISH methods.
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Objective: To determine the degree of concordance between positive HER2 gene amplification detected by chromogenic in situ hybridization (CISH) and detected by fluorescence in situ hybridization (FISH) in the patients with gastric adenocarcinoma.
Method: Tumour tissue samples from 96 patients with radical operation of gastric adenocarcinoma were tested by immunohistochemical methods (IHC) with Hercep test, Code K5204, (DACO, USA), gene amplification was tested by CISH method using HER2 pharm-Dx Kit, Code SK109 (DAKO, USA), and FISH method was carried out by microarray technique using PATH Vysion HER2 (Abbott Vysis, USA). Kappa coefficient was used to determine the concordance rate of the results from CISH and FISH methods.
Results: The following results were found on the IHC: score 0–52,1 %, score 1–24,0 %, score 2–10,4 %, score 3–13,5 % of the patients. In all tumours whith 3+ the HER2 gene amplification exists using CISH and FICH methods. In the category tumours with 2+ the HER2 gene amplification was found in 3 patients using CISH method, and in five patients using FISH method. Kappa = 0,78 ($p < 0.001$).
Conclusion: FISH method is more sensitive and it is recommended in routine practice for determining HER2 gene amplification in the patients with gastric adenocarcinoma.

PS-08-031
Prognostic impact of HER2 and EGFR status on overall survival of advanced gastric cancer patients.
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Objective: This study was conducted to investigate whether human epidermal growth factor receptor 2 (HER2) status and epidermal growth factor receptor (EGFR) status are independent prognostic factors for advanced gastric cancer patients.
Method: Formalin-fixed paraffin-embedded tumour samples were examined for HER2 and EGFR using immunohistochemistry (IHC). Additionally, gene amplification was examined using fluorescent in situ hybridization (FISH) for HER2. Positivity was defined as an IHC score of 3+ or an IHC score of 2+/FISH positive for HER2, and an IHC score of 2+ or 3+ for EGFR.
Results: Of the 96 patients with radical operation, 18 (18,8 %) were HER2 positive and 6 (6,3 %) were EGFR positive. After a median follow-up time of 27,8 months with 76 deaths, there was no significant difference in overall survival (OS) in terms of EGFR status. However, there was a significant difference in OS between HER2-positive and HER2-negative patients [median, 17.0 vs 26.0 months; log-rank = 8,62, $p < 0.01$]. Multivariate analysis showed that HER2 positivity was no an independent prognostic factor for OS [hazard ratio, 0,29 (95 % confidence interval, 0.71–2,26); $P = 0,42$].
Conclusion: The study suggested that HER2-positive status had poor prognostic value, but it is not an independent prognostic factor.

PS-08-032

Expression of P40 ve COX-2 in esophageal Squamous Cell Carcinoma (SCC) in Northeast Anatolia (high-incidence area)

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Objective: ΔNp63—a p63 isoform suggested to be highly specific for squamous/basal cells, which is thought to antagonize the activity of TAp63 and p53. Cyclooxygenase (COX) is a key enzyme in arachidonic acid metabolism. COX-2 expression may contribute to the synthesis of prostanoids, which relate to carcinogenesis and tumour progression.
Method: We performed an immunohistochemical analysis of COX-2 and P40 in 85 human esophageal squamous cell carcinoma tissues and evaluated the relationship with lymphatic invasion, venous invasion, lymph node metastasis, depth of tumour invasion, localizations, age, size, histopathological grading, and TNM clinical classification.
Results: There was a relation between expression of P40 ve COX-2 and differentiation grade, lymph node metastasis, stage and tumour size but not with vascular invasion.
Conclusion: Immunohistochemical detection of expression of P40 ve COX-2 in the primary esophageal squamous cell tumour may be useful for the prediction of a poor prognosis.

PS-08-033

Relationship between HSPA2 expression and prognostic parameters of esophageal Squamous Cell Carcinoma (SCC)

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Objective: Heat shock-related 70 kDa protein 2 is a protein that in humans is encoded by the HSPA2 gene. HSPA2 is expressed in various tumours and in certain types of somatic tissues. is important for cancer cell growth and metastasis. However, the status of HSPA2 expression and its prognostic significance in esophageal squamous cell cancer (ESCC) remain unknown.
Method: Archived and paraffin-embedded samples were obtained from 85 patients with a diagnosis of ESCC, who underwent surgical resection during the period of 2007 to 2014 in Ataturk University, Faculty of Medicine. The expression of HSPA2 in ESCC was analyzed by immunohistochemistry, and correlated with clinicopathological parameters.
Results: HSPA2 mRNA and protein were overexpressed in ESCC tissues compared to paired adjacent noncancerous tissues ($P < 0.001$). Clinicopathological analysis showed that HSPA2 expression was significantly correlated with tumour size ($P = 0.01$), histological differentiation ($P = 0.03$), and tumour stage ($P = 0.001$), lymph node metastases and recurrence, respectively (all, $P < 0.05$).
Conclusion: Our results suggest that overexpression of HSPA2 in esophagus cancer is associated with aggressive progression and poor prognosis and that HSPA2 may be served as a prognostic marker.

PS-08-034

Atypical behavior of early gastric cancer

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Objective: To highlight diagnostic dilemma of early gastric cancer (EGC).
Method: The particular histological features were examined in 30 EGCs diagnosed at three departments of Pathology from Romania (Tirgu-Mures), Poland (Warsaw), and Hungary (Budapest).
Results: Eight out of the 30 cases were signet ring cell (poorly cohesive) carcinomas that displayed a specific aspect: multiple intramucosal foci with loss of E-cadherin and mena protein. In one of them, although invasion was limited to the mucosa, diffuse carcinomatosis of the lymph vessels with re-expression of E-cadherin but not mena was seen in all of the gastric layers, with accompaying lymph node and liver metastases. In other case, diagnosed as pT1b tubular adenocarcinoma, an incidental skip metastasis was identified during sentinel node mapping. The only independent negative prognostic factor was localization of the tumour in the gastroesophageal junction.
Conclusion: An EGC with invasion limited to mucosa and with carcinomatosis of the lymph vessels in submucosa and muscularis propria, which is now classified as pT1a, should be included in pT2, despite the absence of the tumour nests in these layers. Further research should be performed by the gastrointestinal working groups for a proper evaluation of GCs with atypical behavior. The research was founded by project UMFTGM-PO-CC-02-F01-19/2014.

PS-08-035

Gastrointestinal stromal tumours in Romanian patients: Clinicopathological and molecular profile

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Objective: To present the molecular characteristics of gastrointestinal stromal tumours (GIST).
Method: In 13 consecutive cases with GISTs diagnosed at Department of Pathology of Tirgu-Mures, Romania, molecular sequencing was performed to detect the c-KIT/PDGFRA genes mutations.
Results: None of the 13 GISTs presented mutations in exon 12 of the PDGFRA gene. Only one case displayed a PDGFRA mutation (p.D842V) in exon 18 (this case had a deletion in exon 11 of KIT gene). Six cases were KIT/PDGFRA wild-type. In the other six cases, KIT mutations in exon 9 (P456S mut) was detected in one case, whereas exon 11 was affected in the other five patients (insertion - 3 cases, deletion - one case, p.V559G mutation - one case). In one of the cases, diagnosed in a 64 year-old female, one KIT/PDGFRA wild type-GIST was diagnosed in the stomach and, incidentally, a synchronous GIST was identified in the proximal stomach, with insertion in exon 11 of KIT gene.
Conclusion: In Romanian patients, GISTs seems to be predominantly driven by KIT mutations in exon 11. Careful macroscopical examination of the surgical specimens should be performed to identify the synchronous GISTs; the molecular profile of both synchronous tumours is mandatory to be examined for effective targeted therapy.

PS-08-037

Nuclear Factor-Kappa B(NF-KappaB) activation in esophageal Squamous cell Carcinoma (SCC)

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Objective: NF-κB is activated by carcinogens, tumour promoters, inflammatory cytokines. The activation of NF-κB can suppress apoptosis, thus promoting chemoresistance and tumorigenesis. Several studies have demonstrated an antiapoptotic function for Nuclear factor-kappa B (NF-κB), but its role in esophageal tumorigenesis has not been reported.
Method: We obtained archival, formalin-fixed and paraffin-embedded material from surgically resected at esophageal squamous cell carcinoma specimens (85) containing tumour and adjacent normal and abnormal epithelium tissues. Tumour tissue specimens obtained were histologically and immunohistochemical examined. The immunohistochemical expression of NF-κB p65 was investigated relevant clinical parameters (tumour size, metastasis of lymph node, differentiations.)
Results: Immunohistochemical analysis showed enhanced nuclear staining for NF-κB/p65 in both high-grade ($P < .0001$) and low-grade ($P < .003$) cancer specimens, compared to benign tissue. High levels of nuclear immunohistochemical expression of NF-κB p65 were detected in

the esophagus cancers, with significantly higher levels in poor differentiated tumours compared with well differentiated tumours ($P < .0001$). In NF-κB p65 expression level was significantly higher in poorly differentiated tumours than well differentiated ($P < .0001$). High levels of nuclear immunohistochemical expression of NF-κB p65 were detected in the in tumours having large tumour size and a greater number of the lymph node metastasis.
Conclusion: These results demonstrate that expression of NF-κB/p65 in esophageal squamous cell carcinoma is related to tumour progression.

PS-08-038
Scalp melanoma with gastrointestinal metastasis: A case report
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Objective: Metastasis of malignant melanoma has been shown to different organs of the human body with a rare incidence involving gastrointestinal tract. Melanoma by itself is a great mimicker of other neoplastic conditions and may create a major diagnostic challenge.
Method: This report involves, a 38 year old woman suffering from melanoma of the scalp that developed into gastrointestinal metastasis.
Results: In March 2008, our patient was diagnosed with superficial spreading melanoma, amelanotic type (Clark V, Breslow 7 mm), of the scalp. After 10 months, in three lymph nodes of the neck, metastases were detected. In March 2010, after endoscopic biopsy of gastric mucosa, and microscopic examination of the sample, melanoma metastasis were observed, which was confirmed by immunohistochemical analysis: Melan A +, HMB45 +, Pan CK -/+. Diagnosis is complemented by cytological findings, which showed the presence of melanoma cells. Following surgical removal of the stomach, part of the colon, and part of the small intestine, macroscopic mucosal tumour deposits were observed. Microscopic analysis confirmed the presence of metastatic melanoma, with transmural invasion. In regional lymph nodes metastatic deposits were detected.
Conclusion: The behavior of head and neck melanoma is aggressive, and it has an overall poorer prognosis than that of other skin sites.

PS-08-039
Cystic lymphangioma of small bowel mesentery: A case report
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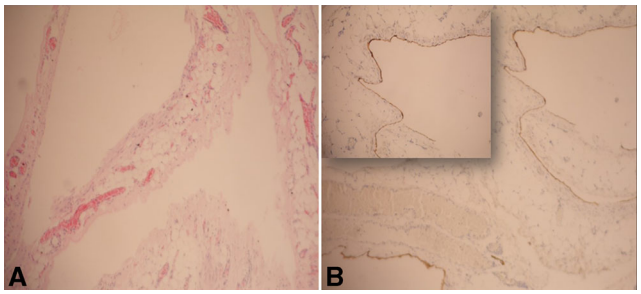
Objective: Intraabdominal lymphangiomas are rare congenital malformations and most are located in mesentery. Although they are generally asymptomatic, they may be complicated by intestinal obstruction or cyst rupture occasionally.
Method: Here, we present a case with cystic lymphangioma of small bowel mesentery.
Results: A-6-year-old boy referred with nausea and vomiting. Abdominal computerized tomography (CT) revealed a cyst 88 × 35 mm in size without significant contrast enhancement and located in right lower abdominal quadrant. Laparotomy was performed and patient underwent a partial small bowel resection. In gross examination, two separated cysts which are 6.7 and 2.5 cm in diameter were detected. The cyts were attached to the mesentery and filled with a serous fluid. The thickness of the cyst wall was only 0.1 cm. Microscopically, cystic spaces were covered by a flattened one-layer epithelium which was stained positive for D2-40 and CD31 immunohistochemically. The cyst wall was composed of fibrovascular stroma and adipose tissue. Diagnosis of cystic lymphangioma was made based on immunohistochemical findings.
Conclusion: Lymphangioma of small bowel mesentery constitutes less than 1 % of all lymphangiomas and shows variable expression of vascular markers, such as D2-40, CD31 and CD34. Mesenteric cysts, cystic mesothelioma, peritoneal inclusion cysts, parasitic cysts should be considered in differential diagnosis.

A) Cystic spaces covered by flattened epithelium (Hematoxylin-eosin, x400), B) D2-40 positivity, immunohistochemistry, x100 (inset:x200):



PS-08-040
Clinicopathological correlation in Gastrointestinal Graft versus Host Disease: Significance of grading
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Objective: Graft-versus-host disease (GVHD) is one of the most common complications of allogeneic hematopoietic stem cell transplantation. Gastrointestinal (GI) tract is among the three major target organ systems of GVHD together with skin and liver.
Method: GI biopsies taken from a total of 133 patients with GI GVHD were graded using Snover's system for severity of mucosal pathology. The correlation of pathological grade with clinical parameters comprising age, gender, primary disease, stem cell source, biopsy time, clinical symptoms, and clinical grade was evaluated using Chi-square and Kruskal-Wallis tests. A p value < 0.05 was considered significant.
Results: Median age of 133 patients was 38 years ranging between 6 and 68 years. Majority of the patients were diagnosed as AML (34.6 %) followed by ALL (21 %). GVHD was found in multiple sites in 56.5 % of the biopsies of which duodenum was the most severely affected site in 60 % of the cases. Pathological grade had no correlation with clinical parameters except for clinical grade ($p < 0.05$; kappa 0.111).
Conclusion: Since GVHD involves multiple sites with varying degrees of severity in GI tract, both clinical and pathological grading seem to be necessary to have a better clinicopathological correlation for follow-up and treatment of the patients.

PS-08-041
Expression profile of antiapoptotic markers in gastric cancer
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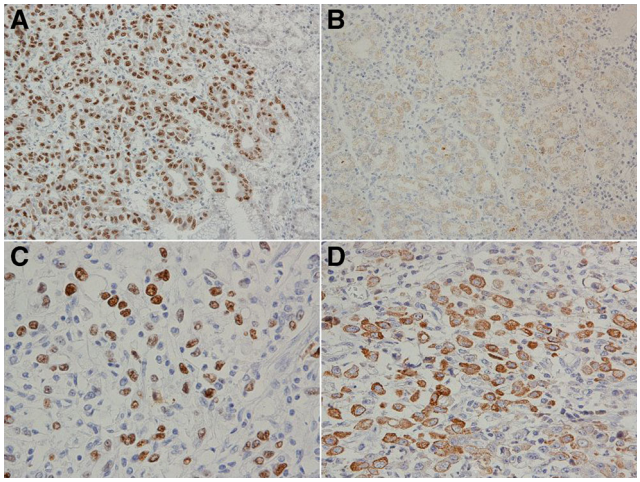
Objective: The aim of this research was to investigate the expression profile of antiapoptotic markers Survivin, Flip-l and Bcl-2 in gastric cancer (GC).
Method: We analyzed tissue samples of GC obtained by partial or total gastrectomy in 87 patients (65 male and 32 female) for immunohistochemical expression of Survivin, Flip-l and Bcl-2. The statistical frequency and correlation analysis of apoptosis related proteins expression and clinicopathological tumour features was performed in SPSS 15.0.
Results: Positive Survivin expression was observed in 36 (41.38 %), Flip-l in 33 (37.93 %), and Bcl-2 in 14 (16.09 %) of the investigated tumours. Bcl-2 expression was more frequent in intestinal type carcinoma compared to diffuse, however this difference was not statistically significant. Bcl-2 and Flip-l expression both significantly correlated with tubular histology of GC ($p < 0.01$, respectively). Expression of Flip-l was

significantly associated with the absence of lymphovascular invasion and low pathologic stage ($p < 0.01$). Nuclear expression of Survivin was also linked to low pathologic stage ($p = 0.02$).
Conclusion: Our results suggested that antiapoptotic markers demonstrate trend of more frequent expression in GC with favorable clinicopathologic features. This inverse correlation between immunohistochemical expression of Survivin, Flip-l and Bcl-2 and tumour aggressiveness in GC requires further elucidation.



PS-08-042
The correlation of mucin phenotype and Klf4 expression in gastric cancer
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Objective: Recent advances in molecular and immunohistochemical methods enabled more accurate classification of gastric cancer (GC) based on mucin phenotype into those with gastric, intestinal, mixed gastrointestinal and unclassified type. The aim of this research was to examine the correlation between Klf4 expression and these phenotypes and clinicopathologic characteristics of GC.
Method: A total of 78 cases of gastric cancer were analyzed for immunohistochemical expression of MUC5AC, MUC2, CD10 and Klf4. Statistical analysis was performed in SPSS 15.0.
Results: MUC5Ac expression was detected in 69.2 %, MUC2 in 30.8 % and CD10 in 15.4 % of analyzed tumours. Based on MUC5AC, MUC2 and CD10 expression, 42 tumours were classified as gastric type, 15 as mixed, 13 as intestinal and 8 as unclassified. Aberrant Klf4 expression was found in 84.6 % of the cases. Gastric phenotype was significantly associated with altered Klf4 expression ($p = 0.023$).
Conclusion: Our results suggest an important role of Klf4 transcription factor in differentiation of gastric mucosa epithelial cells and indicate its potential significance in more accurate diagnostic and prognostic stratification of the patients with GC.

PS-08-043
Metastatic renal cell carcinoma presenting as polyposis of small intestine: Case report
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Objective: The metastatic pathway is not always predictable, especially for renal cell carcinoma known as one of the "greatest mimics encountered in clinical medicine". We report a rare case of a 58-years old male who had nefrectomi 2 years ago, presenting now with unexpected metastatic disease.
Method: The patient was admitted to the emergency room with acute abdominal pain followed by copremesis and gastrointestinal bleeding, therefore segmental resection of the small intestine was performed with primary entero-enteral L-L anastomosis. The gross examination revealed the presence of three polypoid structures measuring from 3 to 8 cm in diameter, causing retraction of the wall towards the intestinal lumen and segmental intussusception. On selected samples immunohistochemical analysis with RCC, CD 10, CKAE1/AE3, Vimentin and EMA were made.
Results: The microscopic examination showed aggregates of cells with clear cytoplasm and round uniform nuclei, surrounded with distinct membrane, infiltrating intestinal wall and ulcerating the mucosa. Immunohistochemical staining for RCC, EMA and CD10 showed positive expresion, that confirmed the diagnosis of metastatic renal cell carcinoma.
Conclusion: The possibility of recurrent renal cell metastasis to the gastrointestinal tract should be kept in mind, although it is rare, considering the complex lymphatic drainage of the kidney.

PS-08-044
Anti-tumoural role of mast cells in gastric neoplasia: New evidence
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Objective: Mast cells (MCs) are considered as important players in neoplasia, current concern being to determine if their role is pro-tumorigenic or anti-tumorigenic. This study, correlating the presence of MCs with gastric neoplasia in Helicobacter pylori (HP) positive and negative patients, brings new data supporting the hypothesis that MCs have a protective role.
Method: We performed a retrospective case-control study including 30 gastric surgical samples with gastric neoplasia and 30 surgical samples with non-tumoural gastric lesions. Half of the patients in each group had HP infection. Giemsa and tryptase stains were used for quantitative evaluation of MCs in one area for the control group and in three areas for case group: intratumoral, peritumoral and normal mucosa.
Results: Presence of HP does not influence the number of MCs in tumoural and non-tumoural cases. MCs were significantly increased in tumoural microenvironment and significantly decreased in the normal distant mucosa comparative with control group ($p = 0.0005$).
Conclusion: MCs are distributed as a collar around the tumour. Their significant decrease in the normal distant mucosa supports the fact that they are part of immune anti-tumoural host response, mobilized to limit tumoural evolution. ACKNOWLEDGEMENT: Partially financed from the European Social Fund and Romanian Government, contract POSDRU/159/1.5/S/137390.

PS-08-045
Eukaryotic translation initiation factors in gastroenteropancreatic neuroendocrine tumours: A TMA based analysis
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Objective: Eukaryotic translation initiation factors (eIFs) are mediators of start codon recognition. Mutation or deregulated expression of eIFs influences cell growth and proliferation, contributing to carcinogenesis. In the course of the neuroendocrine tumour (NET)-study project at the Medical University of Graz, we have analyzed various eIF subunits in gastroenteropancreatic (GEP)-NETs in a tissue microarray (TMA)-based immunohistochemical analysis.

Method: We have investigated several eIF subunits in NET- and neuroendocrine carcinoma (NEC)-samples by analyzing the cytoplasmic expression intensity (score 0, 1+, 2+ or 3+), and the density of cells featuring a positive expression (%). As controls, we have analyzed eIFs in the corresponding normal tissues. We also correlated prognostic parameters, i.e. time-to-relapse and overall-survival, with eIF expression levels.
Results: Our analysis shows a deregulation of eIFs in NETs and NECs, as compared to healthy controls. Interestingly, some eIF subunits are up-regulated in tumour tissue, whilst others are down-regulated in tumours, compared to healthy controls.
Conclusion: As conclusion, eIFs are activated aberrantly in NETs and NECs. Differential expression of eIFs in NETs is likely to influence NET- and NEC-tumorigenesis. In future eIFs may be potentially useful as disease biomarkers, and might serve as therapeutic targets.

PS-08-046
Tumour budding in the intestinal-type adenocarcinoma of the stomach: Prognostic significance
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Objective: We aimed to assess the prognostic significance of tumour budding in the intestinal-type adenocarcinoma of the stomach, determine its relationship with other clinicopathologic features.
Method: Tumour budding was assessed in 52 archival cases of the intestinal-type adenocarcinoma of the stomach using hematoxylin and eosin (H&E) sections; tumour buds were defined as single cells or nonglandular clusters composed of <5 cells. The presence of budding was determined through assessment of all tumour-containing slides, and associations with clinicopathologic features and outcomes were analyzed. Two pathologists participated in an interobserver variability study.
Results: Budding was present in 32 (71,5 %) of 52 cases and was associated with decreased overall survival (log rank = 30,57, $p = 0.001$). High-grade budding was linked to advanced pT classification ($p < 0.01$), lymphatic invasion ($p < 0,01$), blood vessel invasion ($p < 0.01$), perineural invasion ($p < 0.01$), histological grade ($p < 0.01$), nodal status ($p < 0.01$), tumour size ($p < 0.01$), and stage ($p < 0.01$). On multivariable analysis, tumour budding, and stage were prognostically significantly independent of grade, tumour size, nodal status, lymphovascular invasion, and perineural invasion. Inter-observer agreement was considered strong ($k = 0.77$).
Conclusion: The presence of tumour budding, and stage are significant predictors of poor outcomes in patients with the intestinal-type adenocarcinoma of the stomach.

PS-08-047
De novo dedifferentiation in imatinib-naïve Gastrointestinal Stromal Tumour (GIST): Report of two cases, one with rhabdomyosarcomatous differentiation
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Objective: Dedifferentiation associated with loss of diagnostic markers with or without heterologous trans-differentiation is a rare phenomenon in GIST which mainly occur under or following tyrosine kinase inhibition (TKI) therapy. We herein present two cases of dedifferentiated GIST that occurred without prior TKI therapy.
Method: Histopathologic and panel of Immunohistochemical markers were used including CD117, CD34, vimentin, DOG1, desmin, myogenin.
Results: Patients were primarily A 17-year-old girl and a 32-year-old man who underwent distal gastric resection & gastrectomy for multinodular GIST (6 cm) and a huge GIST (25 cm) respectively. Patient 1 is an recent case and remained disease-free at 34 months. Case 1 showed a dominant epithelioid SDHB-deficient GIST (CD117+/CD34+) with a 1 cm focus of anaplastic pleomorphic sarcomatous "MFH"-like component (vimentin-only phenotype). Case 2 showed a DOG1+/CD34+/CD117-negative bland spindle cell component and juxtaposed rhabdomyosarcomatous component (DOG1-/CD34-/CD117-/desmin+/myogenin+) with focal intermingling.
Conclusion: Although rare, dedifferentiation with or without heterologous trans-differentiation do occur rarely in Imatinib-naive GIST and should be considered in the differential diagnosis. Thorough sampling of such cases is necessary for appropriate classification.

PS-08-049
Morphological analysis of the relationship between the duodenal biopsy samples diagnosed as "increased intraepithelial lymphocytes" with Helicobacter pylori gastritis and Celiac Disease
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Objective: We studied retrospectively the histomorphological difference between 25 Celiac or non-Celiac cases with increased intraepithelial lymphosites and no villus atrophy; and the effect of Helicobacter pylori gastritis to this increase.
Method: Duodenal and gastric endoscopic biopsies of 25 patients between 2003 and 2014 were retrospectively analyzed for the two morphological criterias; increased intraepithelial lymphocytes (IELs) and normal villus pattern (Modified Marsh Classification of histologic findings in celiac disease (Oberhuber) -Marsh groups 0, 1, 2). These 25 patients were categorized under two groups; group 1, 11 patients who had clinically diagnosed Celiac disease with incerased IELs and group 2, 14 patients which had increased IELs in duodenum without the clinical diagnosis of Celiac disease. These two groups were re-evaluated histomorphologically and compared statistically according to these parameters: Helicobacter pylori presence in gastric biopsies, the ratio (grade? degree?) of increase in IELs, the presence of active duodenitis, lymphoid follicles and parasitic enfestation in duodenal biopsy samples. Two groups were analyzed statistically using the SPSS ver16.0.
Results: The increase in IELs was not statistically significant between two groups. When the cut-off point was defined as %40, the ratio (?) of increase in IELs were found statistically significant in the clinically diagnosed Celiac disease group ($p = 0.042$). Accompanying Helicobacter pylori gastritis was found statistically significant in group 2 ($p = 0.045$). The presence of active duodenitis was not statistically significant between two groups.
Conclusion: The increase in IELs in duodenal biopsy samples without villus atrophy is associated with Celiac disease if the increase ratio is high. The presence of Helicobacter pylori gastritis may be an important factor for the increased IELs in duodenal endoscopic biopsies.

PS-08-050
Low grade gastric dysplasia: Natural evolution
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Objective: There is, yet, controversy because of the lack of consensus and accurate risk stratification of low grade gastric dysplasia. The current study aims to study low grade gastric dysplasia evolution.
Method: A 10-year retrospective study of 68 patients who were diagnosed with low grade dysplasia, had no endoscopic/surgical treatment, and who had a minimum follow up of 1 year is carried out. All the slides were reviewed and the following variables were analised: age, sex, family history of gastric cancer, presence of Helicobacter Pylori, anatomic distribution, endoscopic mucosa aspects and lesion evolution. A statistical relationship was studied through "Chi Square".

Results: Low grade dysplasia was shown to regress in 66 % of cases, to persist in 19 % and to progress to higher grades in 13 % of cases. There was a case that progressed to invasive carcinoma in the first year of follow up. Of lesions which have progressed, 90 % were multifocal ($p < 0{,}001$); 72 % were in depressed mucosa ($p < 0{,}001$); 54 % failed Helicobacter pylori erradication ($p = 0{,}041$) and 45,5 % had familiar history of gastric carcinoma ($p = 0{,}347$).
Conclusion: In 66 % of cases of low grade dysplasia there was regression, and in 13 % of cases there was progression, which was statistically correlated with multifocality and presence of depressed mucosa.

PS-08-051
Gastric collision tumour: A case report
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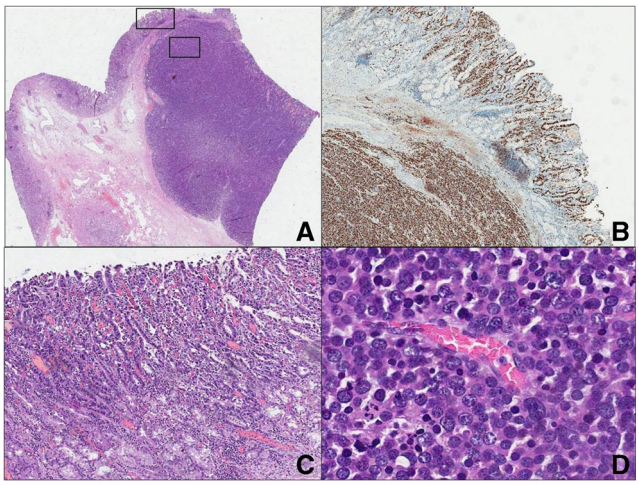
Objective: Mixed gastric carcinoma showed features of both adenocarcinoma (AC) and neuroendocrine carcinoma (NEC) is designated as 'composite tumour' and is not an uncommon entity. Cases in which gastric AC and NEC are not intermixed appearing in a same patient are extremely rare and designated as 'collision tumour'.
Method: A case of gastric collision tumour is presented here.
Results: 71 years old male admitted to the oncology department with a history of abdominal pain, weakness and weight loss. Endoscopy revealed mass lesion of the gastric corpus, biopsy was performed. Histology revealed collision tumour, due to non intermixed AC and NET growth pattern. Tumour cells were positive for CK AE1/AE3, Chromograinin A (NEC only), Synaptophysin (NEC only) and CDX-2. Next subtotal gastric resection was performed. Histology confirmed a collision tumour diagnosis with tumour (NEC component) spreading to subserosal tissue. One regional lymph node showed AC involvement and three nodes were involved by NEC. Thus, collision gastric carcinoma pT3pN2 was signed out.
Conclusion: Gastric collision tumour is a rare entity with less than 20 cases reported to date. Clinical and pathological data on association of AC and NEC should be reported and reviewed.

Microscopic appearance of tumours edges. Moderately differentiated adenocarcinoma (C) and poorly differentiated NEC (D). H&E (A, C, D) and Ki-67 (B) with no evidence of intermixing. Details of A are at C and D:



PS-08-052
Characteristics of gastrointestinal stomal tumours and other synchronous / metachronous tumours: A 14 case series
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Objective: Aim of this study was to investigate simultaneous occurrence of synchronous and metachronous tumours in studied GIST cases.
Method: From the archives of Fundeni Clinical Institute were identified between January 2004 and July 2014, 140 cases of GIST. Data on age, gender, clinical, histopathological aspects, and follow up were collected.
Results: 14 patients out of 140 GIST (10.7 %) had also another tumour, 5 females and 9 males with ages between 38 and 81 being considered for this study. GISTs occurred in the small intestine (9) and stomach (5) with size ranging from 0.6 to 12 cm, 3 of them being highly mitotic (>5/50HPFs). Out of 9 small intestinal GISTs, 3 also associated adenocarcinomas of the stomach, 1 urothelial carcinoma of the bladder, 1 rectal adenocarcinoma, 1 chistadenoma of the kidney, 1 papillary serous chistadenoma of the ovary, 1 neuroendocrine tumour of the small intestine and 1cavernous liver hemangioma. The remaining 5 GISTs of the stomach associated scuamous cell carcinoma of the esophagus, cavernous liver hemangioma, breast carcinoma, gastric neuroendocrine tumour and hyperplastic polyp of the stomach.
Conclusion: The prognosis of these patients is mostly influenced by the malignancy associated therefore the treatment algorithm should be directed on the more aggressive tumour.

PS-08-053
Gastrointestinal neuroendocrine tumours: Diagnostic challenges
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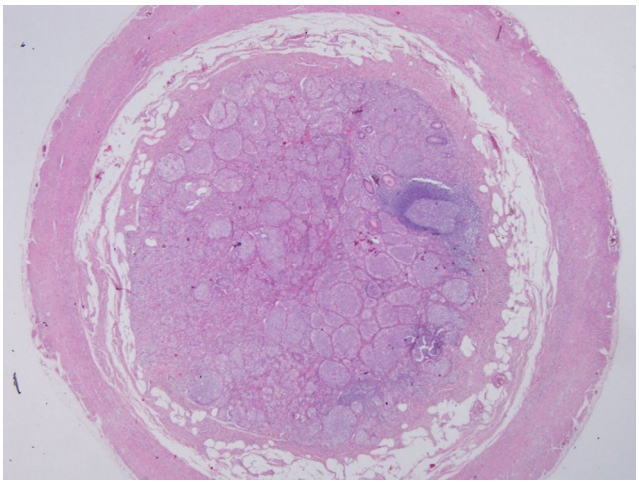
Objective: Gastrointestinal neuroendocrine tumours (GI-NETs) constitute less than 2 % of gastrointestinal tumours. Staging and grading is still controversial due to different proposals as ENETS and AJCC/UICC classifications.
Method: We re-evaluated 196 cases diagnosed between years 2000–2015 according to the ENETS 2006 classification.
Results: Of 196, female:male ratio was 1.27. Median age was 48 ± 15.28. Almost 55 % were located in stomach, followed by appendix (19.4 %), rectum (9.7 %), small bowel (7.6 %), bulbus (5.6 %) and 2.5 % in other parts of colon. Multiple tumours were seen in 20.4 %. Seventy-two percent were grade 1, followed by grade 2 (20.4 %) and grade 3 (4.6 %). Chromogranin positivity was more frequent in stomach ($p < 0.01$). Tumour size differed between 0.1 and 10 cm, while in 83 cases (42.3 %) it could not be determined due to very small size, dispersed nature of the tumour cells and inadequacy of sampling. In 6 (3 %) cases Ki-67 index could not be evaluated due to cauterization artifacts or loss of tumour in serial immunohistochemistry sections.
Conclusion: One of the major limitations for grading in biopsies was small sample size which interferes with Ki67 staining and interpretation. Presence of different staging systems and frequent updates in grading schemes have potential to lead to discrepancy when evaluating recurrent cases and determining time-trends of the tumours.

A grade 1 neuroendocrine tumour located in appendix, Hematoxylin-eosin, x100:



PS-08-054

Is there a correlation between autoimmune and alkaline gastritis?

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Objective: Aim of the study is the investigation of antral mucosa in autoimmune gastritis which in contrast to oxyntic is considered unaffected.
Method: The material consists of H&E and Giemsa stained sections of 1149 consecutive gastric biopsies.
Results: Histological evaluation revealed HP-gastritis in 228(19,84 %), autoimmune gastritis (AIG) in 64(5,57 %), non-specific gastritis in 384(33,42 %), alkaline/chemical gastritis (ALG/CG) in 88(7,66 %), no/minimal changes and others in 385(33,51 %) cases. In AIG was 39 females and 25 males and the mean age was 61,68 (range: 29–81). The atrophy was severe in 48, moderate in 9, mild in 4 biopsies and 3 had no data. In 12 cases pyloric mucosa showed changes of alkaline gastritis. The incidence of ALG in AIG was significantly higher compared to ALG/CG in the whole gastritis setting ($p < 0{,}0001$).
Conclusion: ALG is a rather common finding in AIG which can be ascribed to a higher pH in the antrum due to the low HCL secretion in association with age related sphincter dysfunction.

PS-08-055

Mucin phenotype in gastric hyperplastic polyps: A study of 33 cases

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Objective: We aim to assess mucin phenotypes in gastric hyperplastic polyps (GHPs).
Method: 33 GHPs were recorded over a 7 years period. We reviewed their endoscopic and histological features. MUC2, MUC5AC and MUC6 immunohistochemical expression patterns were studied. The GHP mucin phenotypes were divided into 4 subtypes: the gastric mucin phenotype (G-type), the intestinal mucin phenotype (I-type), the gastrointestinal mucin phenotype (GI-type) and the unclassified mucin phenotype (U-type).
Results: Sex-ratio was 1.6. Mean age was 59.8 years. 80 % patients had a single polyp and 20 % multiple polyps. Size was small than 10 mm in 82 % of GHPs and comprised between 10 and 15 mm in 18 % of cases. Polyps were cardial in 24 % of cases, fundic in 30 % of cases, corporeal in 15 % of cases and antral in 30 % of cases. Focal intestinal metaplasia was present in all cases. The G-types was observed in 63.6 % of cases and the GI-type in 36.3 % of the GHPs. Neither I-type nor U-type were found.
Conclusion: Whereas the expression of mucins and its significance are elucidated in gastric adenocarcinoma, the significance of the mucin phenotype for GHPs has not been well documented and their prognostic value is not yet well established.

PS-08-056

GIST of the stomach with epithelioid and spindle cell morphology: A case report and review of literature

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Objective: Gastrointestinal stromal tumours (GIST) are the most common mesenchymal tumours of the stomach. They usually display immunopositivity for CD117(KIT) and most of them contain KIT- or PDFGRA- activating mutations. A broad morphological appearance of a gastric GIST may suggest an SDH-deficient tumour or may reflect divergent response to targeted therapies.
Method: A 67-year-old male presented with a gastric tumour, measuring 9,5 × 7 cm, protruding into the lumen. A partial gastrectomy was performed. Formalin-fixed paraffin embedded tissue was examined with histology and immunohistochemistry.
Results: Microscopically, a stromal gastrointestinal tumour, characterized by epithelioid cells (with nuclear polymorphism) and spindle cells (with vesicular ovoid nuclei), was revealed. Mitotic figures: 8/50HPF. There also was osteochondromatous differentiation and 3 positive lymph nodes. Immunohistochemically, neoplastic cells were CD117(+ with dot-like pattern in the epithelioid element and + focally in the spindle cell element), CD34(+), DOG-1(+ focally), Ki-67(10 %). The diagnosis was gastric GIST, prognostic group 6a.
Conclusion: In gastric GIST with spindle cell and epithelioid morphology, mitotic count and tumour size are important prognostic parameters, which could suggest the optimal targeted therapy, although the prognosis may be quite unpredictable, simulating SDH-deficient GISTs.

PS-08-057

A case of adrenal cortical carcinoma with metastasis in the stomach and synchronous gastrointestinal stromal tumour

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Objective: To report a rare gastric metastatic case with adrenocortical origin.
Method: A 71-year-old male presented with symptoms suggesting gastric cancer that was confirmed at gastroscopy and was diagnosed as undifferentiated carcinoma at biopsy. The abdominal CT-scan also revealed a tumour located in the right adrenal gland. Total gastrectomy and right adrenalectomy were performed.
Results: Macroscopic examination of the surgical specimens revealed a protruded tumour of the posterior wall of the gastric body covered by intact mucosa and a 13 × 10 × 6 cm-sized encapsulated tumour weighing 500 grams, in the adrenal gland. Histopathologic examination showed an

adrenocortical carcinoma composed by oval-shaped cells with slight eosinophilic cytoplasm with focally hyaline globules, a high mitotic rate (>20 mitoses/50HPF) and large hemorrhagic and necrotic areas. In the adrenal gland, the tumour capsule was crossed and metastasis was seen in the submucosa of the stomach, without lymph node metastases. The final diagnosis was based on the tumour cells positivity for vimentin, inhibin, calretinin, and melan A. A synchronous DOG-1/c-KIT positive gastrointestinal stromal tumour (10 × 10 mm, no mitoses) was also incidentally identified in the stomach.
Conclusion: The gastric bioptic specimens that display undifferentiated carcinomas should be carefully examined to exclude a possible metastatic tumour.
The research was founded by project UMFTGM-CC-13-01-V01-15/2013.

Monday, 7 September 2015, 09.30–10.30, Restaurant
PS-09 Poster Session Gynaecological Pathology

PS-09-002
Atypical polypoid adenomyoma of the uterus: A clinicopathological analysis of 28 cases
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Objective: To investigate the clinicopathological characteristics of uterine atypical polypoid adenomyoma (APAM), including the cases with coexsistent endometroid endometrial adenocarcinoma (EEA).
Method: A retrospective analysis of the clinical data, morphologic features, and immunohistochemistry of 28 consecutive cases of uterine APAM diagnosed in our Department between January 2001 and December 2014 was done.
Results: The mean age of the patients was 41 (range, 26–61). Only five patients were postmenopausal, and seven were undergoing evaluation for infertility. Microscopic examination disclosed endometrial glands with varying degrees of hyperplasia and cytological atypia within a myofibromatous stroma. Squamous metaplasia was present in 25(89 %), and foci of well-differentiated EEA coexisted in 5 (17.9 %) cases. In 4 (14,3 %) other patients moderately-differentiated EEA was present both in APAM and endometrial fragments. Nine patients were initially treated with hysterectomy and the remaining 19 with curettage, polypectomy, or hysteroscopic transcervical resection, followed by hormonal therapy in 10 cases. There was one recurrence documented, while in 3 (13.6 %) of these patients the APAMs persisted up to 2 years. All patients except the one with advanced stage EEA (FIGO stage IIIC) were well and alive 16–147 (mean, 71) months after primary treatment.
Conclusion: Although the clinical behavior of APAM is benign in most cases, it can be associated with sterility and rarely with endometrial carcinoma. Therefore a meticulous pathological evaluation of specimen of APAM is necessary for the detection of the coexistence of EEA.

PS-09-003
Sebaceous adenoma arising in a mature cystic teratoma of the ovary: Case report
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Objective: Sebaceous adenoma arising in a mature cystic teratoma of the ovary is rare, although sebaceous glands are almost always found in benign ovarian teratomas.
Method: We report a case of a 44-year-old female with sebaceous adenoma occurring in an ovarian mature cystic teratoma.
Results: The ovarian teratoma was grossly cystic, with apparent solid mass protruding into the cyst cavity. Microscopically, most of the tumour consisted of a typical dermoid cyst. However, in solid areas the tumour showed lobular or diffuse proliferation of sebaceous cells showing various degree of maturity. Recent report described association of ovarian sebaceous adenomas with Muir-Torre syndrome (a variant of Lynch syndrome). In our case, we ruled out this possibility by immunohistochemical examination with antibodies against mismatch repair proteins (MLH2, PMS2, MSH2, MSH6), which were positive.
Conclusion: We present the seventh reported case of a sebaceous adenoma arising in mature cystic teratoma of the ovary. Acknowledgement: This work was supported by PRVOUK-P27/LF1/1

PS-09-004
The innovative role of p53 unbalance in precancerous lesions for serous ovarian carcinoma
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Objective: Papillary tubal hyperplasia (PTH) is accompanied with detached rounded clusters that are free floating in the lumen of the tube and psamomma bodies. In some studies PHT was associated with ovarian serous borderline tumour (SBT) although being poorly investigated with molecular methods. We investigate p53 and Ki-67 expression in fallopian tubes from patients with SBT and high-grade serous ovarian carcinoma (HGSC).
Method: 58 patients were recruited (34 with SBT, 33 with HGSC and 14 with normal fallopian tubes (control group (CG), p53 and Ki-67 expression were detected in their fallopian tubes.
Results: PHT was diagnosed in 73 % of SBT patients, 20 % of HGSC patients and was not diagnosed in CG ($p < 0.05$). PHT showed weak nuclear and/or cytoplasmic p53 staining, Ki-67 expression was low (<5 %) in 90 %. Serous tubal intraepithelial carcinoma (STIC) was diagnosed in 25 % of HGSC patients and was not revealed in SBT patients and in CG. STIC showed strong nuclear p53-staining and high Ki-67 expression (>10 %), ($p < 0.05$). Patients from CG showed weak p53-staining and low Ki-67 expression in 100 % of fallopian tubes.
Conclusion: Coincidence of PHT and SBT can reflect simultaneous development of precancerous and neoplastic lesions in the fallopian tube and in the ovary. Thus, PHT shows genomic instability, involves wild type h53 stabilization and takes precedence of neoplastic transformation. In addition our results prove the hypothesis about different pathogeneses of low-grade serous carcinoma (through PHT) and HGSC (through STIC).

PS-09-005
Adenosarcoma of the cervix: A case report
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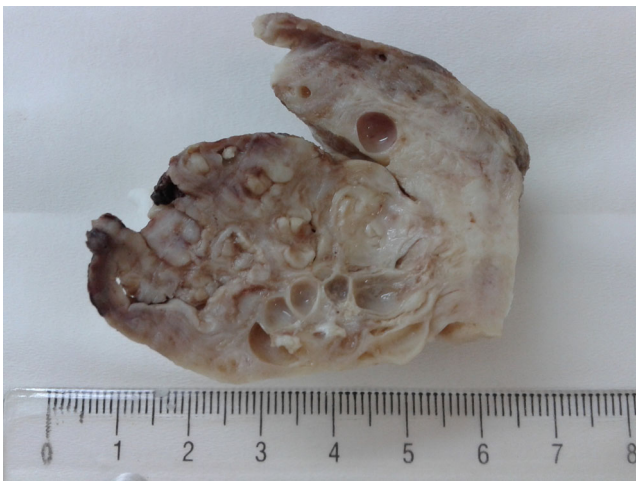
Objective: To present a rare case of cervical mixed Mullerian tumour.

Method: A 47-year-old woman with bleeding out of the cycle of 3 months backward was admitted to hospital. Gynecological finding indicated voluminous tumour with involvement of both the cervical lips. Magnetic resonance imaging showed a tumour with its epicenter in the region of the posterior cervical lip with infiltration of the cervical stroma, without penetration of parametria. Tumour biopsy revealed cervical adenosarcoma. Subsequently, surgical intervention was made.
Results: Macroscopic exam of the surgically resected uterus discovered polypoid formation 47 mm in its greatest dimension confined to the cervix. Microscopically, the tumour was composed of epithelial and stromal elements, which were arranged in leaf-like pattern. Glands were compressed in thin slit-like pattern with evidence of stromal condensation around the glands. Glandular epithelium showed benign histological characteristics with focal multiplied and pseudostratified nuclei without atypia. Stromal cells had moderate cytological atypia with mitoses up to 4/10 HPF. Focally, hemosiderophages and areas of fresh bleeding was found.
Conclusion: Biphasic tumour with clear histological signs of benign epithelial and malignant mesenchymal component allows the diagnosis of cervical adenosarcoma. In differential diagnosis, primitive endometrial tumour propagation in the cervix and papillary fibroadenoma should be considered.

Gross finding of cervical adenosarcoma:



PS-09-006
Evaluation of cyclic glycodelin production in endometrium of patients with chronic endometritis
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Objective: To assess cyclic production of glycodelin (GD) in endometrium of patients with chronic endometritis (CE).
Method: Morphological and immunohistochemical examination was performed of the uterine cavity scraping samples taken during mid-proliferative phase (days 8–11) from 51 patients of reproductive age with dysfunctional uterine bleeding and infertility (Group 1) and 22 control patients (pipelle before ECF) (Group 2).
Results: Morphological features of CE were detected in 26 patients from Group 1. Signs of non-specific chronic inflammation were not found in endometrial samples from Group 2. Immunohistochemistry of samples without CE showed a lack of GD in the glands; it correlates with GD production pattern during normal ovulation cycles in fertile women. Eighty-three percent of patients with CE had GD expression in glandular epithelial cells implying premature GD production in mid-proliferative phase.
Conclusion: Patients with morphologically verified CE have premature GD production in the peri-ovulation period. Synthesis of GD possessing contraceptive activity in this period may contribute to infertility in CE patients.

PS-09-007
An uterine incidental tumour
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Objective: Adenomatoid tumour is a relatively common benign tumour, which has an incidence of 5 %. Its most common location is genital tract and has a mesothelial origin. Adenomatoid uterine tumour (AUT) is found incidentally in routine hysterectomies.
Method: A 55-year-old woman who had an hysterectomy because complex endometrial hyperplasia.
Results: A whitish-yellowish, intramural, circumscribed and 1,5 cm diameter nodule was found. Microscopically, it showed an intramural and well defined nodule of cuboidal cells with pseudoglandular spaces delimiting an adenoid pattern and surrounded by variable-size myometrial smooth muscle fibers. Inmunohistochemistry, it was positive for cytokeratins AE1/AE3 and 7, WT1 and calretinin.
Conclusion: AUT is an incidental and solitary finding. It measures less than 4 cm. It is positive for cytokeratin 7, calretinin and D2-40; negative for cytokeratin 5/6, 20, EMA, vimentin, desmin, MDM2, CDK-4 and CD31 and its mitotic activity ranges between 0,2 and 3 %. It has a characteristic histology, so inmunohistochemistry is not usually necessary; however, certain tumours mimic AUT (lipoleiomyoma, liposarcoma, lymphangioma, haemangioma and adenocarcinoma). AUT is a common tumour, but often we forget its existence and is underdiagnosed. It is required to consider AUT and its differential diagnosis to avoid making big mistakes.

PS-09-008
Metastatic endometrial adenocarcinoma mimicking a primary colon cancer: A case report and review of literature
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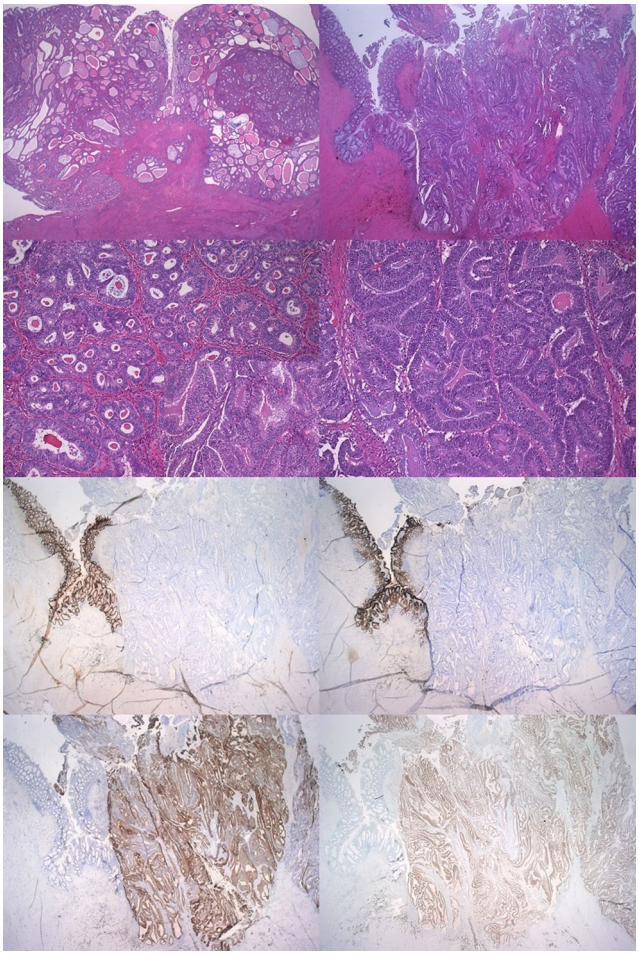
Objective: Present a unique case of endometrioid endometrial adenocarcinoma metastatic to the mucosa of the colon.
Method: Evalute microscopic slides from our archive and perform immunohistochemistry staining. Review literature.
Results: What first appeared to be a tumour primary to the colon showed an immunohistochemical profile typical for an endometrial carcinoma. After reviewing literature we found that the metastasis was unlikely to represent endometrial carcinoma arising in endometriosis.
Conclusion: Our case report underlines the importance of considering metastatic disease as a differential diagnosis even in unusual locations and the value of complementary analyses in identifying the origin of a tumour.

Tumour and metastasis:



PS-09-009

Large cell variant of small cell carcinoma of the ovary, hypercalcemic type

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Objective: Large cell variant of small cell carcinoma of the ovary, hypercalcemic type (SCCOHT), is a rare tumour, usually occurring in young women.
Method: We report a case of 36-year-old female presented with an ovarian tumour 8 cm in diameter.
Results: Grossly, the ovary consisted of partly solid and partly cystic tumour. Microscopically, the tumour consisted of large cells with ample cytoplasm and irregular nuclei with prominent nucleoli. In some areas, the tumour cells were arranged in solid sheets, in others, there was pseudofollicular arrangement. Immunohistochemically, the tumour cells were positive for vimentin, cytokeratin (AE1/AE3) and alpha-smooth muscle actin. Moreover, the tumour cells shows loss of Brg1 expression. Other markers examined including S-100 protein, desmin, CD31, CD34, D2-40, alpha-inhibin, and BerEP4 were negative.
Conclusion: We described a case of large cell variant of SCCOHT. This variant is rare, only few cases have been reported to date. Recently, it has been shown that SCCOHT is associated with SMARCA4 gene mutation. Mutation of this gene is associated with loss of Brg1 protein expression. As immunophenotype of SCCOHT is non-specific, loss of Brg1 can be used as a helpful marker in differential diagnosis of these tumours. Acknowledgement: This work was supported by PRVOUK-P27/LF1/1

PS-09-010

Ovarian hemangioma: Report of three cases associated with concomitant stromal luteinization

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Objective: Ovarian hemangiomas are rare tumours with less than 60 reported cases in the English literature. These lesions may rarely be associated with systemic manifestations. Conditions associated with ovarian hemangiomas include stromal luteinization, ascites, thrombocytopenia, endometrial hyperplasia or carcinoma.
Method: We report three cases of ovarian hemangiomas: Ovarian tumour was detected in 69 year old female with known diagnosis of diffuse large B-cell lymphoma. A 68 year old female presented with ascites. Preoperative checkup suggested pelvic malignancy. Adnexal mass was discovered incidentally in 81 year old female.
Results: Histopathologic examination of every case showed ovarian hemangioma with concomitant stromal luteinization. Moreover, in one case a component of Leydig cells was present.
Conclusion: Ovarian hemangiomas can be rarely associated with stromal luteinization, we report additional three cases.

PS-09-012

A rare case of superficial vaginal myofibroblastoma

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Objective: Superficial vaginal myofibroblastoma is a rare mesenchymal tumour. We present a 59-year-old woman with 4-cm polypoid mass located in lamina propria of the vagina. Tumour excision was performed.
Method: The diagnose was confirmed by immunohistochemistry.
Results: The tumour was not encapsulated, had gray, gelatinous, soft consistency, microscopically with spindled cells with elongate nuclei, mild pleomorphism, different zones: predominantly - with high cellularity and myxoid foci with lace-like pattern resembling mucin. Immunophenotype: Desmin (+), Smooth Muscle Actin (+), Er (+) 30 % nuclei, CD34(+), EMA(-), CK1,7,20(-), CD10(-), Ki67 2 % allowed to distinguish it from mixed tumour of the vagina (spindle cell epithelioma), SFT, fibroepithelial stromal polyp and confirmed benign nature of tumour.
Conclusion: Uncommon vaginal tumours, characterized by a predominance of spindle stromal-type cells with different patterns, myxomatous background may cause issues in identification stromal and pseudoepithelial or epithelial components, with mucin-like foci. Immunophenotype may be variable in different areas.

PS-09-013

Expression of Osteopontin as a prognostic indicator in grading of Malignant Epithelial Tumours of ovary

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Objective: To determine if Osteopontin expression by Immunohistochemisrty (IHC) can correlate with grade of Malignant Epithelial Tumours of Ovary.
Method: The present work was done at Dept of Pathology, J. N. Medical College, Belgaum, Karnataka, India, from Jan 2010 to June 2013 for evaluation of marker and data analysis. The study included 120 surface epithelial Ovarian tumours confirmed histopathologically. In all the cases, Osteopontin expression was studied with IHC on paraffin sections.
Results: This study included 95 (79.2 %) benign tumours and 25 (20.8 %) malignant tumours. All Benign epithelial tumours were negative for Osteopontin expression. All high grade (III) malignant Ovarian epithelial tumours showed increased expression of Osteopontin of +++ and low grade (I & II) tumours expressed +/++ Osteopontin. High grade serous

carcinoma was seen to be common malignant tumour. With Fisher Exact test, p value < 0.0001 was significant for expression of Osteopontin.
Conclusion: Osteopontin expression was seen in all the malignant epithelial tumours of Ovary. Osteopontin expression was significantly higher in high grade epithelial carcinoma of ovary as compared to low grade tumour. Hence Osteopontin is a good prognostic indicator in grading of Malignant Ovarian epithelial tumours.

PS-09-014
p 16: A new marker for differentiating between endometrial polyps and endometrial hyperplasia on curettage and Pipelle biopsy
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Objective: One of the most frequent causes of abnormal vaginal bleeding is endometrial polyps (2–23 %) and endometrial hyperplasia (14 %). Most of the time, both lesions are easy to recognize on hysteroscopic and microscopic examination however they may pose diagnostic problems due to the overlap in morphology in both situations. The aim of this study was to distinguish endometrial polyps from endometrial hyperplasia based on the stromal positivity of p16, generally used for other purposes in gynecologic pathology.
Method: We examined 44 cases, 24 endometrial polyps (15 atrophic, 8 functional, 1 hyperplastic) and 20 endometrial hyperplasia (9 simple, 1 simple with atypia, 10 complex with atypia). In all cases, stromal cell positivity for p16 (p16- DB Biotech, clone R19-D) was classified into 4 grades: grade 0 (0–10 %), grade 1 (≥10 < 25%), grade 2(≥25 < 50%), and grade 3(≥50%).
Results: Stromal p16 positivity was 70.8% in polyps and 0% in hyperplasia, respectively (highly statistically significant, $p = 0.0001$). Most of the 24 polyps (65%) had grade 3 stromal positivity. There was no difference in glandular p16 expression between endometrial polyps and hyperplasia.
Conclusion: The significant difference in p16 stromal positivity justifies this markers's usefulness in the differential diagnosis between these two lesions with different treatment (polypectomy vs. hormonal/ hysterectomy in hyperplasia).

PS-09-015
Uterine tumour resembling ovarian sex cord tumour
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Objective: Uterine tumours resembling ovarian sex cord tumour (UTROSCT) is rare group of stromal neoplasms exhibiting prominent sex cord-like diferentiation. UTROSCT was first presented by Clement and Scully in 1976.

Method: We report case of the patient 42 years old which appears because of metrorrhagia lasting past 4 years.
Results: Intrauterine tumour mass size 5 × 2,5 × 2,5 cm was detected and surgically removed. The tumour grossly resemble polypoid mass. Stromal component is arranged in solid structures. Epitheloid tumour component (represented about 60% of the tumour mass) is arranged in adenoid, tubular and follicular structures, as well as, cribriform and solid groups, bands and nests. Mitoses, with pathological forms were numerous, more than 9/10 high power field. The infiltrative tumour ingrowth in the myometrium was detected. Immunohistochemical tests show tumour mass immunoreactivity for vimentin, calretinin, CD56, AE1/AE3, focally for desmin, CK7, melan A, HMB45 with coexpression of PR and CD99. Ki-67 was positive up to 10% of cells. Tumour was diagnosed as uterine tumour resembling ovarian sex cord tumour.
Conclusion: Most UTROSCT have unpredictable clinical behavior. Besides that, we presented a case with high mitotic index and infiltrative tumour growth. Clinical forms of UTROSCT are highly variable and individual approach in therapy is the key, as well as further research in connection with this tumour.

PS-09-016
A rare case of aberrant migration of primordial germ cells: Uterine yolk sac tumour
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Objective: Yolk sac tumour of uterus is a very rare tumour that that usually arises in the testis or ovary, it's depelop in the uterus is a result of aberrant migration of primordial germ cells. It is important to be aware of such entities to ensure correct diagnosis and hence patient management.
Method: We present a case of 57 years old woman in climax presenting with postmenopausal bleeding and elevated serum alpha-fetoprotein. CT scan showed an enlarged uterus measuring 9.2 cm in length. Biopsy report suggested non-keratinized epidermoid carcinoma microcellular with areas of clear cell carcinoma, poorly differentiated G3, with areas of infarction and acute inflammation associated. The mass was excised and sent to our pathology department for histopathological examination. We reported Yolk sac tumour of uterus with hepatoid pattern T2aN0M0. The section from the uterin cervix and ovary did not show any remarkable pathology.
Results: We discuss the clinicopathological features of the case and review the literature for previously reported yolk sac tumours.
Conclusion: Germ cell tumours in post-menopausal patients are extremely rare, with very few case reports in the literature. These cases show aggressive behavior and very poor prognosis.

PS-09-017
Endometrioid carcinoma with squamous differentiation of the uterus and ovaries - synchronous primary tumours or metastasis: A case report
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Objective: Endometrioid carcinoma simultaneously involving the uterus and ovaries are problematic when establishing whether they are synchronous malignancies or a single primary and associated metastasis. We present a case of such challenging diagnosis in a young woman.
Method: A 38 year-old woman with personal history of Hodgkin lymphoma, presently in remission for 10 years and fibrocystic breast disease was admitted to our hospital for uterine and bilateral ovarian masses and metrorrhagias. After surgical intervention, on histopathological examination we found endometrioid carcinoma with squamous differentiation in the uterus, cervix and ovaries. In order to establish tumour origin, histopathological features were analyzed and immunohistochemistry for vimentin, ER, PR, CDX2 was performed.
Results: High positivity for vimentin, ER, PR for both ovaries and endometrium, and weak positivity for CDX2, together with morphopathological characteristics concluded endometrioid endometrial carcinoma with squamous differentiation, FIGO grade 1, with cervical extension and bilateral ovarian metastasis, pTNM stage IIIA.
Conclusion: Immunohistochemistry is important in differentiating synchronous from metastatic tumours, especially in places with limited resources, as for providing accurate diagnosis and staging so the patient can benefit of optimal therapeutic management.

PS-09-018

Atypical localization of endometriosis, bowel endometriosis

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Objective: Endometriosis is the presence of endometrial tissue outside the endometrium that describe endometrial glands and stroma. By the localization of ecoptic endometrium, endometriosis can be classed as internal endometriosis and external endometriosis. Internal endometriosis-adenomyosis is the presence of endometrium in the uterine muscle. In external endometriosis the ecoptic endometrium is positioned outside the body of the uterus: ovarium, peritoneum tube, ileum, cervix, vagina.
Method: External endometriosis is the form of smaller or larger fields of fresh or old bleeding or hyperemic nodal changes bluish to dark brown in color. The 33 years old female was hospitalized after showing the symptoms of suboclusion. During preoperative diagnosis and preparation, resection of terminal ileum was performed with the presence of a submucous lesion along the muscular layer, up to 10 mm long. A transverse section showed that it is of "spongy structure", cystic in appearance, color brownish-red. Segments were fixed in the 10% formaldehide, paraffine and cut by the microtome to 5 μm sections and colored HE method. The muscle wall of the small bowel revealed numerous gland foci and endometrial stroma. Surrounding the glands were a large number of macrophages filled with haemosiderin. Immunohistological analyses were carried: CD10, ER.
Results: External endometriosis is a rare localisation. Diagnostics is based on the patohistological analysis. The microscopic picture of endometriosis shows the presence of endometrial glands and stroma surrounded by inflammatory infiltrate.
Conclusion: The patohistological diagnostics of external bowel endometriosis is the key to identifying this change. The recessed part of the bowel is analyzed on the tissue cultures colored by a standard HE method and immunohistochemical analyses.

PS-09-019

Metastatic tumours of the ovary: Difficulties of the histological diagnostics

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Objective: The ovary is a common site of metastases. Clinical and histological features of metastatic tumours frequently mimic primary ovarian malignancies causing serious diagnostic problems for the surgical pathologist. Frozen section is widely used in the intraoperative assessment of patients with ovarian tumours but it can be very difficult to distinguish certain types of primary ovarian tumours and metastases from other sites.
Method: We examined 152 cases of secondary ovarian neoplasm diagnosed in The National Institute of Oncology, Hungary from 2000 to 2014.
Results: Colorectal cancer was the most common primary tumour (58 cases), followed by breast (33 cases), endometrium (30 cases) and stomach (13 cases) cancer. The differential diagnosis the most difficult was when endometrioid and mucinous tumours were presented in the ovaries. Metastases of colorectal and gastric adenocarcinomas may simulate benign or borderline cystadenomas too. In 74 cases frozen section was performed but metastatic origin of the tumour was successfully identified only in 32 cases (43%).
Conclusion: The knowledge of the patient's history and immunhistochemical stains were helpful for distinguishing these secondary ovarian tumours from primary ovarian neoplasms. Frozen section is only moderately successful in distinguishing primary ovarian malignancies from tumours metastatic to the ovaries.

PS-09-020

Clinical and morphological features of uterine myomas in women of reproductive age

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Objective: To identify the features of myomas of different size in women of reproductive age.
Method: We analyzed 30 cases of large size myomas in women of reproductive age, who were in barren marriage. In all cases patients underwent hysteroresectoscopy and endoscopic conservative myomectomy. Morphological study was conducted on the basis of the pathology laboratory at the National centre of obstetrics and gynecology of the RK.
Results: In 11 cases we observed single myomas, while in 19 women we found multiple myomas. Myomas were predominantly located on the back wall. We found out that large myomas (61 to 70 mm) were prevalent. In 20 cases we noticed a deformation of the uterine cavity due to submucosal and intramural myomas. During the histological examination in large myomas we observed degenerative changes including edema, mucilaginization, cyst formation, focuses of necrosis, calcification with reactive focuses of inflammation. We also noticed focuses of adenomyosis.
Conclusion: The prevalance of large size myomas in women of reproductive age is a sign of hyperestrogenia. We believe that infertility in this groups could be explained not only by deformation of uterine cavity, but also by necrosis, calcification, focuses of inflammation in large myomas. The latter indicates 'fast growth', caused by ademomyosis. Morphological findings allows us to assume that there are certain differences of growth patterns in large myomas and myomas of medium and small size.

PS-09-021

Morphological characteristics of endometriosis in women older than 40 years of age

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Objective: To analyze cases of endometriosis in women older than 40. We noticed that endometriosis in these category is a major morphological finding after histological analysis of surgical material.
Method: We analyzed 38 cases of endometriosis in women (40 to 67 year old), who experienced radical surgery, including hysterectomy and bilateral salpingo-oophorectomy because of leiomyomas of the uterus. In accordance with the classification of the American Society for Reproductive Medicine we diagnosed Stage II endometriosis (12 cases) and Stage III (26 cases). The research was undertaken based on the materials of pathology laboratory of the National centre of obstetrics and gynecology we analyzed all cases of endometriosis diagnosed in 2014 (within the frameworks of the research project on clinical and laboratory diagnostics of endometriosis).
Results: After hystological study of 38 cases of endometriosis, in 21 case we diagnosed endometrial hyperplasia (complex hyperplasia

with atypia). In all cases we diagnosed focuses of mild proliferation of fallopian tube epithelium. In four cases we observed cellular leiomyomas.
Conclusion: Results of our research show the connection between Stage II and Stage III endometriosis and proliferation of endometrium and of fallopian tube epithelium. Moreover, endometriosis influences rate of proliferation of leiomyomas.

PS-09-022
Does serous tubal intraepithelial carcinoma explain the origin of all serous carcinomas?
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Objective: Since 2001, the theory of pelvic serous carcinogenesis, the origin of serous carcinomas from STIC (serous tubal intraepithielial carcinoma) has been proposed and nowadays it is widely accepted. The aim of this study is to find out the incidence of tubal lesions in pelvic serous carcinomas in our institution.
Method: One hundred forty four pelvic serous carcinomas (ovarian, tubal, peritoneal) had been operated at our institution from 2005 to 2014. The fallobian tubes of patients were examined by SEE-FIM (sectioning and extensively examining the fimbriated end) protocol. All tubal hematoxylin-eosin sections with anomalies (nuclear crowding, hyperchromasi) were further evaluated with immunohistochemical p53 and Ki67 staining.
Results: STIC was identified in 27 of 144 (18.75 %) patients. STIC was found in 2 (7.4 %) peritoneal, 8 (29.6 %) tubal and 17 (63 %) ovarian carcinomas.
Conclusion: Almost nearly one fifth of pelvic serous carcinomas, most of them ovarian, had STIC in the fallobian tubes. The other serous carcinomas might be originated either de novo in the ovary/peritoneum or tubal intraepithelial carcinoma might have been disappeared during carcinogenesis.

PS-09-023
The characteristic of connective tissue of myometrium in women with pelvic organ prolapse
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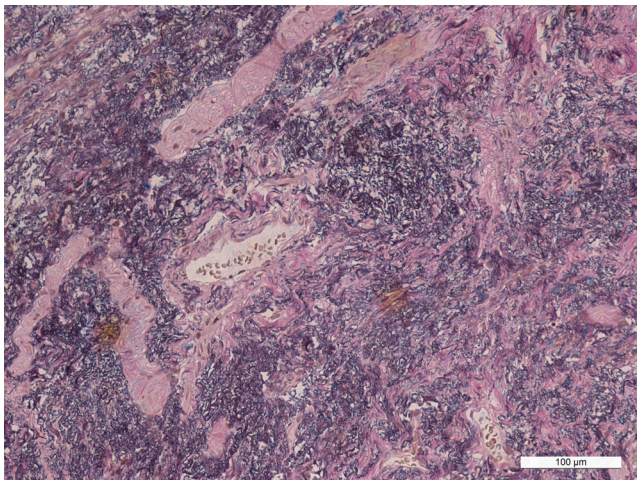
Objective: To investigate the myometrial stromal component (MSC) of the uterine body in postmenopausal women with pelvic organ prolapse (POP).
Method: Normal myometrium (n = 15) and myometrial samples of the women with POP (n = 30) were stained with hematoxylin-eosin, Verhoeff-van Gieson stain (VVG), collagen I, III, V, fibronectin, fibulin-5, matrix metalloproteinase 1, 9, tissue inhibitor matrix metalloproteinase 1, 2 (TIMP-1, 2).
Results: In MSC of the women with POP we observed perivascular VVG-positive black deposits, that were also positive for collagen III, a decrease average expression of collagen I (4,6 ± 4 vs 54,8 ± 3 %, p < 0,01); collagen V (14 ± 2 vs 65 ± 9,3 %, p = 0,02), fibronectin (10,9 ±v8 vs 14,7 ± 4 %, p = 0,03) and fibulin-5 (0,6 ± 0,2 % vs 11, 7 ± 1,2 %, p < 0,01). The ratio of collagen I and III type was 1:6,3 vs 1,8:1 (in normal myometrium). TIMP-1, 2 were negative. The same changes were found in myometrial veins. A strong negative correlation was detected between collagen V and fibronectin (r = −0,9, p < 0,05, in control r = −0,8, p = 0,3).
Conclusion: POP is accompanied by the connective tissue remodeling of the uterine body.

Pelvic organ prolapse. Black filamentous deposits in the stroma of the myometrium, VVG x 200:



PS-09-024
Local agressive tumour of vulva: Unique presentation of aggressive angiomyxoma
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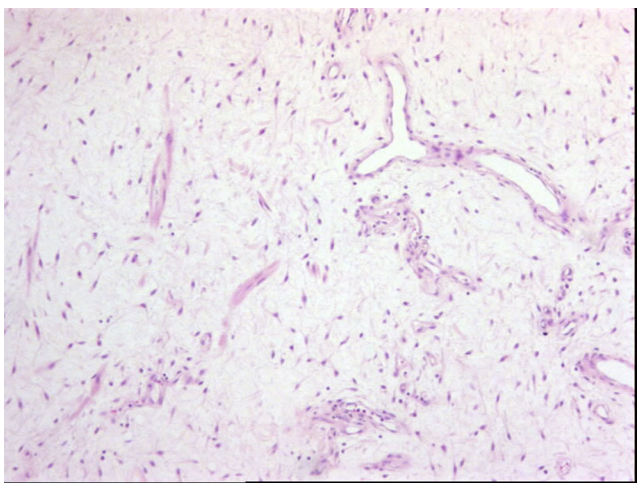
Objective: Aggressive angiomyxoma (AA) is a rare, locally agressive tumour of pelvis and perineal region with mesenchymal origin. This tumour tends to grow slowly with a low tendency to metastasize, but it shows a local agressive behavior and local recurrence.
Method: A 25 year old Turkish woman revealed to clinic with vulvar mass. After physical and gynecological examination surgical resection was performed.
Results: In light microscopic examination tumour was consisted of spindle and stellate shaped cell embedded in a loose-myxoid stroma. In immunohistochemical examination tumour cells expressed vimentin, desmin, smooth muscle actin (SMA) and estrogen (ER). Tumour cells were negative for CD34 and progeterone (PR). Based on the pathological findings tumour was diagnosed as AA of vulva.
Conclusion: AA is believed to arise from specilized mesenchymal cells of perineal and pelvic region cells which are reactive to estrogen and/or progesterone. Because of this these tumours usually expresses ER and/or PR. Our case is also expressing ER.



PS-09-025

An immunohistochemical and ultrastructural study of the stromal component of myometrium in women during labor with Marfan-like Syndrome (MFS)

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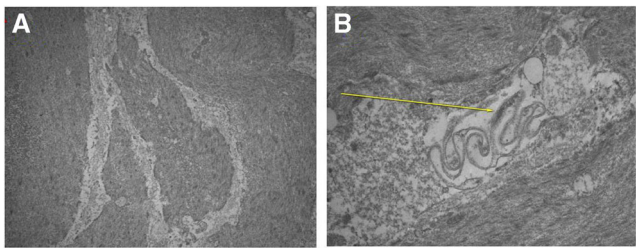
Objective: To investigate the stromal component of myometrium in women with Marfan-like syndrome and weak uterine contractions during labor.
Method: Biopsies of the lower uterine segment were studied at the time of a cesarean delivery in women with MFS (n = 15) versus in ones without MFS, pathology of uterus and complications of childbirth (n = 10). All samples were stained with hematoxylin and eosin, Van Gieson, collagen types I, III and V, fibronectin, fibulin-5, matrix metalloproteinase (MMP-1, -9), tissue inhibitor of matrix metalloproteinase (TIMP-1, -2), connexin-43. Electron microscopy (EM) and electron immunocytochemistry (EIC) using an antibody against connexin-43 were performed on six samples.
Results: There was a decreased expression of collagen I (3,7 ± 2,8 vs 67, 9 ± 17 %, p < 0,01), collagen III (14,7 ± 2,2 vs 32,3 ± 14 %, p = 0,03), fibulin-5 (2,6 ± 1,9 vs 15,4 ± 0,7 %, p < 0,01) and TIMP-1,-2. The collagen type I/III ratio was 1:4 vs 2:1 in the reference group. EM and EIC showed a reduction of gap junctions between smooth muscle cells and a decreased connexin-43 expression in smooth muscle cells and telocytes.
Conclusion: Pathological remodeling of the stromal component of myometrium and a decreased connexin-43 in myometrium can possibly lead to weak uterine contractions during labor.

EIC. A) The reduction of gap junctions between smooth muscle cells, x 10000; B) lack of connexin-43 expression in smooth muscle cells and telocyte (arrow), x 20000:



PS-09-026

A rare uterine tumour

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Objective: The term "Müllerian adenosarcoma with sarcomatous overgrowth" (MASO) is defined as the presence of pure sarcoma occupying at least 25 % of the tumour, usually high grade in nature and without a benign glandular component. In this report we present a MASO case with heterolog elements, derived from uterine cavity.
Method: A 52-year-old postmenopausal woman presented with vaginal bleeding and pelvic pain. Vaginal examination revealed enlarged uterus and ultrasound scans revealed a large heterogeneous mass in the uterine cavity.
Results: On gross examination a friable polypoid mass arrised from uterine corpus. On microscopic examination revealed a biphasic tumour in which glands were scattered throughout the stromal component. The later formed broad polipoid fronds that typicaly projected into the glands The stroma were more cellular around glands and formed characteristic periglandular cuffs. There were bizarre cells and rhabdomyoblasts that were varied from round to strap-shaped and eosinofilic cytoplasm with cross striations. Immunoreactivity with desmin and skeletel muscle markers (myogenin and myo D1) were identified in rhabdomyoblasts and small cells.
Conclusion: Uterine adenosarcoma is relatively rare tumour and is hard to diagnose without immunohistochemistry. The most important adverse prognostic factors are deep myometrial invasion, sarcomatous overgrowth and heterologous elements, especialy rhabdomyosarcoma.

PS-09-027

Expression and prognostic value of GAL-3 in endometrial carcinoma

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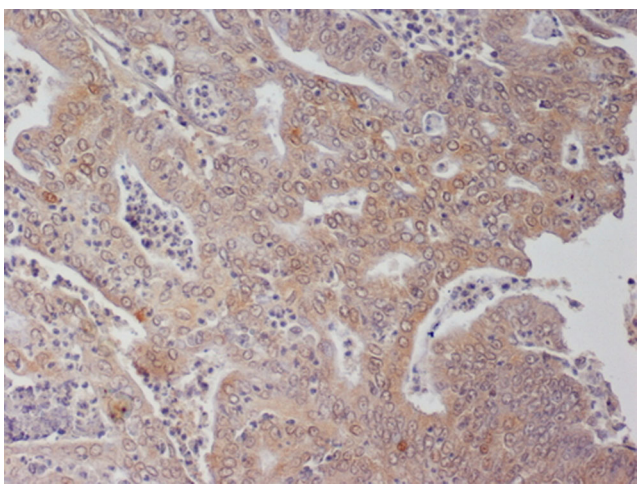
Objective: Endometrial adenocarcinoma is the most common malignant neoplasia of the female reproductive system, in most developed countries with an annual incidence of up to 25/100,000. In the present study, we evaluate immunohistochemically the expression of GAL-3 in endometrial carcinoma and its correlation with prognosis and patient survival. Review of the literature reveled that up-regulation of galactin-3 has been associated with adverse clinicopathologic factors in several types of malignancies and indeed it has been suggested that inhibition of galactin-3 may provide a novel therapeutic approach in some tumours.
Method: GAL-3 expression was assessed by semi-quantitative immunohistochemistry in 46 primary endometrial carcinomas. Results were statistically analyzed in relation to standard diagnostic clinicohistopathological parameters.
Results: GAL-3 expression was detected in all patients with endometrial carcinoma (45.7 % with mild, 15.2 % medium and 39.1 % high expression) and exhibited statistically significant correlation with the histological type, disease stage, differentiation and myometrial invasion. The 5-year survival for mild and medium GAL-3 expression was 100 %. However for patients with high GAL-3 expression, the 1-year survival rate was 83.33 %, the 2-year was 44.44 % and the 5-year survival rate was 33.33 %.
Conclusion: GAL-3 expression is associated with poor prognosis and could be used as an independent prognostic factor in patients with endometrial carcinoma. Nevertheless, there are relatively few investigations of GAL-3 in endometrial carcinoma, thus, its role in the carcinogenetic process and on effective therapies in those tumours awaits further elucidation.

GAL-3 expression in moderate differentiation endometrial carcinoma. Original magnification X200:



PS-09-028

Immunohistochemical expression of p53 and BRCA1 in high grade endometrial carcinoma

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Objective: Identification of tumours with BRCA dysfunction has therapeutic and prognostic implications proven for breast and ovarian but still debatable for uterine carcinoma. The aim of this study is to evaluate the expression of p53- and BRCA1-proteins, detected by immunohistochemistry, in high grade endometrial in comparison with high grade serous ovarian carcinomas (HGSOC).
Method: The investigation was performed on 13 cases of endometrial carcinoma with serous and non-serous G3 morphology and 13 age-matched cases of HGSOC using monoclonal anti-p53 and BRCA1 antibodies. Two of the uterine cases - one with serous and one case with mixed histology (serous and G3 endometrioid) had history for previous breast carcinoma.
Results: All 13 HGSOC and 5 out 13 endometrial cancers showed p53 overexpression. Twelve of thirteen ovarian carcinomas revealed no expression of BRCA1 and therefore are suspicious for BRCA1-mutations. In the uterine group the same pattern was observed only in the two cases with previous breast carcinoma which were p53 positive.
Conclusion: Combination of serous morphology, p53 overexpression and history for previous or synchronous breast cancer or HGSOC could be included as criteria for stratification of patients with endometrial carcinoma suspicious for BRCA1-mutations and suitable for genetic testing.

PS-09-029

Primary strumal carcinoid of the ovary as an uncommon form of ovarian teratoma: A case report

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Objective: Strumal carcinoid (SC) is a rare variant of ovarian teratoma, characterized by an intimate mixture of thyroid tissue and carcinoid structures in a variable proportion. Primary ovarian carcinoids form 5 % of ovarian teratomas and 0, 5–1, 7 % of all carcinoid tumours.
Results: Case Description: We present a case of strumal carcinoid occurring in 45-year-old woman. The pacient with short history of constipation underwent an unilateral salpingo-oophorectomy for cystic tumour of the left ovary detected by the ultrasonography. Histopathological analysis of the tumour mass revealed SC of typical morphology. The woman subsequently underwent abdominal hysteradnexectomy and omentectomy without residual tumour structures. No subsequent therapy was indicated. Currently, the patient has no signs of relaps.
Conclusion: Primary ovarian carcinoid tumours represent a group of ovarian monodermal teratomas, occuring in middle-aged or older women. Most patients are asymptomatic or may have unspecific symptoms of abdominal distention, a minority has carcinoid syndrom or a constipation. These tumours are classified into five groups according to their histological patterns: insular, trabecular, mucinous, strumal and mixed. Only few cases have malignant course. SC, when confined to the ovary, is almost always benign.

PS-09-031

Impaired endometrial receptivity in infertile patients with external genital endometriosis

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Objective: To study the morphological and molecular substrate of impaired endometrial receptivity in fertile patients with external genital endometriosis who enter an assisted reproductive technology program.
Method: 140 infertile patients, including 50 women with grade 1-2 external genital endometriosis (a study group), 44 with endometrioid ovarian cysts (a comparison group), and 54 with tuboperitoneal factor of infertility (control group) were examined. All the patients underwent aspiration pipelle endometrial biopsy on 6–8 days following ovulation. Serial paraffin-embedded sections were used to determine the count of pinopodia and the expression of leukemia inhibitory factor (LIF), HOXA10, glycodelin A, integrin avβ3, and aromatase in the superficial epithelium, glandular epithelium, and endometrial stroma.
Results: The patients with external genital endometriosis had significantly lower pinopodium counts ($p < 0.05$), decreased expression of LIF, HOXA10, integrin avβ3, and glycodelin A in the superficial epithelium and a significantly increased expression of aromatase in the superficial epithelium, glands, and endometrial stroma cjmparing with control ($p < 0.05$). The highest expression of aromatase was seen in patients with endometrioid ovarian cysts.
Conclusion: Changed endometrial receptivity may be one of the leading causes of infertility and lower efficiency of the assisted reproductive technology program in patients with external genital endometriosis.

PS-09-032

Transitional cell carcinoma of the endometrium: A case report

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Objective: Endometrial transitional cell carcinoma (TCC) is a rare tumour with a few cases reported in the available literature. We present a case of endometrial transitional cell carcinoma in a 43 years old patient presented with profuse bleeding. After curettage and diagnosis of TCC was made, the patient underwent operation.
Method: The operative material contained the uterus with both adnexa. The uterus (720 gr weight) contained an intracavitary, polypoid mass which infiltrated the whole myometrium, serosa and the left ovary. The tissue specimens were fixed in 10 % buffered formalin and embedded in paraffin. Immunostainings with CK7, CK20, Vimentin, Estrogen receptor, Progesteron receptor and Thrombomodulin were made.
Results: Microscopically, the tumour was composed of solid sheets and tightly packed papillary structures with thin fibrovascular cores lined by many layers of transitional cells showing moderate to severe atypia. The neoplastic cells were positive only for CK7 and Vimentin. The patient had FIGO stage III A. Pulmonary and liver metastases occurred after the chemotherapy and the patient passed away 11 months after diagnosis.
Conclusion: TCC is a distinct type of endometrial carcinoma which has to be recognized. It broadens the spectrum of endometrial neoplasms.

PS-09-033

Sertoli - Leydig cell tumour with heterologous elements

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*Faculty of Medicine Skopje, Dept. of Pathology, Republic of Macedonia

Objective: Ovarian Sertoli-Leydig cell tumour of intermediate differentiation with heterologous elements is a rare ovarian tumour that belongs to the group of sex cord stromal tumours. This tumour affects mainly young women, with an incidence of less than 0,5 % of ovarian tumours. We present a case of unilateral ovarian tumour in a 34-year old patient.
Method: The tissue sections were conventionally fixed, embedded, stained with HeEo and immunostained with Calretinin, Inhibin, CK7, CK20, Vimentin, CD99 and Synaptophysin.
Results: Gross examination of the pathologic specimen showed an ovarian mass with a diameter of 14 cm, with smooth intact external surface. The cut section revealed solid tumour with cystic areas filled

with clear fluid. The histopathologic examination showed cysts lined by cuboidal cells and mucinous and goblet cells of intestinal type. The solid part of the tumour consisted of Sertoli cells forming retiform and tubular structures and clusters od Leydig cells. The Sertoli cells were positive for CK7, Inhibin and Vimentin, focally for Calretinin and CD99, and negative for CK20 and Synaptophysin. The tumour was FIGO stage IA.
Conclusion: Since the overall prognosis of SLCTs is good, recognizing this specific entity and it varieties is essential for further proper management of the patients.

PS-09-034
Adenocarcinoma of the fallopian tube. Report of five unsuspected cases found in gynecological specimens with other malignancies
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Objective: To describe five cases of unsuspected primary fallopian tube carcinomas discovered during the examination of hysterectomy with oophorectomy specimens due to gynecological malignancies and review the literature.
Method: Patient's age ranged from 34 to 70 years. Four cases were preoperatively diagnosed as ovarian carcinomas and the fifth as an advanced-stage adenocarcinoma of the endometrium. Two cases received neoadjuvant chemotherapy. One patient had BRAC1-2 mutation, not tested in the remaining cases.
Results: All cases were high-grade serous adenocarcinomas, bilateral in one. Stage ranged from pTis to pT3cpN1pM1. The immunohistochemical profile was WT1+, p16+, ER+, RP+, PAX8+. p53 was positive not only in the infiltrating component but also in the contiguous tubal intraepithelial carcinoma (TIC) identified in all cases. Tubal neoplasms were synchronous with other gynaecologic malignancies in three cases: one ovarian malignant müllerian mixed tumour, one ovarian endometrioid adenocarcinoma and one advanced-stage endometrioid adenocarcinoma of the endometrium.
Conclusion: Thorough examination of the fallopian tube in hysterectomy with oophorectomy specimens because of gynaecologic malignancies can reveal non-suspected primary tubal neoplasms. The identification of tubal intraepithelial carcinoma (TIC) and PAX8, p53 positivity supports its primary origin and the theory that at least a proportion of high-grade serous ovarian adenocarcinomas are in fact tubal in origin.

PS-09-035
Adenosarcoma of the uterine cervix. Report of a case with tubal-type epithelium with high-grade dysplasia and review of the literature
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*Hospital Puerta de Hierro, Dept. of Pathology, Madrid, Spain

Objective: To describe one case of a biphasic neoplasm of the uterine cervix with unusual features and review reported variants of these tumours.
Method: A 47 year-old female consulted because of vaginal bleeding. Physical examination showed a polypoid mass protruding from the external os resected with a presumptive diagnosis of "endocervical polyp vs myoma". After the pathological diagnosis she underwent hysterectomy with oophorectomy.
Results: Histology revealed a biphasic neoplasm composed of medium-to-large glands lined by ciliated, tubal-type epithelia with high-grade dysplasia set in a sarcomatous, mitotically active background that consisted of spindle cells with low-to-moderately pleomorphic nuclei. Stromal cells were concentrated around glands displaying a "phyllodes-like" pattern. Stromal cells were vimentin+ and actin, desmin, CD10 and cytokeratins negative. Dysplastic epithelia was CK7+ and negative for CEA and p16. p53 immunoreactivity was found in both components. No residual tumour was found in the subsequent surgical specimen.
Conclusion: Since the epithelial component of an adenosarcoma is, by definition, benign, cases with high-grade epithelial dysplasia are difficult to classify. Whether the presence of high-grade epithelial dysplasia affects or not their prognosis is still to determine. Once excluded extension of a primary uterine neoplasm, the differential diagnosis includes adenofibroma, atypical polypoid adenomyoma and mesonephric adenocarcinoma with malignant spindle-cell component.

PS-09-036
Vulvar angiomyofibroblastoma: A case report of rare solid tumour clinically mimicking Bartholin cyst
P. Lewitowicz*, A. Wincewicz, A. Horecka-Lewitowicz, O. Adamczyk-Gruszka, S. Sulkowski
*Jan Kochanowski University, Dept. of Pathology, Kielce, Poland

Objective: Vulvar angiomyofibroblastoma is rare solid neoplasm of benign course. This vulvar entity of 49-year old woman is reported here.
Method: The surgically removed tumour underwent formalin fixation and was sampled for H&E and immunohistochemical evaluation.
Results: The tumour grew at left vulvar labia and clinically mimicked Bartholin cyst. On cut surface the 3,5 cm-in-diameter tumour was whitish, flesh, solid with myxoid outlook. Hypocellular and hypercellular fields were mixed in the neoplasm. Microscopically the tumour was composed of proliferation of small thin walled vessels with adhering cuffs and islands of epithelioid, spindle and occasionally vacuolizated plasmacytoid cells. Tumour cells sprouted from perivascular regions and accumulated in nearby of vascular branches in pattern of pericyte-like proliferation. Some aggregations of cells with vascular compression resembled a bit haemangiopericytoma pattern. Myxoid intercellular matrix constituted pas -alcjan blue-positive, hypocellular areas. The tumour co-expressed vimentin and desmin with no immunoreactivity for CKAE1/AE3 and SMA. Such an immunofentype is thought to share myofibrolastic origin despite SMA negativity.
Conclusion: Thus, it could be speculated that our case of angiomyofibroblastoma is an example of tumour that probably derives from perivascular stem cells with further acquisition of some myoid features.

PS-09-037
Ovarian anastomosing hemangioma: A case report and review of the literature
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*5th Multiprofile Hospital, Dept. of Clinical Pathology, Sofia, Bulgaria

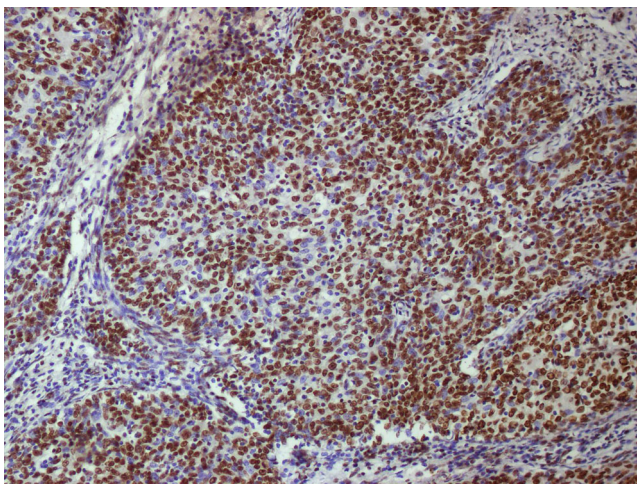
Objective: In 2009, Montgomery and Epstein described a novel variant of capillary hemangioma with an unusual sinusoidal pattern reminiscent of splenic parenchyma and coined the term "anastomosing hemangioma". The lesion was considered unique for genitourinary system with predilection to kidney. In the literature we found only four cases of this entity in ovaries.
Method: A 70-year-old woman presented with cystic formation of the right ovary, intraoperatively diagnosed as serous cystadenoma. The section of the ovary revealed a fortuitous finding in the cortex: circumscribed lesion, 7 mm in diameter, with mahogany brown, spongy appearance.
Results: Microscopic examination of H&E-stained slides manifested well-demarcated but un-encapsulated vascular proliferation, composed of tightly packed capillary-sized blood vessels with an anastomosing sinusoidal-like architecture. Endothelial lining featured only mild cytologic atypia and lack of mitotic figures. Tortuous large caliber feeding and draining vessels were present and the lesion was surrounded by luteinized

ovarian stroma. Immunohistochemical examination with CD34 and CD31 highlighted endothelial cells.
Conclusion: The analysis of all five cases with ovarian anastomosing hemangioma pointed the following clinico-morphological features: accidental finding in menopausal age, small sized lesion often in combination with stromal luteinization and serous cystadenomas but the significance of this combination is still uncertain.

PS-09-038
Differences of the ARID-1 ALPHA expressions in squamous and adenosquamous carcinomas of uterine cervix
D. Solakoglu Kahraman*, G. Diniz, S. Sayhan, M. Uncel, D. Ayaz, T. Karadeniz, T. Akman, U. Solmaz, A. Ozdemir
*Tepecik Training and Research Center, Dept. of Pathology, Izmir, Turkey

Objective: AT-rich interactive domain 1A (ARID1A) is a tumour suppressor gene involved in chromatin remodeling. This retrospective study was designed to evaluate the differences of tissue expressions of ARID1A in a spectrum of cervical neoplasms.
Method: One hundred patients recently diagnosed as cervical intraepithelial neoplasms or invasive squamous cell carcinoma with or without adenomatous component at the Tepecik Training and Research Hospital were identified using pathology databases.
Results: In this series, there were 29 low and 29 high grade cervical intraepithelial neoplasms, 27 squamous cell carcinomas and 15 adenosquamous carcinomas. Statistically it was determined that the expression of ARID1A was significantly down-regulated in adenosquamous carcinomas when compared with in non-invasive or invasive squamous cell carcinomas ($p = 0.015$).
Conclusion: Our findings were demonstrated to link of ARID1A expression and the adenomatous differentiation of uterine squamous cell carcinomas. Therefore it may be suggested that ARID1A gene may act as a role of pathogenesis of cervical adenosquamous carcinomas.

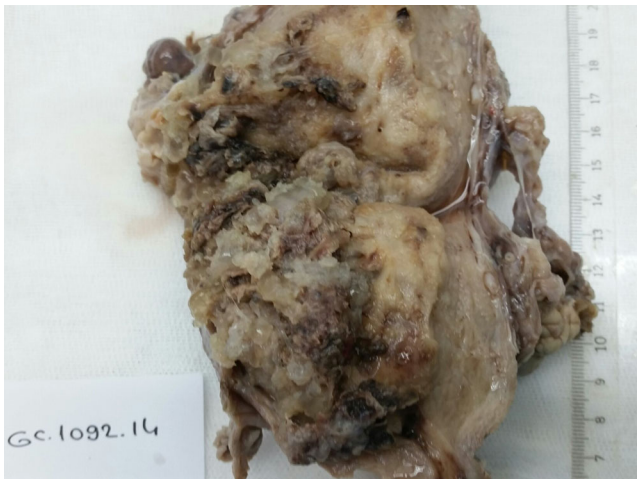
High ARID1A expression in a SCC sample (DAB X100):



PS-09-039
Invasive mole of the uterus: Report of two rare cases and review of the literature
D. Solakoglu Kahraman*, S. Sayhan, T. Karadeniz, D. Ayaz, Y. Koca, M. Sanci
*Tepecik Training and Research Center, Dept. of Pathology, Izmir, Turkey

Objective: Gestational trophoblastic neoplasias (GTN) are rare tumours that constitute less than 1 % of all gynecological malignancies. Invasive mole is a distinct subgroup of GTN, which if not diagnosed and treated early, can result in serious complications like uterine perforation and haemoperitoneum.
Method: We present two rare cases of an invasive mole of the uterus, which developed following the evacuation of a molar pregnancy. They were 43-year-old and 49 -year-old patient with vaginal bleeding after endometrial curettage and have a continuous high level of human chorionic gonadotropin (hCG).
Results: We performed hysterectomy to the two patients who completed the parity. They were given a diagnoses of invasive mole of the uterus and successfully treated before any major complications could arise.
Conclusion: After molar pregnancy curratege, 15–20 % patients can develop postmolar gestational trophoblastic diseases. The vaginal bleeding that continues after molar pregnancy curettage, high or not decrease value of hCG and the persistant theca lutein cysts are the most frequency findings. The patients must be researched for metastasis. Usually, chemotherapy should be given after curettage and sometimes hysterectomy can be done.

Gross: Invasive mole:



PS-09-040
Rare subtype of gestational trophoblastic disease: Placental site trophoblastic tumour
H. S. Toru*, G. Erdogan, M. Sakinci, H. E. Pestereli, F. S. Karaveli
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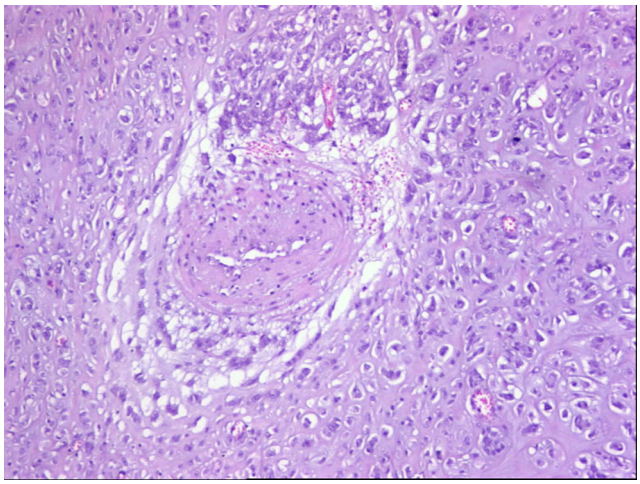
Objective: Placental site trophoblastic tumour (PSTT) is a rare gestational trophoblastic disease (GTD). The most important difference between PSTT and other GTD is slow growth and chemotherapy resistance of PSTT.
Method: The aim of this report is to present a unique entity of GTD and challenges in differential diagnosis.
Results: A 27 year-old woman revealed to clinic with menometrorrhagia. In sonographic and magnetic resonance imaging intramural mass resembling myoma uteri and right adnexial multiloculated cyst was obtained. In clinical history patient had a pregnancy 5 years before and baby was alive and healthy. Surgical excision was performed for intramural mass and adnexial cyst. In histopatholgoical evaluation mononuclear and multinuclear trophoblasts were infiltrating myometrium and uterine vessels. This finding was representing a trophoblastic neoplasia and beta-HCG serum levels was negative. With clinical and histopathological findings PSTT was diagnosed. After the histerectomy and bilateral salphingoopherectomy diagnose was confirmed and chemotherapy was given.

Conclusion: PSTTs are exceptional subtype of GTD tumours, encountering difficult clinical and histological diagnosis. Consequently, novel therapeutic strategies are still needed with better efficacy and less toxicity, in particular for those with drug-resistant disease. Centralized care of GTD should be made worldwide as this will likely save more young lives.

Figure 1:



PS-09-041

A clinicopathologic study of early stage Placental Mesenchymal Dysplasia (PMD)

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Objective: To elucidate the clinical presentation, complications, microscopic features, and differential diagnoses of early stage (gestational age less than 20 weeks) PMD.
Method: 10 cases of PMD were clinicopathologically analyzed. Immunohistochemical study of p57 (Kip2) (p57), which is products of a paternally imprinted, maternally expressed gene, was also done.
Results: Maternal ages ranged from 23 to 40 years. Gestational periods ranged from 12 to 19 weeks. Five patients were initially diagnosed as partial mole (PM) and one was as complete mole (CM) with twin on ultrasound examination. One case was associated with BWS. 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. Cytotrophoblasts were positive for p57 in all cases, and 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 is useful for differential diagnoses in equivocal cases. It is important to identify PMD cases prenatally to reduce fetal morbidity and mortality.

PS-09-042

Mesonephric adenocarcinoma of the Uterine Cervix with HNF 1-Beta, Amacr positive, ER/PR negative and wild type p53 expression

G. Kir*
*Umraniye Egt. Aras. Hastanesi, Dept. of Pathology, Istanbul, Turkey

Objective: Mesonephric adenocarcinoma (MA) is a are tumour of the female genital tract, mainly in the cervix and vagina. Here we report a case of cervical MA having morphological and immunohistochemical features of clear cell carcinoma in a 48-year-old woman.
Method: In curettage specimen, there were large areas with pseudoendometrioid pattern and focal area with clear and hobnail cells. All areas were HNF 1-β, Amacr positive, Napsin A, ER/PR negative and p53 was wild type.
Results: The curettage diagnosis was adenocarcinoma with features of clear cell carcinoma. In resection specimen there was mesonephric adenocarcinoma in the cervical wall with mesonephric hyperplasia at the periphery of the tumour.
Conclusion: The presented case of cervical mesonephric adenocarcinoma revealed HNF 1-β, Amacr positive, ER/PR negative and wild type p53 immunostaining results, this may result diagnostic confusion particularly on a small biopsy specimen.

PS-09-043

Morphofunctional aspects of blood at preeclampsia

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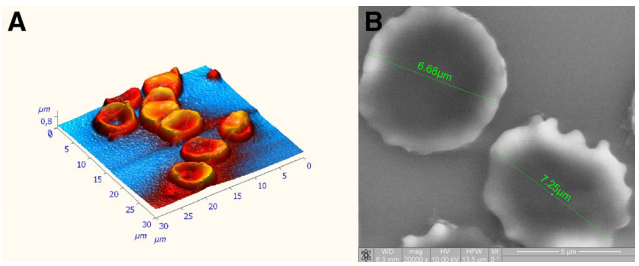
*Belgorod State University, Dept. of Pathology, Russia

Objective: Preeclampsia renders significant influence on condition of mother, fetus and newborn, being the most dangerous and frequently occurring complication of pregnancy.
Method: The condition of erythrocytes of 85 pregnant women was researched with help of raster electron microscopy with elemental analysis and atomic power microscopy.
Results: The content of discocytes decreased till 56 ± 1,6 % (85 ± 1,6 % in control group). Pathological forms of cells have appeared. The content of normocytes were in limits of 68 % from general number of discocytes. 20 % of them were microcytes and 12 % were macrocytes. The depth of cavity of discocyte was 0,38 ± 0,05 (0,24 ± 0,04), the ratio of erythrocyte's diameter to size of cavity was 38,6 units(25,5). Their diameter was 7,43 ± 0,5 (6,75 ± 0,3 μm) in average. Cells of extended form were revealed, what may testify about breach of elasticity of membranes as well as about difficulties of passage through microcirculatory vessels due to alteration of its structure. The content of cytoplasmic bridges between cells was increased, what led to stasis, sludging and thrombosis. The concentration of oxygen in erythrocytes decreased on 18 %.
Conclusion: Revealed alteration pose a threat to condition of mother and fetus due to development of hypoxia and ischemia of tissues.

Fig 1:



PS-09-044

New morphofunctional methods of research of blood stream at diffuse toxic goiter on background of pregnancy

T. Pavlova*, E. Malutina, V. Petrukhin, D. Kolesnikov, I. Goncharov, I. Bashuk, V. Markovskaya
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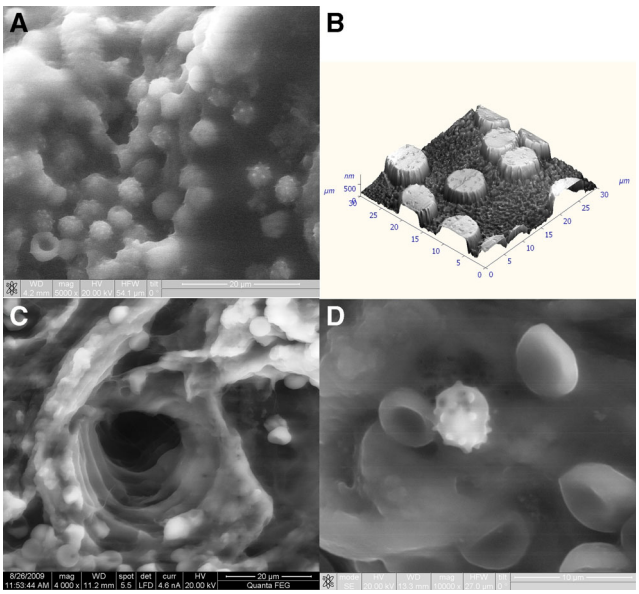
Objective: Dysregulation of metabolic processes at pathology of thyroid gland in mother can lead to violation of vital functions in mother's organism as well as in fetus.
Method: Examined 54 women with diffuse toxic goiter as well as blood vessels and erythrocytes of skin, uterus, umbilical cord and placenta were researched by light microscopy, atomic power microscopy, transmissional and raster microscopy with elemental analysis.
Results: The blood vessels of chorion are full-blooded. The surface of endothelial cells is smoothed with decreasing of number of folds. Local sites of necrosis are observed. The content of magnesium, phosphorus as well as oxygen in erythrocytes decreased till 23,01 ± 2,65 % (45,12 ± 2, 31 % - control group).The number of sodium, potassium and calcium is increased. Blood vessels of skin are full-blooded. Blood vessels of myometrium are full-blooded and thrombosed. The content of macroelements is decreased. Form of vessels of myometrium is violated. Fragmental sites of necrosis are detected. The content of studied macronutrients in erythrocytes decreased. Pathological forms of cells appears.
Conclusion: The destruction of endothelium, violation of blood circulation as well as alteration in content of some microelements at diffuse toxic goiter in skin, uterus, placenta render unfavorable influence on condition of mother and fetus.

Fig 1:



PS-09-045
Use of methods of scanning microscopy at pathology of placenta
T. Pavlova*, E. Malutina, V. Petrukhin, A. Nesterov, I. Bashuk, D. Kolesnikov, I. Goncharov
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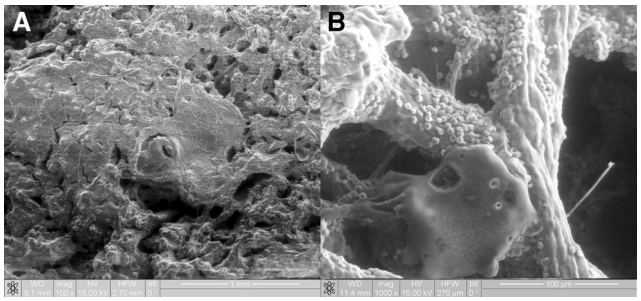
Objective: Stability of biochemical and morphological constants is one of important and mandatory conditions of normal functioning of organism. The risk of breach of hemostasis is possible at presence of pregnancy, especially on background of endocrine pathology.
Method: The 60 placentas of women with pathology of thyroid gland with hypofunction, hyperfunction and euthyroid state were researched by light, atomic power, transmissional and raster electron microscopy.
Results: At research of macro- and microelements in blood vessels of chorion it was showed that the content of oxygen is decreased rapidly at diffuse toxic goiter (23,01 ± 2,65 %), composing in control group 45, 12 ± 2,31 % on background of growing destruction of structures. The quantity of sodium, potassium and calcium was increased. The content of oxygen in intervillous space is decreased significantly as in hyperthyroidism (22,43 ± 1,34 %), and hypothyroid condition (37,91 ± 2,10 %) at comparison with control group. The quantity of potassium and sodium was increased. Blood clots and fibrionoid were revealed.
Conclusion: The use of scanning microscopy extends the opportunities of research of content of macro- and microelements at various types of pathology, being an express-method. Received data testifies about rapid decreasing of oxygen and other elements, what can effect negatively on condition of mother and newborn.

Fig 1:



PS-09-046
Primitive neuroectodermal tumour of the ovary
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Objective: The primitive neuroectodermal tumours of the ovary are rare tumours, which belong to the monodermal teratoma group. These tumours manifest in three forms: differentiated (ependymoma), primitive (neuroblastom, PNET, ependymoblastoma), anaplastic (glioblastome multiforme). The PNET often exhibits aggressive clinical behavior. There have been a small number of case reports of PNET arising in the ovary. They are most frequently large, localized unilaterally, solid but maybe partially cystic. We present a case of pelvic PNET arising in the right adnex.
Method: Fifty eight-year-old woman presented with a large mass in the abdomen. The gross pathological examination showed 12 × 9 × 3 cm tumour which had nodular appearance in the right adnex and revealed grayish-pink fleshy cut surface, accompanied by foci of hemorrhage and necrosis. Hematoxyline-eosin sections showed diffuse small, round blue cell tumour with focal rosette formations. The tumour cells showed immunopositivity with vimentin and neuron spesific markers, GFAP but no CD 99 immunoreactivity. By FISH analysis, LSI EWSR1 translocation was found.
Results: With immunohistochemical and molecular results we diagnosed the case as a monodermal teratoma, PNET.
Conclusion: Pelvic PNETS should be included in the differential diagnosis of pelvic masses.

PS-09-047
Primary Malignant Melanoma (MM) of the vagina: A case report
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*Hospital Center Studenica, Kraljevo, Serbia

Objective: We present 49 years old patient with primary malignant melanoma of vagina, infrequent neoplasm which constitutes about 5 % of all malignant vaginal tumours and less than 1 % of all melanoma cases.
Method: Patient came to ginaecology department with abnormal vaginal bleeding where two separate tumour masses of upper third of vagina were

observed. During gynecological examination they appeared as lobulated, fragile, dark brown mucosal prominences.
Results: After surgical excisional removal, histology revealed primary malignant melanoma. Immunohistochemistry has been done to complete diagnosis. Tumour cells showed positivity for Melan-A and HMB-45. There was no evident vascular invasion evaluated with CD31. The proliferative marker Ki67 was positive in about 35 % of the melanoma cells.
Conclusion: Our case is important because the primary malignant melanoma of vagina is a very rare neoplasm with no accepted system of histopathological prognostic parameters.

PS-09-048
Low grade Endometrial Stromal Sarcoma (ESS) arising within uterine leiomyoma: A case report
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Objective: ESS is a rare neoplasm usually arising in the endometrium composed of uniform, oval to fusiform cells with scant cytoplasm that resemble proliferative endometrial stroma.
Method: A 61-year old woman underwent routine abdominal hysterectomy with bilateral salpingo-oophorectomy due to abdominal mass and vaginal bleeding. Macroscopic and histological examining revealed an enlarged uterus with numerous fibroids except one that contained "nodes within node". There were also enlarged ovaries, endometrial polyp of usual type, and hyperplastic endometrium. "Nodes within node" consists of solid cords and clusters of hypercellular tissue that is reminiscent of proliferating endometrial stroma and sex-cord-stromal-like areas. Foci are surrounded by bundles of smooth muscle cells which do not differ from those in other fibroids of the same uterus. There was lympho-vascular invasion.
Results: Foci showed immunohistochemical positivity for vimentin, S-100, CD99, calretinin, α inhibin, CK7, CKMNF116, EMA, CD10, WT1, MelanA, CD117 and Cyclin D1 while negative for SMA and desmin.
Conclusion: It seems that in the occurrence of tumours such as this, stem cells have a crucial role as thay have the potential of differentiation in various directions when they are appropriately stimulated. Bilateral stromal hyperplasia of the ovaries with persistent ovarian hormone secretion should be considered as a possible factor of influence on the stem cells differentiation.

PS-09-049
Extragonadal dermoid cyst of the great omentum: An incidental finding
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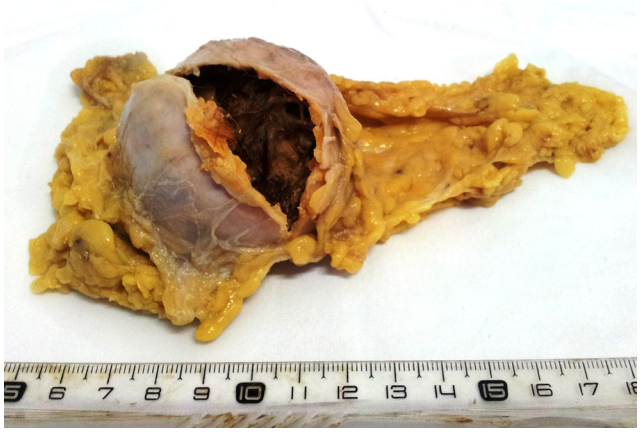
*Sintandrei, Romania

Objective: Dermoid cysts (mature cystic teratomas) usually develop in the ovary. However, extragonadal dermoid cysts are extremely rare with less than 35 cases reported so far, most of them developed in the omentum, usually coexisting with same lesion in the ovary. The etiology of these this tumour is not well known'.
Method: A 46-year-old woman was admitted to hospital for abdominal pain and abnormal uterine bleeding for 2 months. Physical examination revealed a palpable umbilical mass. Ultrasound and CT scans showed a 6 cm submucosal leiomyoma and a calcified cystic mass, located posterior to the anterior abdominal wall. Preoperative tumour marker tests revealed no elevation of cancer antigens.
Results: At laparotomy, a 5.5 × 4 cm cystic, well-defined mass attached to the great omentum was observed and was completely excised. Pathologic examination revealed hair and sebaceous material on cut surface, microscopically corresponding to a mixed of different types mature tissues, with a rim of an atrophic ovarian stroma at the periphery.
Conclusion: While the left ovary was present at anatomical site and normal, the patient's right ovary was absent at normal site during laparotomy and possible auto-amputation of the ovarian tissue with consequently development of the tumour might be suggested in this case.

Extragonadal dermoid cyst of the great omentum:



PS-09-050
Efficiency of intreaepithelial neoplasia diagnosis using liquid-based cytology, P16/Ki67 dual immunostaining and HPV testing for women younger and older 30 years
L. Jiajing*, E. Kogan
*First Moscow State Med. University, Dept. of Pathological Anatomy, Russia

Objective: The aim of our study is to evaluate the effectiveness of liquid basic cytology, HPV-test and P16/Ki67 dual stain immunocytochemistry in screening and diagnosis of cervical precancer pathology for women younger and older 30 years.
Method: Matelial from 30 women younger 30 years and 124 women older 30 years were examined using histology, liquid basic Cytology, immunocytochemistry and HPV-test (RT-PCR). Histological diagnosis has been seed like a "golden standard".
Results: For women younger than 30 years, the efficiency of the the HPV-test was bed (81.8 % sensitivity and 30.4 % specificity). For women older than 30 years, the highest efficiency of the cytological technique was revealed in case of ≥ CIN2 (71.4 % sensitivity and 97.2 % specificity); that of immunocytochemistry (ICC) in ≥ CIN2 (100 % sensitivity and 92.3 % specificity).
Conclusion: The effective use of all the three techniques to detect cervical pathology (cytology, HPV-testing, and ICC) enables one to solve the problem of not only the diagnosis of cervical precancer and cancer, but also their screening for women older than 30 years.

PS-09-051
Small cell neuroendocrine carcinoma of the endometrium: A case report
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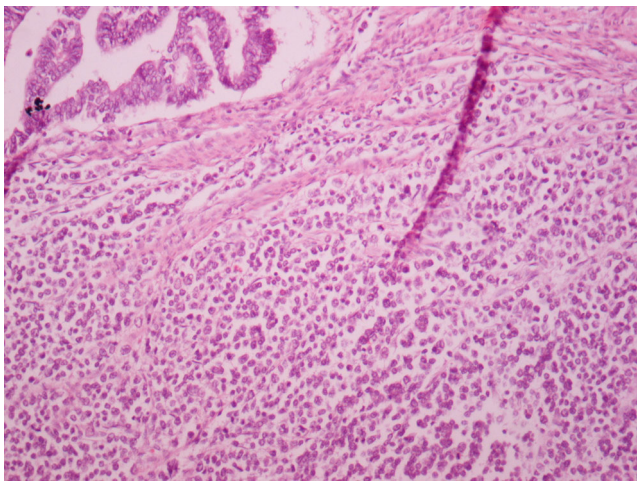
*General Hospital Tzaneio, Dept. of Pathology, Athens, Greece

Objective: Small-cell neuroendocrine carcinoma of the endometrium (SCCE) is an aggressive very uncommon tumour of definite endometrial origin resembling SCC of the lung and other organs, comprising <1 % of

all endometrial malignancies and usually admixed with more conventional types of endometrial cancer
Method: A 55 years old postmenopausal woman underwent a total hysterectomy and salpingoophorectomy because of a diagnosis from a curettage material of a grade 2 endometrioid carcinoma associated with a very small component of an undifferentiated neoplasm. Macroscopic examination revealed a bulcky polypoid intraluminal and full-thickness myometrial infiltration mass.
Results: Histopathologic examination showed a malignant tumour composed of two distinct components: A superficial grade 2 endometrioid carcinoma and a more invasive (transmural) and aggressive component composed of small to intermediated sized hyperchromatic cells forming solid sheets, extensive necrosis, high mitotic rate and angiovascular invasion. Strong and consistent expression of three neuroendocrine immunohistochemical markers (synaprophysin, CD56, NSE) confirmed diagnosis of a small cell carcinoma.
Conclusion: SCCE is extremely rare with limited reported cases to date. Although it's characteristic morphology may be misdiagnosed as undifferentiated carcinoma, sarcoma, melanoma etc in the absence of immunohistochemical analysis. A correct diagnosis is leaded by using of morphological examination, immunohistochemistry, detailed clinical information and radiology findings.

Small cell neuroendocrine carcinoma:



PS-09-052
Different morphological types of uterine leiomyoma
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*Institute of Pathology Skopje, Republic of Macedonia

Objective: Benign uterine leiomyomas are the most common pelvic tumour in women. Uterine smooth muscle tumours are classified according to their morphologic features that include architecture, growth pattern, cellular characteristics, number of mitoses and constituents of the intercellular stroma. The aim of this paper is to present different types of uterine leiomyoma diagnosed in our institution.
Method: In this retrospective study, 1510 gynecological specimens collected over a period of 1 year were studied. A detailed macroscopic and microscopic examination of all tumours of myometrium were made after fixation and staining of samples with routine HE and immunohistochemical techniques.
Results: Benign neoplastic lesions of the myometrium were diagnosed in 556 (36.8 %) of the total 1510 specimens. All benign tumours were leiomyomas, except 12 cases that were adenomyomas. Leiomyoma was the most common tumour of the myometrium accounting for 97.8 %. Usual leiomyoma constituted for 94.42 % and variants of leiomyomas were 5.58 %. We have established the presence of the following variants leiomyomas: appoplectic, cellular, epitheliod, hydropic, lipoleiomyoma, mitoticall active, myxoid, neurilemmoma-like, symplastic, leiomyoma with erythropoiesis.
Conclusion: Variants of leiomyomas and their partial presence were relatively rare, but it is important to differentiate them from malignant tumours of the myometrium.

PS-09-054
Primary ovarian trabecular carcinoid with stromal luteinization: A case report
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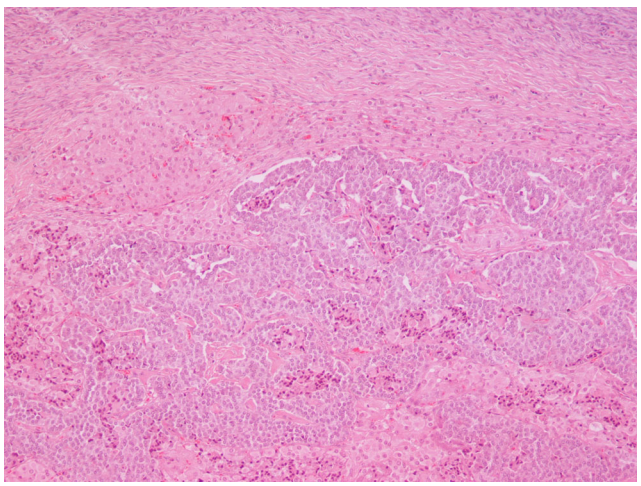
*General Hospital Tzaneio, Dept. of Pathology, Athens, Greece

Objective: Primary ovarian carcinoid tumours (POCTs) comprising less than 0,1 % of all ovarian neoplasms. They are subdivided in to four types: insular, trabecular, strumal and mucinous but mixed types also occur. Primary trabecular carcinoid usually arises in association with teratomatous elements. Pure forms are very rare.
Method: We report a case of 2,3 cm sized, solid, firm, oval with a smooth outline, yellow right ovary tumour in a 70 years old woman. The patient had vaginal bleeding and a mature cystic teratoma / epidermoid cyst of controlateral ovary. No history of hormonal disorders.
Results: Microscopically the tumour composed of trabeculae and ribbons surrounded by large eosinophilic cells resembling luteinized or Leyding stromal cells. The trabeculae's and ribbon's cells had ovoid or elongated nuclei. No mitotic activity nor necrosis were found. Immunohistichemical analysis showed strong positivity of trabeculae's cells for neuroendocrine markers as well as cytokeratins (Cam5-2) and positivity of eosinophilic stromal cells for vimentin, a-inhibin, calretinin. MIB:<1 %. A diagnosis of primary ovarian trabecular carcinoid with luteinized stromal cells was done.
Conclusion: Because of the rarity and heterogenity of POCTs (which occasionally may resemble a sex cord stromal tumour), combination of morphologic criteria, immunohistochemical findings and the clinical history can put a definitive diagnosis.

Trabecular carcinoid with stromal luteinization:



PS-09-055
Malignant Brenner Tumour
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*General Hospital Subotica, Dept. of Pathology, Serbia

Objective: A description of a rare malignant ovarian tumour in a 20-years old patient.
Method: To a 20-years old patient performed right ovariectomy with a large tumour alteration of diameter 16 cm of white-yellow color, of homogeneous appearance. Several tissue fragments have been biopsed from the Douglas cavum, omentum and peritoneum.
Results: Histologically tumour tissue is built of atypical cells that look like transitional epithelium, oesinophilic cytoplasm, hyperchromatic oval nuclei with clear nucleolus and longitudinal nuclear grooves like those in granulosa cell tumour. Malignant cells build islands, stripes, adenoid and pseudoglandular formations surrounded by a massive stroma of fibroblastic appearance. Smaller centers of necrosis and areas corresponding a benign Brenner tumour. Tumour ovarian tissue with implants from Douglas cavum, omentum, and perioneum shows imunophenotype: CK7+, CK20-, inhibin-, calretinin-, CD99-, WT1 citoplasmatic +. Based on the morphological characteristics and imunophenotype the following diagnosis has been set: Malignant Brenner with stromal invasion and peritoneal implants pTb(FIGO IIIB).
Conclusion: Malignant Brenner is a rare ovarian surface epithelial neoplasms, composed of transitional (urothelial)-type epithelial cells. Makes 1–2 % of all ovarian tumours. It usually appears in the sixth decade of life, unulateral (90–95 %), and it's extremely rare in young women. Histological appearance can be like carcinoma of transitional epithelium or planocellular, granulosa cell tumour and non-differentiated carcinoma. It's necessary to implement immunohistochemical methods. Therapy is syrgical and adjuvant chemotherapy.

PS-09-056
Evaluation of the results of the first circle of organized cervical screening in R. Macedonia
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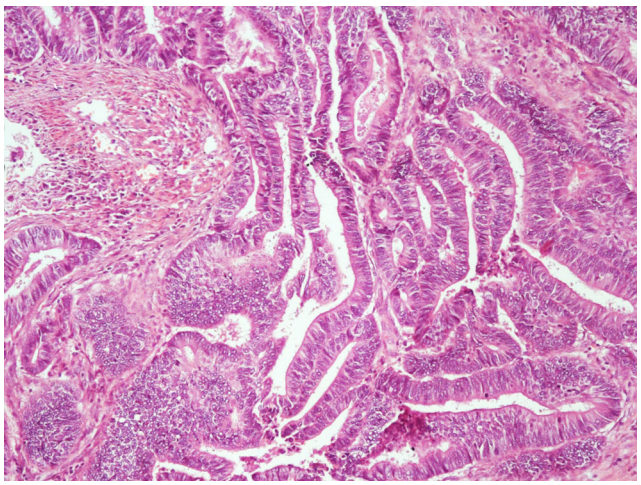
Objective: To determine the distribution of cervical squamous intraepithelial lesions (SIL) and invasive cervical carcinoma depending on the age of the women included in a 3-year cervical cancer screening.
Method: This retrospective study includes the results of the first cycle of the organized screening program, where 112.842 pap smears were screened. This was realized in a 3-year period (2012–2014). Reporting was done using the 2001 Bethesda system.
Results: Epithelial cell abnormalities were detected in 7.390 (6.55 %) of the total number of analyzed tests. Low grade squamous intraepithelial lesions (LSIL) were found in 69.37 %, high grade squamous intraepithelial lesions (HSIL) were in 10.93 % of the patients, and cervical cancer was suspected in 0.18 % of the cases. The youngest age group (24–35 years) has highest percentage of SIL (9.76 %), but 79.82 % of them were LSIL, and only 8.15 % were HSIL. The middle age group (36–48 years), has abnormal Pap tests in 5.06 %. HSIL is more often detected in this age group (17.18 %). The oldest age group (49–60 years) has the least detected abnormalities (1.90 %), but the highest rate of invasive cervical cancer (2.53 %).
Conclusion: In the older target groups, abnormal tests are less often detected, but if present, they more often belong to the category of HSIL, or even invasive cervical cancer. Detailed and careful analysis of the pap smears is essential to prevent false negative results, especially in older patients where serious epithelial lesions can mimic benign atrophic changes.

PS-09-057
Correlation between hormonal expression and proliferative index with stage and histologic grade in type 1 endometrial carcinoma in Mexican Mestizos
B. Saenz Ibarra*, G. S. Gómez Macías, O. Barboza Quintana, R. Garza Guajardo, J. Ancer Rodriguez
*Hospital Universitario Monterrey, Dept. of Anatomy Pathology, Mexico

Objective: To correlate cell proliferation index and hormonal expression with pathological stage in type 1 endometrial carcinoma.
Method: We designed an observational, descriptive, cross-sectional study. The sample included 107 patients with primary type 1 endometrial cancer. In each tissue sample, immunohistochemical markers of Ki-67, estrogen receptors and progesterone receptors were performed. Endometrial carcinoma was staged according to the FIGO. Clinical information was retrieved from the medical records.
Results: A total of 107 patients with primary type 1 endometrial carcinoma were included in the analysis. The mean age of presentation was 56 years. In respect to grade of differentiation, 2.8 % were classified as well differentiated, 76.6 % as moderately differentiated, and 20 % as poorly differentiated. The proliferative index by Ki-67 was positively correlated to the clinical stage and histological grade. Estrogen receptor and progesterone receptor positivity had a negative correlation to the clinical stage and histologic grade.
Conclusion: Estrogen and progesterone receptor positivity correlated negatively to higher histologic grade and clinical stage by FIGO, while proliferation index had a positive correlation.

Endometrial Cancer with moderate differentiation:



PS-09-058
Ovarian sclerosing stromal tumour: Case report and review of the literature
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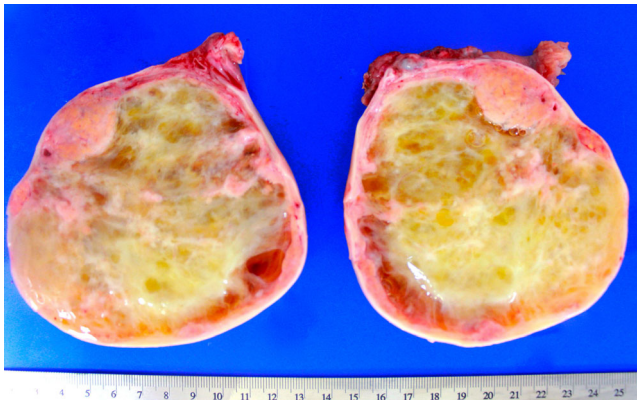
*Hospital Universitario Monterrey, Dept. of Anatomy Pathology, Mexico

Objective: To present a case of an ovarian sclerosing stromal tumour and a literature review of the topic.
Method: We identified a case from our University Hospital "Dr. José Eleuterio González" in northeast Mexico.
Results: A 19-year old patient, without any relevant history, presented to the gynecology clinic because of abdominal pain. The pain had started 5 days earlier and was colic. A pelvic ultrasound revealed a left adnexal mass. The result of tumour marker CA-125 was reported 98.3 U/mL (normal range: <35 U /mL). The lesion was surgically excised. The macroscopic evaluation showed a 10 × 10 cm tumour with an intact capsule. At section, the tumour was solid with some areas showing cystic degeneration, white and yellow alternating regions with fibrosis. Microscopic examination revealed a lobular growth pattern with alternating areas of hypocellularity and hypercellularity composed of spindle-shaped cells producing collagen and round to oval cells with lipid-rich cytoplasm; additionally interlobular fibrosis was observed. Inhibin staining was positive.

Conclusion: Ovarian sclerosing stromal tumour is rare tumour derived from the sex cord stroma that usually affects women in their second and third decade of life. A high level of suspicion is warranted to identify the tumour distinctive histological characteristics.

Ovarian sclerosing stromal tumour:



PS-09-059

CD34 expression in stromal cells of HPV induced cervical lesion: Possible role in tumour invasiveness

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*University Clinical Center Tuzla, Dept. of Pathology, Bosnia and Herzegovina

Objective: To determine whether loss of subepithelial CD34+ fibrocytes is associated with invasive squamous cell carcinoma of the cervix and could be considered as a finding of early stromal invasion.
Method: A retrospective-prospective study wich comprised 140 tissue samples from 100 female patients who had histopathological verified cervical lesions and known HPV status. A immunohistotochemical staining for CD34 (DAKO, monoclonal mouse anti-human CD34 klasa II, Clone QBEnd-10) was performed on all tissue samples in order to establish the distribution and intensity of expresion in stromal fibrocytes.
Results: Median value of CD34 expression in precancerous cervical lesions was significantly higher than in a cancerous lesions in both groups (HRHPV + and HRHPV-) ($p < 0{,}001$). CD34 expression is signicicantly differ in preinvasive and invasive cervical lesion, and has very high sensitivity (over 95 %) and specificity (over 42 %).
Conclusion: Loss of CD34+ fibrocytes is specific for stromal changes associated with early stromal invasion and invasive cervical carcinoma. Therefore CD34 represent sensitive marker in detection of small fields of invasion.

PS-09-060

Ovarian adenosarcoma with sex cord elements: An uncommon diagnosis

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*Centro Hospitalar do Porto, Serviço de Anatomia Patológica, Portugal

Objective: Mullerian adenosarcomas, uncommon neoplasms characterized by a mixed benign epithelial component and a malignant stromal component, are more common in the uterus, but have been described in the ovary, peritoneum and more rarely in the vagina. Occasionally, the stromal component of adenosarcomas contains sex cord-like elements.
Method: We report a case of a 86-year-old woman who presented with left abdominal pain and was found to have a large left-sided pelvic mass, probably arising from the ovary, on ultrasound and computed tomography scan. She underwent left salpingo-oophorectomy.
Results: Macroscopically there was a 19 cm multi-cystic mass with smooth walls, yellowish watery fluid content and a mamilonated area of 6,5 cm with a whitish, rubbery cut surface. Histologically, a benign tubal epithelium lined polypoid projections of low-grade malignant stroma. Underneath the epithelium and dispersed in the stroma there were nests of sex cord-like elements resembling granulosa cells. This component was imunorreactive for inhibin. There is no evidence of disease on a 2-year follow-up.
Conclusion: Sex cord-like elements can occur within the stromal component of adenosarcoma, including in areas of sarcomatous overgrowth, and may exhibit a true sex cord immunophenotype. Sex cord-like areas seem to occur within a higher proportion of ovarian than uterine adenosarcomas.

PS-09-061

On the issue of extragenital endometriosis morphology: Endometriosis of a postoperative cicatrix

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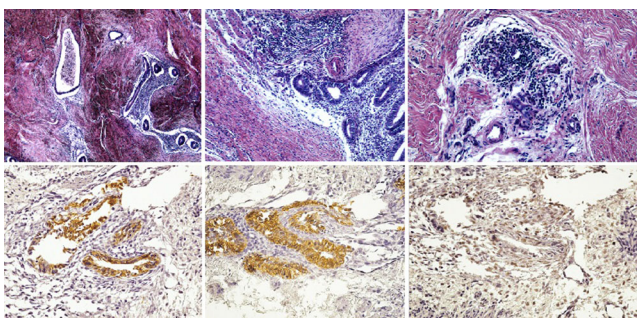
Objective: To study morphological manifestations of one of the most rare and poorly explored extragenital endometriosis localisation - endometriosis of a postoperative cicatrix (EPC).
Method: We observed three patients, aging 23–41 years old, which have got through the excision of postoperational cicatrix, that formed after gynecological operations.
Results: In all patients, during macroscopical research we found a soft tissue formation of mildly-elastic consistency from 2,0 up to 4,5 cm which was gray-pink colored on the section, with thin capsule and local hemorrhages under the capsule and also a deposition of a brown pigment sized up to 0,3–0,5 cm. Microscopicly we observed foci with highly developed glandular component with cystic transformation in some parts, focal flattering of a gland covering epithelium.
Conclusion: In immunohistochemical research, with the usage of monoclonal antireceptor antibodies to estrogen(ER), progesterone (PR), cytokeratins 7 and 18 (CK7, CK18), in endometrioid foci we found the expression of PR, cytokeratins 7 and 18 and poor expression of ER. Morphological presentation and immunophenotype match the diagnosis of focal endometriosis. Modern approach to the treatment of patients with endometriosis must consist in combining the surgical method with the morphological verification of a process.

Microscopy and immunohistochemistry of a cicatrix:



PS-09-062

Bilateral benign Brenner tumours mimicking metastases of colon adenocarcinoma

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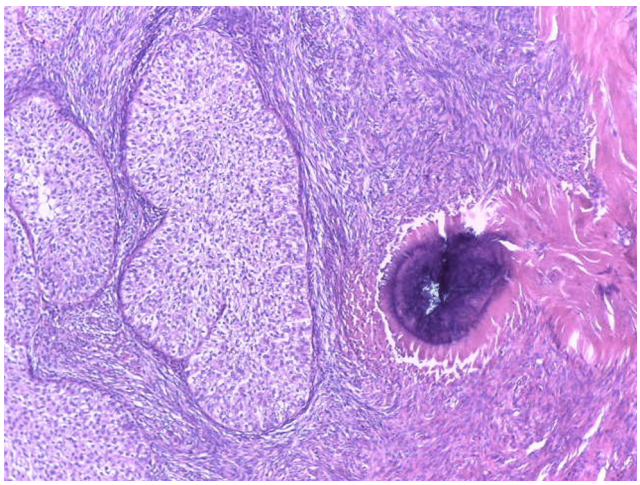
Objective: Brenner tumours are rare neoplasms, usually benign and asymptomatic that include less than 2 % of all solid ovarian tumours.

Usually, the tumours are unilateral and occur in women aged over 40, mostly as incidental findings with the incidence being higher for post menopausal patients.
Method: We report the case of a 64-year-old woman admitted to the Emergency University Hospital Bucharest, after being diagnosed with colon adenocarcinoma. During the segmentary colectomy the surgeons also found two masses in the right and left ovaries. Taking into consideration the possibility of the ovaries being malignantly transformed, a bilateral ovariectomy was performed as well.
Results: The histopathological examination validates the diagnosis of G2 colon adenocarcinoma, staged pT2N0. On the other hand, the ovarian metastases were infirmed. The microscopic examination showed an incidental finding: bilateral benign Brenner tumours of the right and left ovaries.
Conclusion: It is difficult to diagnose Brenner tumour based on imaging techniques or gross examination because the appearance of the tumour is nonspecific. As a result, Brenner tumours can easily be confused with other tumours of the female genital tract and even with metastases, especially in patients with synchronous malignant tumours. Therefore, the importance of an accurate pathological examination for differential diagnosis is emphasized.

Typical Brenner tumoural cell nests with a nearby stromal dystrophic calcification. H.E. ob.x10:



PS-09-063
Uterine Tumour Resembling Ovarian Sex Cord Tumour (UTROSCT): Case report
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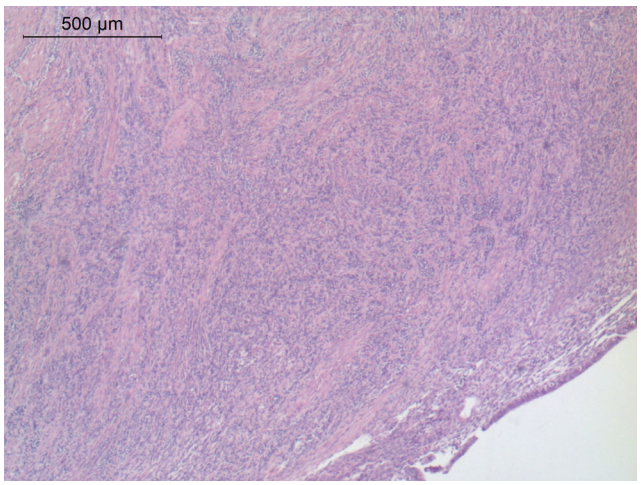
Objective: We describe a case of a uterine tumour resembling ovarian sex cord tumour (UTROSCT).
Method: 41 year old woman with hypermenorrhoe and myomatous uterus was curretaged. Finding of scarce round epithelial cellular elements of unknown significance was demonstrated within secretory endometrium. Rebiopsy was recommended. Hysterectomy was performed.
Results: Gross: we received a uterus with a subendometrial well demarcated homogenous polypoid yellow nodule, 15 mm in diameter. Microscopy: uniform small round cells with pale nuclei, scarce cytoplasm growing in insular, trabecular and solid patterns separated by a reticular stroma. Immunohistochemistry demonstrated positivity for Vimentin, SMA, CKAE1/AE3, calretinin, Estrogen, Progesteron, Androgen, CD99, and only focal positivity for inhibin-A and Melan-A. Desmin, caldesmon, CD10, CK7, EMA, CEA, Chromogranin-A, S-100, LCA were negative. A diagnosis of UTROSCT was made.
Conclusion: The origin of UTROSCT is still debatable, suggested from pluripotent uterine mesenchymal cells. These rare tumours differ from endometrial stromal tumours with sex-cord like elements (ESTSCLE) by behavior and molecular profile. Their immunoprofile aids in differentiating them from epithelioid smooth muscle tumours and endometrial stromal tumours. Although they generally have a benign course, few reported cases of metastases might suggest the augmentation of a less reserved therapeutic approach.

Uterine tumour resembling ovarian sex cord tumour (HE):



PS-09-065
Uterine adenolipoleiomyoma: A case report and review of the literature
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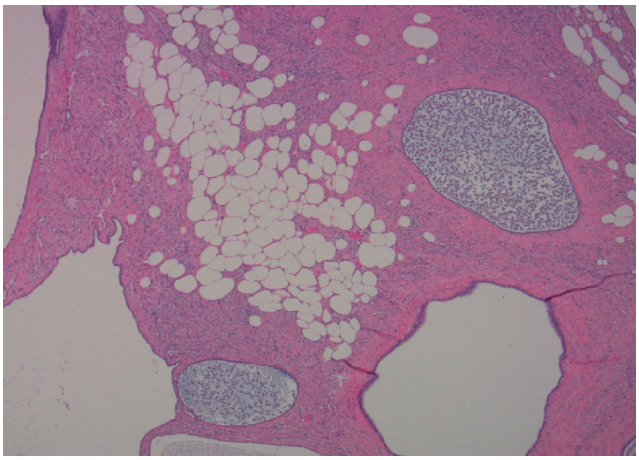
Objective: Uterine adenolipoleiomyoma, also termed adenomyolipoma or lipoadenofibroma, is a rare benign lesion, considered to be a variant of a benign mullerian mixed tumour.
Method: A postmenopausal 69-year-old woman presented with left abdominal pain. Imaging studies revealed an uterine heterogeneous cystic mass and a total hysterectomy and bilateral salpingo-oopharectomy were performed.
Results: On gross examination, an intramural nodular mass of 3, 5 × 3 × 3 cm was found in the uterine fundus along with an endometrial olyp. The cut surface of the mass was extensively cystic with solid whitish areas. Microscopically, it was composed of epithelial and mesenchymal elements with cystic glands lined by cuboid, tubal-type and focally endometrial-type epithelium, surrounded by endometrial stroma and

smooth muscle intermingled with abundant mature adipose tissue. Neither the epithelial nor mesenchymal components showed atypia, mitosis or necrosis. The glandular epithelium was immunoreactive for cytokeratins; the endometrial stromal cells were positive for CD10; smooth muscle cells were positive for smooth muscle actin and the adipocytes were positive for S100

Conclusion: This appears to be third report presenting as an intramural mass and the tenth case of this unusual lesion. It occurs most frequently in postmenopausal women. One report showed aggressive behavior as a massive local recurrence.

Uterine adenolipoleiomyoma:



PS-09-066

Dysgerminoma in a case of 46 XY partial gonadal dysgenesis

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Objective: Disorders of sex development (DSD) among 46 XY individuals are due to the abnormalities of karyotype, gonadal formation, androgen synthesis and androgen action. Here we present a case of 46 XY with partial gonadal dysgenesis.

Method: 22 year old patient (175 cm height, 62 kg weight) presented with primary amenorrhea and infertility. She was phenotypically female with female external genital appearance. Laboratory results revealed low estradiol levels (<20 pg/mL, normal range:20–40 pg/mL), high follicle stimulating hormone levels (93.96 mlU/mL), low free testosterone levels (3.96 pg/mL, normal range:0.29–3.18 pg/mL). Karyotype analysis showed 46 XY genotype. Transvaginal ultrasonography showed athrophic uterus (40 × 25 × 20 mm) and atrophic gonads. According to surgeon's intraoperative observation, there was fibrotic, band like 10 × 7 mm area which can be a potential right gonad. And there was 20 × 17 mm mass at left tubaovarian region. Patient had normal müllerian structures, streak gonads. Histopathological examination of right gonad showed ovarian stroma without follicles, sertoli cell only atrophic tubules, leydig cell hyperplasia, tumoural areas identical with dysgerminoma.

Conclusion: 46 XY DSDs are complete/partial gonadal dysgenesis, gonadal regression, ovotesticular DSD. Tumour development in cases with partial gonadal DSD is a rare condition. Apropriate time of prophylactic gonadectomy depends on various factors. Any evidence of malignancy warrants gonadectomy.

PS-09-067

Sclerosing stromal tumour of ovary: A case report

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Objective: We present a 30-year-old woman who was asymptomatic.In an ultrasound guidance heterogeneous solid mass in left ovary was observed.

Method: Unilateral oophorectomy was made. Macroscopically left ovary was replaced by a solid lesion, circumscribed, smooth surface and 5 cm in maximum dimension. It presented a edematous, translucent and yellowish center and rubbery consistency at the periphery.

Results: Histological study showed a heterogeneous tumour of irregular distribution that was more cellular at the periphery. The central zone showed a pseudo-lobed pattern, with cell nests separated by an edematous or collagenized stroma. The vasculature was prominent throughout the lesion with thin-walled vessels and irregular hemangiopericitoide type light. The tumour was composed of two types of cells: spindle and luteinized cells with vacuolated cytoplasm. Some of the luteinized cells acquired morphology of signet ring cells, so it was mandatory rule out metastatic tumour (krukenberg); PAS negativity and lack of expression of cytokeratin did it. In addition, neoplastic cells displayed immunohistochemical expression of calretinin, inhibin (in luteinized cells) and actin (in the spindle cells).

Conclusion: The morphological pattern and immunohistochemical profile was compatible with sclerosing stromal tumour.

PS-09-068

A study of secondary urothelial tumours in ovary and primary ovarian tumours of urothelial-like appearance: Diagnostic dilemma

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Objective: Transitional cell carcinoma of the ovary, malignant Brenner tumour and metastatic transitional cell carcinoma in ovary pose a diagnostic difficulty due to their histological similarities. Differentiation being more important considering differences in biological behavior and in prognosis.

Method: The case of a woman aged 56 years. Pelvic sonography showed a tumour of the left ovary, abdominal computed tomography demonstrated the osteolytic changes in the lumbar vertebrae and sacral bone and tumour enlarged right kidney. After a total hysterectomy, bilateral salpingooophorectomy and histopathological analysis of ovarian tissue is sent to the Institute of Pathology, Medical Faculty in Belgrade. Differential diagnosis included the possibility of metastatic transitional cell carcinoma originating in the kidney, malignant Brenner tumour and primary trasitional cell carcinoma of the ovary.

Results: Macroscopically tumour of the ovary was of partly solid and partly cystic structure. Histologically observed tumour consisted of epithelioid cells with hyperchromatic nuclei and emphasized nucleoli, that build nests and multilayered lining of the cystic spaces. Immunohistochemical staining has shown that tumour is CK7+, CK20+, WT1-, Ca125-, CEA-, p63+, uroplakin +, thrombomodulin + and negative for estrogen and progesterone markers (Fig.1).

Conclusion: In conclusion considering histological characteristics and immunophenotype of differentially considered tumours (Fig.2) we have concluded that findings point to metastatic tumour of urothelial origin and that the biopsy of enlarged kidney should be performed, suggesting clinicopathological correlation should be done.

Figure1 Figure 2:

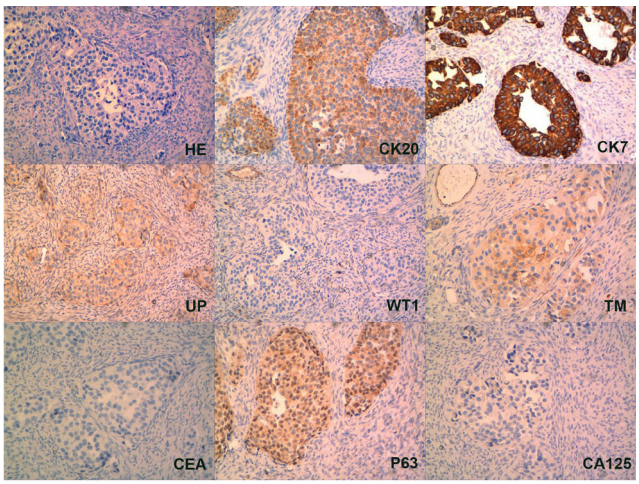

Figure 1. Ovarian tumor tissue, magnification 40X, immunohistochemical staining showing CK7+, CK20+, WT1-, Ca125-, CEA-, p63+, uroplakin(UP) +, thrombomodulin(TM) + markers.

Figure 2. Immunophenotype of transitional cell carcinoma of the ovary (TCCO), metastatic transitional cell carcinoma originating in kidney (MTCCK) and malignant Brenner tumor (MBT).

	TCCO	MTCCK	MBT
CK7	+	+	+
CK20	-	+	+
WT 1	+	-	+
CA 125	+	-	+
CEA	+	-	+
P63	-	+	+
Uroplakin	-	+	+
Thrombomodulin	-	+	+

PS-09-069

Parasitic ovarian granulosa cell tumour of the descending colon presenting as acute abdomen: Case report

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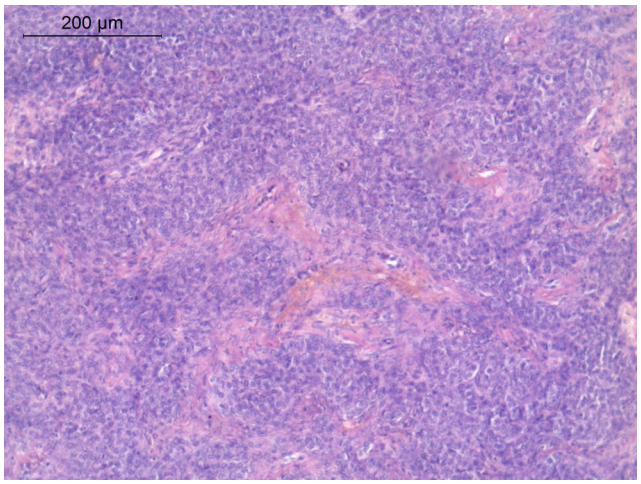
Objective: Here we present a case of parasitic ovarian granulosa cell tumour on the serosa of the descending colon.
Method: A 41 year old woman with history of right adnexectomy and left ovarian cystectomy was admitted with abdominal pain. Imaging demonstrated a peritoneal heterogenic solid-cystic 87 × 72 × 63 mm lesion extending to the small pelvis, and an oval hypoechogenic mass in the left mesogastrium. The patient developed acute abdomen. On laparotomy, large amount of fresh blood was found, the solid cystic lesion corresponded to a chronic hematoma. An oval solid 50 × 40 × 25 mm tumour was found attached with a bleeding vascular pedicle to the epiploic appendix of the descending colon.
Results: Macroscopically, the solid tumour was whitish yellow, on cut surface whitish to brown, hemorrhagic, with small cystic cavities in one pole. Microscopy demonstrated granulosa cells growing in trabecular and insular pattern in a fibromatous stroma. Mitotic count was 5MF/10HPF. Immunoprofile: CKAE1/AE3, CAM5.2, Calretenin, Estrogen, CD56, Inhibin-A, CD99 positivity, CK7, CK20, EMA, WT1, Desmin, SMA, HMB45, Chromogranin, CD10, CD117, CD34 negativity. Diagnosis of ovarian granulosa cell tumour of the adult type was made.
Conclusion: Most reported parasitic ovarian tumours are teratomas. In our case, we cannot exclude recurrence from previously undiagnosed cystic granulosa cell tumour.

Parasitic ovarian granulosa cell tumour of the descending colon (HE):



PS-09-070

Absence or presence of high grade squamous intraepithelial lesion in cervical specimens: A study of 452 cases

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Objective: To determine the frequency of negative cervical excision findings following a diagnosis of high-grade squamous intraepithelial lesion (HSIL).
Method: A total of 452 patients who underwent cervical excision after a diagnosis of HSIL between 2004 and 2014 were enrolled. Data regarding patient age, prior cytological and histological diagnosis, HPV status (Cervista® HPV high-risk test), and size of specimen were obtained from medical and pathological records.
Results: The overall incidence of negative excisions at our institution was 14 %. The lowest incidence was among women with concordant preceding cytology and biopsy diagnoses (11 %, 29 out of 265 cases). The highest incidence was among women with HSIL biopsy/LSIL cytology (20 %, 6 out of 30 cases) and women with LSIL biopsy/HSIL cytology (20 %, 30 out of 146 cases). No statistically significant differences were found between positive excision group and negative excision group regarding age (mean 36 vs 34 years, respectively, $p = 0.25$), size of specimen (mean 27 vs 26 mm, respectively, $p = 0.87$), and hr-HPV negative status (33 vs 38.5 %, respectively).
Conclusion: Multiple factors may contribute to negative excision. We did not detect a difference in frequency regarding age, size of specimen or hr-HPV status between positive and negative cervical excision findings.

PS-09-071

Low grade endometrial stromal sarcoma: A case report

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Objective: Low grade Endometrial Stromal Sarcoma (LGESS) is a rare tumour for the uterus accounting for only 0,2 % of all genital tract malignant neoplasms. In general ESSs affect younger women than other uterin malignancies. The mean age ranges from 42 to 58 years and 10–25 % of patients are premenopausal. We report a case of low-grade ESS.
Method: A 47 year-old female, reported with complaints of irregular bleeding par vaginum. Ultrasound of the pelvis suggested a globular

mass. The clinical impression was that an atypical leiomyomatous. The patient was opered and a hysterectomy with bilateral salpingo-oophorectomy was performed.
Results: The uterus cut surface showed multiple masses in myometrim ranging from 0,5 to 5,5 cm, poorly definited. The nodules appeared yellow to tan and had a softer consistency. The uterine cavity was free. Ovaries were multi-cystic. Microscopic examination showed a densely cellular tumour composed of uniform, oval to spindle-shaped cells of endometrial stromal-type. Atypia, pleomorphism and mitosis were minimal. Areas of sex cord-like differentiation were seen.The tumour involved the well of the uterus without exceeding. Both ovaries showed follicular cysts.
Conclusion: ESS is a rare malignant tumour, presenting as abnormal uterine bleeding in perimenopausal women. The usual preoperative diagnosis is uterine leiomyoma and definitive diagnosis is achieved only after histopathology of uterus. An early diagnosis is essential because patient survival is directly related to tumour stage.

PS-09-073
Benign epithelial inclusions in pelvic lymph nodes associated with uterus squamous carcinoma
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*Sarajevo, Bosnia and Herzegovina

Objective: To present a case of benign inclusions in lymph nodes which could be related to an inflammatory process or a tumour. Our aim was to alert pathologists towards a group of lesions which can imitate metastatic carcinoma, and especially towards those inclusions which present together with malignant neoplasias of the female genital tract.
Method: To present a case of benign inclusions in lymph nodes which could be related to an inflammatory process or a tumour. Our aim was to alert pathologists towards a group of lesions which can imitate metastatic carcinoma, and especially towards those inclusions which present together with malignant neoplasias of the female genital tract.
Results: Invasive squamous carcinoma of the cervix, pT1b1N0Mx, was found in association with benign glandular inclusions in a pelvic lymph nodes. Epithelium of the endocervix looked regular morphologicaly. Diagnostic features of benign inclusions like bland nuclear cytology, absence of mitosis, necrosis and desmoplastic stromal reactions helped with the in achieving a correct diagnosis. Benign iclusions were found in one pelvic lymph node from the right side and in one pelvic lymph node from the left side.
Conclusion: Benign inclusions can be found in lymph nodes of individuals with or without a malignant disease. Their appearance is similar to the epithelium of the uterine tube and, as such, they may imitate carcinoma metastasis. Therefore, it is very important to create awareness of this rare entity among pathologists to prevent misdiagnosis or overdiagnosis of malignant disease, especially on frozen sections.

PS-09-074
Mucinous carcinoma of the cervix, gastric variant: A case report
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Objective: Mucinous carcinoma of the cervix, gastric type is a mucinous adenocarcinoma that shows gastric type differentiation. We report on a 50 years old female patient with 7-month history of vaginal bleeding.
Method: A Pap-test and an endometrial biopsy were performed. The Pap-test revealed a significant atypical columnar cell population in papillary aggregates and isolated neoplastic cells with mucous secretion. The endometrial biopsy showed well-differentiated variably sized, often cystic glands with mucinous, pyloric type epithelium, invading the endocervical stroma.
Results: Immunohistochemically, the tumour cells were positive for CK7, CEA and focally for p53. Gastric type adenocarcinoma of the cervix, is most often not associated with high-risk HPV and is hence negative for p16.
Conclusion: This rare subtype of mucinous carcinoma is thought to have a worse prognosis compared to the usual types, despite its extremely well-differentiated appearance and is associated with more frequent peritoneal and abdominal spread.

PS-09-075
Unexpected expressions of cell adhesion molecules in ovarian carcinoma
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*University of Medicine Iasi, Romania

Objective: Our study aimed to analyze E-cadherin and CLDN3 expression in ovarian cancer (OC), and their correlations with clinico-morphological parameters.
Method: The study group consisted of 21 cases of OC classified as follows: 10 cases as stage I, 5 cases as stage II, and 6 cases as stage III. The histopathological subtypes were: serous (10 cases), endometrioid (7 cases), clear cells (1 case), mucinous (2 cases), and mixed (1 case); 4 cases were assessed as G1, 6 cases as G2, and 11 cases as G3. The tissue fragments were immunohistochemically processed using anti-E-cadherin and anti-CLDN3 antibodies.
Results: E-cadherin expression was positive in 13 cases (61.90 %) and negative in 8 cases (38.09 %). CLD3 expression was positive in 17 cases (80.95 %) and negative in 4 cases (19.04 %). The statistical analysis revealed significant differences between E-cadherin and tumour grade ($p = 0.014$) and stage ($p = 0.013$), and between CLD3 and histological subtypes ($p = 0.047$), respectively.
Conclusion: E-cadherin and CLDN3 expressions associated with advanced stages and poor differentiation are not concordant with the expected role of adhesion molecule, as we expected their disruption and loss during tumour progression. These data suggest that E-cadherin and CLDN3 might have a different behavior in OC compared to other malignancies.

PS-09-076
Immunohistochemical expression of P16INK4a in inflammatory, preneoplastic and neoplastic cervical lesions
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Objective: p16INK4acan be considered as a surrogate marker of active HR-HPV infection in dysplastic and neoplastic cells of the cervix. Aim of the researchwas to determine the presence and level of p16INK4a expression in inflammatory, preneoplastic and neoplastic lesions.
Method: The study was performed on 109 samples of cervical biopsy. Cervical cancer was diagnosed in 36 patients, in 34 patients a preneoplastic change and in 39 a nonspecific inflammatory process. In all samples, immunohistochemical analysis using antibodies to p16INK4a was performed.
Results: The expression of p16INK4a was verified in all cases of cervical cancer, in 67.65 % of cases in dysplastic cervical lesions and 38.5 % of inflammatory lesions. Statistically highly significant difference was found in the presence and level of expression among neoplasic, dysplastic and inflammatory lesions of the cervix (= 76.02, $p < 0.001$). The expression was more frequent and had a higher level in neoplastic and high grade dysplastic lesions compared to expression in inflammatory lesions and low grade dysplasias.
Conclusion: The analysis of the presence of p16INK4a can differentiate nonneoplastic, high grade preneoplastic and neoplastic changes of the cervix. The use of p16INK4a in interpreting of borderline lesions of the cervix can enable a rational therapeutic treatment of patients.

PS-09-077

Clinicopathological, histochemical and immunohistochemical study of mucinous tumours of the ovary about 29 cases

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Objective: The aim of the study was to analyze the clinical characteristics of mucinous ovarian tumours by reclassifying them according o the latest classification of 2008 and to study the histochemical and immunohistochemical profile of these tumours.
Method: There were 29 cases of mucinous ovarian tumours diagnosed in the pathology departement of the Military Hospital of Tunis between 1990 and 2012. We noted 26 benign tumours, 2 borderline tumours and one case of adenocarcinoma. We undertook clinicopathological, histochemical and immunohistochemical studies of these tumours.
Results: Mucinous cystadenoma represented 26 cases (90 %). The average age of patients was 40 years. Eighty-eight percent of these tumours were without atypia, with 65 % of endocervical type, 22 % of intestinal type and 13 % of mixed type. Mucinous cystadenoma with focal atypia (12 %) were all intestinal type. There were two mucinous borderline tumours one of endocervical type and the other of intestinal type. The mucinous adenocarcinoma and borderline mucinous tumours screted more sulfomucins than mucinous cystadenoma. Mucinous adenocarcinoma secreted more neutral ucins than mucinous cystadenoma. Benign mucinous tumours of intestinal type sereted more sialomucines than endocervical type. Benign mucinous tumours were positive for CK7 and negative for CK20 in 22 cases among 25 (88 %). The 2 mucinous borderline tumours and the mucinous adenocarcinoma were all positive for CK7 and negative for CK20.
Conclusion: The histochemistry is useful in assessing the risk of recurrence of mucinous cystadenoma. The immunohistochemistry using the couple CK7/CK20 helps to determine the primary or secondary character of mucinous adenocarcinoma.

PS-09-078

When urinary bladder looks uterus

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Objective: To present common lesions in uterus and very rare in bladder with therapeutic implications. In one hand, bladder endometriosis and endocervicosis which are uncommon pathologic findings, with a common embryological origin and in the other hand secondary tumours of the urinary bladder, all of them less than 2 % of all urinary bladder neoplasm.
Method: We reviewed all transurethral resections and cystectomies in our Hospitals in the last 10 years looking for Müllerian lesions or metastatic neoplasm from uterus.
Results: We found endometriosis (5), endocervicosis (1), endometrioid adenocarcinoma (3) and squamous carcinoma from cervix (1).
Conclusion: Is important to recognize these benign lesions of endometriosis and endocervicosis to not make a wrong diagnostic of metastatic carcinomas and recognize metastatic endometrioid carcinoma and squamous carcinoma of the uterus and make the differential diagnosis with primary adenocarcinoma of the bladder and urothelial carcinoma with squamous differentiation, for their therapeutic implications.

PS-09-079

Clear cell renal cell carcinoma metastatic to the ovary: A case report

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Objective: Although renal cell carcinoma (RCC) is known to metastasize to unusual sites, it rarely metastasizes to the ovaries, and it must be distinguished from a primary clear cell carcinoma.
Method: A case of ovarian metastasis from a clear cell RCC is reported. The patient developed unilateral ovarian metastasis 8 years after the nephrectomy.
Results: A 46-year-old woman presented with abdominal pain. Radiological work-up revealed a tumoural mass in the left adnexal region. Intraoperative consultation was made without the knowledge of the previous history of RCC. Grossly, the left ovary was measured 13 × 12 × 7 cm. It was replaced by a tumour mass with widespread cystic and myxoid changes with focal yellowish solid areas. Because of the extensive degenerative changes a definite diagnosis could not be given. After thorough sampling, permanent sections revealed small foci of clear cell tumour arranged in a solid, alveolar and cystic pattern some of which filled with blood, which may be a clue for RCC. Immunohistochemically, the neoplastic cells were positive for EMA, CD10, vimentin and PAX-8, and negative for CK7.
Conclusion: Possibility of metastasis from RCC should be considered in clear cell ovarian tumours. It is important to differentiate between the two since the management of clear cell ovarian carcinoma and RCC is different.

PS-09-080

Serous adenocarcinom of the fallopian tube: Case report

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Objective: We report a case of primary fallopian tube serous adenocarcinoma in 69-year-old woman.
Method: The patient was at routine gynecological examination revealed a tumour mass in the region of the right ovary. Was hospitalized and underwent exploratory laparotomy. Taken a few fragments of tumour tissue for analysis.
Results: At histopathologic analysis delivered two clips tissues. The first clip was soft, yellowish gray, partly papillary surface. The second clip was part of the fallopian tube with ovarian tissue. At the intersection of the lumen of the fallopian tubes filled with yellowish-gray tumour tissue. Ovary was grayish in color, made of mostly softer finely-nodular tissue. Histological examination of the clips presented tumour composed of complex papillae with stratified epithelium producing irregular slit-like spaces and small epithelial tufts. The cells were large, eosinophilic cytoplasm with high grade nuclei with abundant mitotic figures. Some nuclei were vesicular and nucleoli and sam nuclei were hyperchromatic. Immunohistochemical tumour cells were positive for EMA, CK7, WT1, p53, p16ink, and negative for Calretinin, indicating that the tumour, serous adenocarcinoma, origin of the fallopian tubes.
Conclusion: Although rare, one should always think of the possibility that the serous adenocarcinoma origin of the fallopian tubes.

PS-09-081

Superficial spreading Squamous Cell Carcinoma (SCC) of the uterine cervix involving the endometrium, bilateral fallopian tubes and unilateral ovary: A case report

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Objective: When squamous cell carcinoma (SCC) of the cervix invades the uterus this usually occurs in a direct way, however it rarely spreads superficially to the inner surface of the genital tract.
Method: Morphological features of the total laparoscopic histerectomy and bilateral salpingo-oophorectomy specimen from a 53 years old patient are described.
Results: On gross examination the uterus was measured 12 × 10 × 5 cm. Macroscopically there was no visible tumour in the cervix and uterine cavity. The fallopian tubes and the ovaries were unremarkable.

Microscopically, the cervix was involved by moderately differentiated non-keratinizing SCC. Maximum diameter of the invasive tumour was 8 mm and the depth of invasion was 3 mm. Endometrial epithelium was focally replaced by superficial spreading SCC with glandular involvement without invasion of the stroma and myometrium. Mucosa of the both fallopian tubes was also focally replaced by SCC without subepithelial invasion. A tumour implant over the left ovarian surface and a small focus of tumour entrapped in the ovarian cortical stroma were seen.
Conclusion: Superficial extension of SCC of the cervix to the endometrium and the adnexae without invasion is uncommon. Because of the rarity of such cases, it is unclear whether they behave similar to the SCC invading directly into the uterine wall.

PS-09-082
Aberrant Prostatic Tissue in the Uterine Cervix
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Objective: Prostatic tissue has rarely been described in the lower female genital tract. Possible theories of histogenesis include a developmental anomaly, metaplasia of preexisting endocervical glands, and derivation from mesonephric remnants.
Method: We present an incidental finding of aberrant prostatic tissue in a cone biopsy of the cervix of a 34 old woman for high-grade epithelial dysplasia.
Results: The microscopic investigation of the cone biopsy, besides the high-grade epithelial dysplasia, showed a cluster od tubuloalveolar glands, linned with two-layered epithelium comprised of flattened basal cells and overlying secretory cells, with an overall appearance of prostatic glands. Immunohistochemical studies confirmed the histological suspicion of aberrant prostatic tissue differentiation: secretory cells were positive for PSA, while the basal cells were positive for CKHMW antigen and the surrounding stroma was marked by SMA staining.
Conclusion: The presence of ectopic prostatic tissue in the lower female genital tract may be more common than appreciated. Once the possibility is considered, the diagnosis is easily confirmed with additional immunohistochemical stainings. However, such glands must not be overlooked on standard HeEo staining in the first place. Aberrant Prostatic Tissue in the Uterine Cervix.

PS-09-083
Xanthomatous Endometritis
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Objective: Xanthomatous changes are unusual lesions in endometrium. The term "xanthomatous endometritis" refers to morphological changes frequently induced by estrogen stimulation. An 43 -old female attended our gynecology clinic with complaint of abnormal uterine bleeding. It was performed diagnostical curettage to patient. Histopathologic features are lipid-containing histiocytic cells in endometrium. These cells were stained with CD68.
Conclusion: These lesions may lead to diagnostic confusion. Therefore, the differential diagnosis should be made.

PS-09-084
Coexpression of VEGF-C and VEGF-R3 in ovarian cancer: Positivity versus negativity
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Objective: Our study aimed to find a possible statistically significant difference between VEGF-C and VEGF-R3 expression pattern and classic clinicopathological parameters (tumour stage and grade, histopathological type), in ovarian carcinoma (OC).
Method: The study group included 21 patients with the following histopathological diagnosis: high grade serous OC - 8 cases, low grade serous OC - 2 cases, high grade endometrioid OC - 5 cases, low grade endometrioid OC - 2 cases, clear cells OC - 1 case, mucinous OC - 2 cases, and mixed OC - 1 case. A semiquantitative evaluation of VEGF-C and VEGFR3 immunohistochemical reaction was performed using a scoring system based on positive cells percent (P) and immunostaining intensity (I).
Results: VEGF-C - VEGF-R3 expression pattern has been noticed in the ensemble of study group, 18 cases being dominantly double positive or double negative. The other 3 cases showed a VEGF-C negative / VEGF-R3 positive pattern. Although the statistical analysis did not reveal significant differences between the expression of the two markers and clinicopathological parameters, we noticed VEGF-C - VEGF-R3 positive expression association with late stages and high grades.
Conclusion: VEGF-C - VEGF-R3 co-expression supports the capacity of dissemination by lymphatic pathways, by its pro-lymphangiogenic potential, and therefore indicates a high potential of tumour aggressivity.

PS-09-085
Evaluation of the caveolin-1 and arid-1 alpha expressions in uterine smooth muscle tumours
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Objective: This retrospective study was designed to evaluate the importance of tissue expressions of caveolin-1 and ARID-1A which are known as signal regulator and tumour suppressor in differential diagnosis of uterine smooth muscle tumours.
Method: Thirty patients were included in this study and immunohistochemical stains for caveolin-1 and ARID-1A were performed.
Results: In this series, there were 10 leiomyosarcomas (LMSs), 10 uterine smooth muscle tumours of uncertain malignant potential (STUMP) and 10 leiomyomas (LMs). Cytoplasmic Caveolin-1 expression was determined In 9 LMSs and 2 STUMPs; while perivascular expression was determined in 5 LMSs and 2 STUMPs. Statistically it was determined if the tumour becomes malignant and more invasive, it gains the perivascular Caveolin-1 expression ($p = 0.029$). On the other hand, the mean nuclear staining rate for ARID1A in LMSs (63 ± 23.4 %) was higher than both STUMPs (60 ± 18.5 %) and LMs (%34.5 ± %16.5). Statistically it was determined that the expression of ARID1A was significantly down-regulated in LMs when compared with STUMPs and LMSs ($p = 0.004$).
Conclusion: Our findings were demonstrated that perivascular Caveolin 1 expression was seen to be a marker for malignancy of uterine smooth muscle tumours. Similarly we found to link of ARID1A expression and the aggressiveness of SMTs.

PS-09-086
The clinicopathological significance of the ARID1A expression in ovarian serous tumours
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Objective: AT-rich interactive domain 1A (ARID1A) is a tumour suppressor gene involved in chromatin remodeling and it encodes the ARID1A protein. The aim of this study was to investigate the association between tissue ARID1A expression and the clinicopathological features of ovarian serous tumours.

Method: ARID1A expression was studied in a total of 82 formalin-fixed, paraffin-embedded ovarian serous tumours specimens and its association with different clinicopathologic parameters was evaluated.
Results: In this series, there were 36 benign (43.9 %), 12 (14.6 %) borderline and 34 (41.5 %) malign serous tumours. Mean age of patients was 43.9 ±1 4.4 years (17 to 72 years). Statistically it was determined that the expression of ARID1A was significantly down-regulated in benign serous tumours when compared with borderline serous tumours and serous carcinomas ($p = 0.001$). The decreasing ARID1A expression was found in 83.3 % ($n = 30$) of serous tumour samples but only in 16.7 % in borderline serous tumour and 8.8 % in serous carcinomas.
Conclusion: Our findings were demonstrated to link of ARID1A expression and the aggressiveness of ovarian cancer. But unlike previous studies, the ARID1A expression was down regulated in benign tumours. Therefore it may be suggested that ARID1A may act as a prognostic biomarker in ovarian cancers.

PS-09-087
Utility of PTEN, MLH1, ARID1A, Beta-catenin, Bax and BCL-2 biomarkers in endometrial hyperplasia and endometrioid endometrial carcinoma
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Objective: We aimed to reveal the expression status of PTEN, MLH1, ARID1A, Beta-catenin, Bax and Bcl-2 biomarkers in all types of endometrial hyperplasia (EH) and endometrioid endometrial carcinoma (EC); to understand that on which step of EC development these molecules play roles, and determine the interactions.
Method: 202 cases including EC, simple EH with and without atypia, complex EH with and without atypia and normal endometrium were assesed immunohistochemically with tissue microarray method.
Results: Loss of PTEN, ARID1A, MLH1 ratio is respectively 61, 52.4, 40.2 %% in patients with EC and 87,5, 41,7, 20,8 % in atypical complex EH; 12,7; 4,2; 1,4 % in simple EH without atypia. There were significantly higher weakly Bax staining in grade III EC in comparison to grade I and II. Severe membranous Beta-catenin expression is significantly higher in EC, complex EH with and without atypia than in simple EH with and without atypia.
Conclusion: It has been shown that PTEN, ARID1A and MLH1 has a role in transition from simple EH to atypical complex EH, also MLH1 has a role in the transition from aytpical complex EH to EC. There were significant concordance in loss of expression PTEN with ARID1A and ARID1A with MLH1 in EC. This condition showed that these three tumorigenesis signaling pathways and protein could have a connection or interaction.

PS-09-088
Ovarian seromucinous carcinoma: A rare case report
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Objective: Ovarian endocervical mucinous type (mullerian) carcinoma has been renamed as seromucinous carcinoma(SMC) by WHO 2014, recently. These type of tumours are frequently bilateral, associated with endometriosis, display acute inflammation in the stroma, composed of endocervical mucinous and ciliated serous type epithelium, and sometimes other cell types. Their clinical behavior is similar to serous tumours.
Method: We report a case of ovarian SMC in a 51 year old woman referred to our hospital with a pelvic mass measuring 24 × 11 × 12 cm on CT. She's underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy and surgical staging procedure.
Results: Macroscopically the main tumour was in ovaries. There was tumour infiltration also in cervix and abdomen. Microscopically the tumour was composed of low grade seromucinous type of cuboidal cells with stroma having inflammatory cells. An endometriotic foci was accompanying the tumour area in cervix. The tumour was diffusely positive for CK7; focally positive for ER, PR, WT1, P53. CD20 was negative.
Conclusion: We present this newly renamed entity to express the new nomenclature and remind its relation with endometriosis.

PS-09-089
Adenoid cystic carcinoma of Bartholin's gland
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Objective: Adenoid cystic carcinoma (ACC) of Bartholin's gland is an extremely rare tumour of the female genital tract, representing about 5–15 % of Bartholin's gland malignancies. Approximately 80 cases have been reported in the literature. The aim of our study is to evaluate the clinicopathological characteristics and treatment of ACC of Bartholin's gland.
Method: We report a case of a 44-year-old women, presented with a growing vaginal painful swelling for 1 year. On examination, there was a redness and heat induration measuring 1.5 cm at the left lateral surface of the vagina. The patient had simple mass excision of the left Bartholin's gland.
Results: Microscopic examination revealed a malignant infiltrative epithelial proliferation tubulo-trabecular and compact with a mucoid susbstance into the lumen. The stroma was hyalinized and there was an infiltration of perineural spaces. We concluded to an ACC of Bartholin's gland with positive margins. So the patient underwent a vulvectomy with bilateral inguinal lymphadenectomy. After 6 months of the initial diagnosis, the patient continues to survive and she does not have metastasis.
Conclusion: ACC of Bartholin's gland is a slow growing tumour locally very aggressive with a high capacity for local recurrence and lung metastasis. Surgery is the most common and useful treatment.

PS-09-090
Cancer of corpus uteri: Histopathological and immunohistochemical prognostic factors
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Objective: Uterine corpus cancer is the third malignancy of european women. However, in general surgical pathology these cancers are rare, patients being directed to hospitals with department of gynecology or oncology. We evaluate histopathological and immunohistochemical features of cancers incidentally diagnosed in a hospital with general surgical profile.
Method: We performed a retrospective review of 25 consecutive uterine cancers surgically removed and diagnosed at Colentina Hospital and 21 cases submitted in consultation in our department from 2008 to 2015.
Results: Of the 25 cases diagnosed in our clinic, 15 (60 %) were endometrioid carcinomas, 4 (16 %)-serous carcinomas and 6 (24 %)-sarcomas; according to 2009 FIGO staging, 9 (36 %) were stage I, 5 (20 %)-stage II, 8 (32 %)-stage III and 3 (12 %)-stage IV; 10 (40 %) cancers were poorly differentiated; angiolymphatic invasion was find in 11 (44 %) cases, cervical and serosa involvement in 6 (24 %) and 3 (12 %) cases, respectively; the depth of myometrial invasion was more than ½ in 10(40 %) cases. Most of the cases submitted in consultation were moderately differentiated endometrioid carcinomas. All poorly differentiated cases were negative for hormonal receptors and overexpressed proliferative factors.
Conclusion: Uterine corpus cancer can occur in any department of pathology disregarding the profile of the clinic. Complex approach (clinical,

imagistic, histopathological and immunohistochemical examinations) is necessary in order to classify these tumours.

PS-09-091

Case report of a monodermal mature teratoma: Struma ovarii in a 43-years old woman

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Objective: Since its firs description in 1895 by Von Kalden, Gottschalk in 1899 and Mayer in 1903, only 150 cases of struma ovarii were reported in the medical literature. The diagnosis of struma ovarii is usually made after surgical resection of the pelvic tumour, on histological exam. We report a case of unilateral monodermal mature teratoma, struma ovarii type, in a 43-years old patient with benign ascites.
Method: A 43-years old woman presented at out Hospital of Obstetric-Gynecology with pelvic pains and repeated metrorrhagia. Total hysterectomy with bilateral oophoro-salphingectomy was preformed.
Results: Histopathological examination, macroscopically: uterus increased in dimensions 200/180/100 mm that show in anterior wall a leiomyomatous nodule of 40/30 mm, right ovary - with cystic transformation 60/50 mm, left ovary - normal aspect 40/30 mm. Microscopy showed proliferative endometrium, leiomyomatous myometrium, right ovary - monodermal mature teratoma, struma ovarii type, left ovary - follicular cyst, fallopian tubes without modifications, ascites liquid without atypical cells. No symptoms of hyperthyroidism were observed, including the post-operative period.
Conclusion: Benign and unilateral struma ovary was diagnosticated in a 43-years old woman. The patient show no hyperthyroidism symptoms before and after surgery. No complication in postoperative period. Struma ovarii is a rare type of teratomas, difficult to identify without histopathological examination. Surgery is the only treatment because can cause symptoms of pelvic mass and compression, also malignant alteration is possible.

PS-09-092

Synchronous endometrial serous carcinoma and cervical Squamous Cell Carcinoma

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Objective: Uterine serous carcinoma (SC) is a very aggressive tumour which often presents with extra-uterine spread. Synchronous occurrence of primary endometrial SC and cervical squamous cell carcinoma (SCC) has not been reported in English literature so far.
Method: A 60-year-old diabetic woman with elevated body mass index presented with vaginal bleeding. Fractional curettage revealed invasive SCC and clusters of atypical cells suspicious for adenocarcinoma. Total abdominal hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy was performed. Grossly, an exophytic cervical mass measuring 3.9 cm was observed; the endometrium was atrophic.
Results: Histological examination revealed invasive cervical SCC (stage pT1b1N0) and extensive serous endometrial intraepithelial carcinoma (SEIC) with focal superficial myometrial invasion and spread to cervix, fallopian tube, ovary and an iliac lymph node (stage pT3a1N1). Immunohistochemically, SC was positive for CK 7, CK 8/18 and vimentin, and negative for ER, p53 and WT1.
Conclusion: In patients with synchronous primary malignancies of the female genital tract, the stage of the disease of either tumour at the time of diagnosis is the most important predictor of survival. Cases of SEIC require careful pathologic examination to demonstrate invasive disease and/or extra-uterine spread, and avoid understaging of the tumour. Surgical staging is recommended when SC is suspected.

PS-09-093

Evaluation of CINtec PLUS test diagnostic accuracy in benign and low grade cervical lesions and comparison with wesults of cervical biopsy p16/Ki-67: Double immunolabeling

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Objective: The aims of this study are twofold. Firstly, to trial the diagnostic accuracy of cervical cytology CINtec PLUS in benign, reactive, and low grade dysplasia (LGD) diagnosed by Pap smear. Secondly, to compare dual cytology staining results with 'gold standard' of cervical biopsy double immunolabeling (DIL).
Method: 19 suitable cases were accrued. A CINtec PLUS test was +ve if ≥ 1 cell showed both brown cytoplasmic p16, and red nuclear Ki-67 staining. Positive p16 in tissue sections was diffuse staining, and Ki-67 was +ve if upper $^{2}/_{3}$ epithelial nuclei were +ve.
Results: Pap smear results were as follows; LGD 7, ASC-H 5, ASCUS 3, Negative 3, HPV alone 1. Of 8 CINtec +ve cases, biopsy yielded CIN 3 in 4 cases, LGD in three cases, and a single case of HPV alone. Of 11 CINtec -ve cases, biopsy was LGD in four cases, HPV alone in two cases, and five benign reactions.
Conclusion: CINtec proved highly specific for detection of high grade lesions. The negative predictive value for all dysplasia was 87 %, higher than the positive predictive value of 64 %. Sensitivity for any dysplasia was 87 %, and specificity 64 %. Comparison of the 8 CINtec +ve with DIL disclosed one discrepant case, a CINtec false +ve, with HPV histology. Of the 11 -ve cases, 9 were also DIL -ve. The remaining 2 p16 +ve, Ki-67 -ve cases were both HPV effect with LGD. Architectural assessment remains an advantage.

PS-09-094

Synchronous melanocytic lesions in the female genital tract: Atypical melanocytic proliferation of the uterine cervix and vulvar malignant melanoma

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Objective: Melanocytic lesions of the uterine cervix are extremely rare and poorly studied with variations and uncertainties regarding the terminology. Melanosis, blue nevus and melanomas are the most commonly encountered pigmented lesions with this location. The aim of the present paper is to describe an unusual atypical melanocytic lesion of the uterine cervix in a patient with vulvar melanoma.
Method: A 60-year-old female patient has undergone surgery for a suspected HSIL diagnosed on cytology and a vulvar tumour. Additional sections from paraffin blocks containing cervical and vulvar lesion were IHC investigated using anti-HMB45, S100, CKAE1/AE3, vim, CD31 antibodies.
Results: In the tissue sections from the exocervical mucosa we observed squamous epithelium without atypia and an increased number of enlarged melanocytes with nuclear atypia in the basal layer of the epithelium, with extension until the inferior 1/3 of it. No HSIL lesions were identified.
Conclusion: Melanocytic lesions of the uterine cervix are extremely rare, the presented case being, to our knowledge, the only one reported in the Romanian medical literature. The increased number of melanocytes and limited extension of atypical cells in the epithelial thickness made the diagnosis difficult. The synchronous presence of the vulvar melanoma advances the suspicion of a multifocal pigmented lesion in the genital tract, likewise primary acquired melanosis with atypia of the conjunctiva, from which one evolved into nodular melanoma.

PS-09-095

PEComa of lymph nodi associated with endometrial cancer of the uterus

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Objective: Case report of PEComa of Lymph nodi associated with endometrial cancer of the uterus. PEComa are a collection of generally rare tumours, defined by the World Health Organization as "mesenchymal tumours composed of hystologically and immunohistochemically distinctive perivascular epitheloid cells". These are rare tumours that can occur in any part of the human body. It is especiall rareness for them to be found associated with endometrial cancer of the uterus.
Method: Biopsy and operational material that is processed and analyzed in the laboratory.
Results: Patient in menopause at the age of 60 is received on the department because of operational treatment uterine cancer. After classical hysterctomy with adnextomy, the material is during the pathohystological processing colored with methodes HE (Hematoxylin eosin) and IHH (Immunohistochemical color). After the procedure, the "ADENOCARCINOMA ENDOMETRIOIDES ENDOMETRII" (G2, NGII; FIGO IA) is diagnosed. Beside that, in one of the lymph nodi is noted to be mesenchymal proliferation with the predominantly trabecular hystological formation, which is composed of spindle elonged cells with bright or granular cytoplasm and central oval nuclei. Immunohistochemical verification: VIMENTIN strongly positive, SMA-alfa strongly positive, DESMIN positive, HMB 45 positive, MELANIN-A negative and S-100 is negative.
Conclusion: It is concluded that PEComa of lymph nodi indicates the primary cancer, and not the metastatic uterine cancer.

PS-09-096

Primary peritoneal serous tumour: Two cases with unusual initial symptoms

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Objective: Primary peritoneal serous carcinoma (PPSC) is a rare malignant epithelial tumour and it diffusely involves the peritoneal surface.
Method: We reported two cases of PPSC in a female patients aged 78 and 67 years occurred with symptoms of vaginal bleeding.
Results: Initial patohistological diagnosis after curettment was serous carcinoma of endometrium. Hysterectomy with bilateral salpingooophorectomy, as well as tissue of the peritoneum and omentum were removed. In both cases macroscopic and histological analyses showed tumour infiltration of uterus body, starting massively from serosa to the surface of endometrium. Tumour was present in the surrounding adipose tissue and parts of the removed thickened omentum. Fallopian tubes and ovaries were intact. Tumour was composed of complex papillary and solid areas with large cells and pleomorfic nuclei. The immunohistochemical analysis showed positive staining for beta-catenen, E-cadherin, vimentin, VEGF and p53 while calretinin was negative. Mitoses were numerous (10-14/10 hpf). Previously performed MR and CT scan excluded the presence of a primary tumour on another locations or organs. Tumour, in the both cases, was diagnosed as high grade primary peritoneal serous carcinoma.
Conclusion: As a rare neoplasam, we wanted to present two cases with unusual initial symptoms that led to PPSC diagnose.

PS-09-097

Regression of endometrial carcinoma with progestational agent

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Objective: Endometrial cancer is the most common gynecologic malignancy in developed countries and effects predominantly postmenopausal women. Definitive treatment for this dissease is total hysterectomy with bilateral salpingooophorectomy.
Method: We report a case of 24 year old nulliparous woman with grade 1 endometrioid adenocarcinoma and desire for in vitro fertilization.
Results: Initially, patohistology of curettmen showed voluminous tumour tissue of endometrium with no microsatellite instability. Strong desire to maintain fertility in spite of potential oncologic risks led to conservative treatment with progestational agent megestrol acetate (Megace) with 320 mg/day for 3 months. After that diagnostic hysteroscopy with biopsy showed slight regression of carcinoma but still tumour was present. Next there months, again patient admitted same therapy but last 3 weeks she had combination of 320 and 480 mg/day of same drug. On hysteroscopy biopsy specimen tumour regression was evident and only small part of carcinoma was present. Next 3 month same protocol of Megace was admitted in high dosages of 320 and 480 mg/day. On follow up complete regression of carcinoma has been established. Patient is now in in vitro fertilization protocol.
Conclusion: In young women with endometrial carcinoma fertility-sparing procedures and hormonal therapy are recommended in order to preserve reproductive potential.

PS-09-098

Disseminated peritoneal adenomucinosis arising from ovarian mucinous cystadenoma: Case report

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Objective: Disseminated peritoneal adenomucinosis (DPAM) is a paucicellular mucinous ascites most commonly associated with appendiceal mucinous neoplasms and rarely originating in primary ovarian tumours.
Method: A 47-year-old female was admitted at the gynecology department for progressive abdominal distension and pain. Clinical, ultrasound and CT scan examinations revealed a large multiloculated cystic mass occupying the pelvis, with high suspicion of pseudomyxoma peritonei (PMP). At surgery the peritoneal cavity was filled with seven liters of abundant gelatinous material. Many small mucinous nodules were seen on the peritoneal surface. Bilateral salpingo-oophorectomy, omentectectomy, appendicectomy and peritoneal lavage were performed.
Results: Macroscopic examination showed a 26 × 23 × 9 cm multiloculated cystic left ovarian tumour with intact capsule and smooth walls, with mucinous content. One of the cysts had a greasy material with hair. Light microscopic examination revealed a mature cystic teratoma and mucinous cystadenoma with CK7+/CK20+ immunohistochemical profile of epithelial cells. The appendix had acellular mucin on the serosal surface, but the entire mucosa was unremarkable. Pools of mucin entrapped in adipose tissue without neoplastic epithelial cells were seen in the omentum, peritoneal nodules and parametrium, confirming the disseminated peritoneal adenomucinosis.
Conclusion: We report a rare case of DPAM produced by an ovarian mucinous cystadenoma developed on a mature cystic teratoma.

PS-09-099

Mitotically active cotyledonoid dissecting leiomyoma of the uterus: A new feature in a rare neoplasm

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Objective: Cotyledonoid dissecting leiomyoma (CDL) is a very rare variant of leiomyoma, with only 48 cases reported in the literature. All

described cases of CDL lack histological features suggestive of malignancy - cytological atypia, necrosis or increased mitotic activity. We report the first case of mitotically active CDL.
Method: A 43 year-old woman, with a pelvic mass extending into the left pelvic cavity, was submitted to total hysterectomy and bilateral adnexectomy.
Results: A multinodular uterine tumour was identified, with close similarities with placental cotyledons, involving the uterus, left Fallopian tube and ovary. Histologically, the tumour was composed of spindle, and focally epithelioid smooth muscle cells, separated by connective tissue with marked hydropic changes and dilated vessels. The majority of the nodules had low mitotic index (MI) and mild cytological atypia. However, some areas with high MI (10 mitoses per 10 HPF) were observed. No coagulative tumour cell necrosis or vascular invasion were observed.
Conclusion: This is the first reported case of mitotically active CDL. Despite the benign behavior of the previously reported CDL, the existence of high MI areas highlights the possibility of classifying this case as a smooth muscle tumour of unknown malignant potential (STUMP).

PS-09-100
Placental features in a patient with Mycobacterium tuberculosis infection
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Objective: Mycobacterium tuberculosis (MTb) infection is highly prevalent in many countries. However, just around 400 cases of congenital/perinatal tuberculosis (Tb) have been reported and, of these, very few have proven involvement of the placenta.
Method: A 31 year-old pregnant woman, with the diagnosis of miliary Tb since the 23rd gestational week and medicated with an adequate tuberculostatic therapy scheme since the diagnosis, gives birth with 40 weeks+6 days.
Results: Macroscopically, the placenta had firm and white plaques. Microscopically, typical but rare granulomas with caseous necrosis and giant cells, some of Langhans-type, in the intervillous space and in relation with decidua, were seen.
Conclusion: With scanty cases reported in the literature, this case contributes to describe the affection of placenta in mothers with Tb. The location of granulomas in proximity with decidua supports disease transmission therethrough.

PS-09-101
Expression of caveolin-1 in the peritumoural stroma is associated with invasiveness in uterine cervical carcinomas
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Objective: Previous studies have demonstrated that Caveolin-1 ambiguously behaves as a tumour suppressor or as a tumour promoter in different tumours depending on the type of cancers. Some findings also revealed that cell proliferation, migration and invasion were attenuated by knockdown of Caveolin-1 expressions. However, the functional and prognostic significance of Caveolin-1 was not fully understood in most tumours. The aim of this study was to investigate the association between tissue Caveolin-1 expression and the pathological features of uterine cervical tumours.
Method: Caveolin-1 expression was studied in a total of 107 formalin-fixed, paraffin-embedded uterine cervix tumours specimens and its association with different clinicopathologic parameters was evaluated.
Results: In this series, there were 59 noninvasive and 48 invasive cervical tumours. Mean age of patients was 47.9 ± 12.8 years (20 to 80 years). Tumoural caveolin-1 expression was determined In most noninvasive tumours (n = 45,76.3 %); while stromal expression was determined in most invasive tumours (n = 27, 56.3 %). Statistically it was determined if the tumour becomes more aggressive and invasive, it gains the stromal caveolin-1 expression (p = 0.001).
Conclusion: Our findings were demonstrated to link of caveolin-1 expression and the aggressiveness of cervix tumours. Therefore it may be suggested that Cav-1 may act as a differential diagnostic biomarker in cervical neoplasms.

PS-09-102
Squamous Cell Carcinoma (SCC) of cervix extending to endometrium and left fallopian tube
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Objective: Squamous cell carcinoma of the cervix is a common gynecological malignancies and can involve the uterin corpus by direct extension or through parametrium by lymphatic invasion to the uterin wall.
Method: We report here a case of invasive cervical cell carcinoma in a 61 year old female with superficial extention to the endometrium and left sided fallopian tube.
Results: Superficial spread of squamous cell carcinoma of the cervix to the endometrium is a rare antitiy. Also tubal involvement due to direct spread is rare.

PS-09-103
Sertoli-Leydig cell tumour of the ovary
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Objective: Sertoli-Leydig cell tumour (SLCTs) of the ovary is a rare sex-cord tumour that account for less than 1 % of all ovarian tumours, occurring most commonly in young women with the average age of 25, and are almost unilaterally. The aim of our study is to discuss the clinical, radiological and pathological features of this rare tumour.
Method: We present two cases of a 17-year-old and 21-year-old women, who presented with a 6 month history of menometrorrhagia with irregular menstrual cycles and dysmenorrhea. Preoperative ultrasonography revealed an heterogeneous and echogenic right latero-uterine mass measuring respectively 69 and 65 mm, well vascularised in Doppler. A right kystectomy was performed and the peritoneal wash cytology was positive to malignancy in the first case and negative in the second one. The two patients underwent right unilateral adnexectomy with omentectomy, and appendectomy.
Results: The histopathologic exam confirmed a well differentiated SLCTs in the first case, and SLCTs with heterologous element in the second case. The immunostaining for CD99 and calretinin was positive.
Conclusion: The prognosis of SLCTs depends on the type of SLCTs. The treatement consists in conservative surgery.

PS-09-104
Triple synchronous carcinomas of the female genital tract in a patient with a history of leukemia: A case report and review of the literature
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Objective: Three primary synchronous cancers in the female genital tract are extremely rare, with only 4 cases reported in literature, showing three distinct neoplasms. We present the first case of a triple invasive carcinoma of the female genital tract in a patient with a past history of malignant disease, with a brief review of the literature.

Method: Case report: A 38-years-old woman with a past history of acute lymphatic leukemia, with a diagnosis of endocervical adenocarcinoma, usual type, stage Ib1 (FIGO) as well as an adnexal mass, underwent radical hysterectomy with bilateral adnexectomy. Pathologic examination of the surgical specimen and detailed immunohistochemical analysis (p16, pCEA, ER, Vimentin) revealed a mucinous adenocarcinoma of the cervix (G2), an intramucosal well differentiated (G1) endometrioid endometrial adenocarcinoma, with focal mucinous and tubaric differentiation of the uterine corpus, mucinous adenocarcinoma of the left ovary. Thirteen months after appropriate treatment the patient is free of disease. Current criteria to discriminate between primary endometrial and endocervical adenocarcinomas (especially in cases with peculiar morphology) are also discussed.
Conclusion: The diagnosis of multiple primary tumours is often a post-operative incidental finding. Multiple synchronous gynecologic cancers have a better prognosis (usually being low-grade/low stage tumours) than metastatic or advanced primitive disease. Determining whether these tumours are multiple primaries or metastases is helpful to predict their malignancy and to select proper treatment.

PS-09-108

Immunohystochemical and ultrastructure features of interstitial Cajal like cells in placental villi in case of intauterine grouth restriction

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Objective: The aim of study is analysis of morphological features of interstitial Cajal like cells (ICLCs) in placenta villi with intauterine grouth restriction (UGR).
Method: Groups of study included 6 patients with UGR and 5 women with physiological pregnancy (PP) of reproductive age. Immunohistochemical analysis with CD117, CD34 were performed. Moreover, ICLCs were detected by transmission electron microscopy.
Results: ICLCs (syn. telocytes or interstitial pacemaker cells) in placenta both in case of UGR and PP were characterized by week CD117, CD34 immunohistochemical positive staining. ICLCs were usually small, with little cytoplasm and long thin prolongations, had exiguous amount of polyribosomes and granular endoplasmic reticulum, located perinuclear or in the dilated portions. In normal placenta ICLCs were localized in terminal and intermediate villous stroma, below the trophoblastic basement membrane, surrounding of the outline of capillaries by their processes. The cells created a three-dimensional network by connecting to each other and other cell types. ICLCs located in large blood vessel walls of stem villi could regulate of vascular tone. In case of UGR ICLCs were with vacuolated cytoplasm, deformed nuclei, they contained lipid drops. ICLCs probably have a high plasticity, acquired similarity with fibroblasts, myofibroblasts.
Conclusion: Thus, ICLCs may participate in the regulation of angiogenesis and feto-placental circulation.

PS-09-110

Aggressive angiomyxoma of the vulva: A rare clinical entity

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Objective: Aggressive angiomyxoma (AA) is a rare slow-growing soft tissue tumour with a predilection for the pelvis and perineal regions of adult women. The term "aggressive" denotes the locally infiltrative and recurrent nature of this neoplasm.
Method: A 48-year-old woman presented with a mass in the left labia majora, which had gradually increased in size. Clinical examination revealed a sausage-like, non tender mass, measuring approximately 20 cm in greatest diameter and having a soft consistency with normal overlying skin. The tumour was considered to be a bartholin gland cyst and was totally excised.
Results: Microscopic examination revealed a neoplasm composed of spindled or stellate cells in a myxoid stroma with scattered vessels of varying caliber. Neither nuclear pleomorphism nor mitoses were observed. The neoplastic cells were stained intensely for cytoplasmic vimentin, desmin and few were estrogen and progesterone positive. The ki67 was <2 %. The diagnosis was aggressive angiomyxoma of the vulva.
Conclusion: AA must be distinguished from benign proliferations with a low risk of recurrence as well as from fully malignant myxoid neoplasms. The optimal treatment is wide local excision with tumour free margins. Long-term follow-up and careful monitoring with magnetic resonance imaging are necessary in order to avoid local recurrence.

Monday, 7 September 2015, 09.30 – 10.30, Restaurant
PS-10 Poster Session Molecular Pathology

PS-10-003

Expression but not genetic variations of MTDH is correlated to clinical outcome of colorectal cancer patients

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Objective: Metadherin (MTDH;MIM#610323) is located at chromosome 8q22 and involved in carcinogenesis. Amplification of loci 8q22 has been shown in colorectal cancer (CRC) and other malignancies. MTDH polymorphisms have been related to breast or ovarian cancer susceptibility. The aim of this study was to analyze MTDH genetic alterations and expression and relationship to clinicopathological variables in CRC.
Method: We analyzed variants and expression of MTDH by direct sequencing, qPCR, and/or immunohistochemistry in 593 CRC tumours (including 158 rectal cancer patients from the Swedish clinical trial of preoperative radiotherapy (preRT)).
Results: We described 29 novel exonic/intronic variants in the MTDH gene. 4/8 exonic variants were assessed pathogenic (in silico). MTDH mRNA and protein was up-regulated in primary tumours and metastases compared with normal mucosa ($p < 0.006$). In rectal cancer patients from the Swedish trial of preRT, high MTDH expression correspond with higher risk of distant recurrence and disease-free survival ($p = 0.009$, $p = 0.007$ respectively) only in patients receiving preoperative RT, independently of the tumour stage.
Conclusion: Expression of MTDH is an independent prognostic factor for distant recurrence and disease-free survival in rectal cancer patients after treatment with preoperative RT. We did not find prognostic or predictive value of the MTDH genetic variants in CRC.

PS-10-004

A single-centre report on the clinical impact of widened predictive testing in the RAS genes for anti-EGFR therapy in Czech metastatic colorectal cancer patients

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Objective: Since late 2013 the evidence of wild type KRAS and NRAS in exons 2-4 have been required before initiating anti-EGFR treatment (cetuximab and panitumumab) in Czech metastatic colorectal cancer (mCRC) patients. The aim of this report is to show the importance of

inclussion of exon 4 of KRAS and NRAS exons 2-4 into predictive testing compare with previous testing only in KRAS exons 2-3.
Method: DNA from 219 formalin-_xed paraf_n-embedded tissue, collected between January 2014-March 2015, was isolated using QIAamp DNA Mini Kit or cobas DNA Sample Preparation Kit. Samples with ≥10 % of tumour cells were examined. Macro-/microdisection was applied when needed. Techniques based on real-time PCR and melting analysis (Diacarta;LightMix;Cobas) or multiplex PCR followed by hybridization (StripAssay, ViennaLab) were applied.
Results: KRAS mutations in exons 2 and 3 were in 36.5 %(80/219) patients. Broader testing identified additional 27.3 %(38/139) RAS mutations: 10.8 %(15/139) in KRAS exon 4, 10 %(14/139) and 6.5 %(9/139) in NRAS exon 2 and 3, respectively.
Conclusion: Extension of RAS testing revealed another 17 %(38/219) of mCRC carriers of RAS mutation who are unlikely to benefit from anti-EGFR treatment. Inclusion of other genetic factors related to prognosis and/or prediction is necessary to improve targeted therapy. This work was supported by Charles University in Prague, project PRVOUK-P27/LF1/1.

PS-10-006
Nuclear localization of CXCR4 in colorectal cancer promote liver metastasis
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Objective: The purpose of this study was to assess CXCR4 expression and explore its contribution to colorectal cancer (CRC).
Method: We examined CXCR4 expression in 124 primary colorectal tumours, 35 liver metastases tissues and matched adjacent noncancerous tissues by RT-PCR. Furthermore, the protein expression was analyzed by immunohistochemistry. The relationship between CXCR4 expression and clinicopathological features were analyzed by X2 test, Kaplan-Meier analysis were used to investigate the prognostic value of CXCR4.
Results: The relative mRNA expression of CXCR4 was significantly higher in (CRC) tissues as compared with adjacent noncancerous tissues ($P < 0.001$). The high expression of CXCR4 in cancer cells was significantly correlated with tumour grade ($P = 0.0001$), clinical stage ($P < 0.05$), and lymphatic invasion ($P < 0.05$). Furthermore, patients with CXCR4 nuclear-type expression showed more frequent lymph node metastasis ($p = 0.021$), advanced clinical stage ($p = 0.001$) and lymphatic invasion ($p = 0.03$) than those with cytoplasm staining-type. Kaplan-Meier survival curves revealed that high expression of CXCR4 was associated with poor prognosis ($P < 0.001$).
Conclusion: CXCR4 plays an important role in the progression of colorectal cancer. The present data suggest that high expression of CXCR4 enhance the liver metastases causing poor prognosis. This protein may potentially be used as an independent biomarker for the prognostic evaluation of colon cancer in the Tunisian cohort.

PS-10-007
Rapid BRAF mutation detection in melanoma patients by immunohistochemistry
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Objective: The V600E mutation is the most common (~90 %) activating mutation of the BRAF gene.BRAF mutations have been frequently investigated in melanoma, colorectal cancer and papillary thyroid carcinoma. The importance of the detection of BRAF mutations has been rising by the routine use of Braf inhibitor therapy.
Method: We evaluated the usefulness of the BRAF V600E mutation-specific monoclonal antibody (VE1) in metastatic melanoma patients. To confirm the results of immunohistochemistry (IHC), we used COBAS 4800 BRAF V600 mutation test and PCR amplification followed by Sanger sequencing.
Results: 36 of 105 patients have wild-type BRAF gene, 64 have V600E mutation and 5 of 105 have V600K mutation. Predicting the mutation only with IHC using VE1 antibody, all 58 positively scored specimen were V600E mutant. The V600K, the wild-type patients and seven patients from the V600E mutant group scored as negative. Thus the specificity is 100 % and the positive predictive value is 1 of the IHC method.
Conclusion: After processing our data we could establish a cheaper diagnostic algorithmfor rapid detection of BRAF mutation.

PS-10-008
Lymph node pooling: A cost-effective and feasible way of nodal molecular staging in colorectal carcinoma
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Objective: We propose a new economical method of colorectal cancer (CRC) molecular lymph node (LN) analysis which can be used in daily practice.
Method: We included 457 freshly dissected LN from 23 CRC patients (2 pTis, 3 pT1, 5 pT2, 5 pT3, 7 pT4). Several LN from the same patient were pooled into PCR tubes. We defined the total tumour load (TTL) as the sum of all tumour burden present in all positive LN. Molecular analysis of tumour CK19 mRNA was performed with the automated molecular assay One-Step Nucleic Acid Amplification (OSNA). LN were analyzed with both H&E and OSNA. All primary tumours were positive for CK19 immunohistochemistry.
Results: All H&E positive cases were also positive with OSNA, showing a good correlation between OSNA and H&E results. A median of 17 LN were freshly harvested per case. Pooled LN resulted in a median 2 PCR tubes per patient. Molecular analysis of 457 LN was performed in 57 runs, saving an 87.7 % of laboratory resources.
Conclusion: The concept of LN pooling reduces greatly the costs and allows analyzing a high number of LN with few molecular determinations. It can be used in selected CRC patients This new approach can be easily performed in pathology departments.

PS-10-009
Cten is regulated through the EGFR-Kras axis to control its effect on Cell motility
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Objective: Cten, which is a member of tensin family, is located at focal adhesions and involved in cell motility. It acts as an oncogene. Even the information about Cten mechanism is still limited. We had hypothesized and shown that Kras is capable of regulating Cten and that this is possibly a means of mediating Kras function. However, Kras signaling is activated by many receptor tyrosine kinases and it is possible that the pathways may be different in breast and colon cancer.
Method: In order to test a hypothesis that Cten is regulated by the EGFR-Kras-Braf axis in CRC, we sought to investigate the effect of EGFR on Cten in CRC cell lines. The C32 cells were stimulated with recombinant EGF or DMSO control. Stimulation using EGF resulted in upregulated Kras as well Cten when compared to DMSO.
Results: For the functional effect. C32 cells transfected with anti-Cten siRNA (C32cten-) had reduced cell motility following EGF stimulation compared to cells transfected with scrambled control (C32ssc). Other controls showed that, as expected, EGF did stimulate cell motility (C32ssc/EGF vs C32ssc/DMSO) and knockdown of Cten did cause a reduction in cell motility (C32ssc /DMSO vs C32Cten-/DMSO).

Conclusion: We conclude that the EGFR-Kras-Braf axis could be one of the cell motility regulation pathways in cancer.

PS-10-010

KRAS Status: Predictor in the targeted treatment of metastatic colorectal cancer

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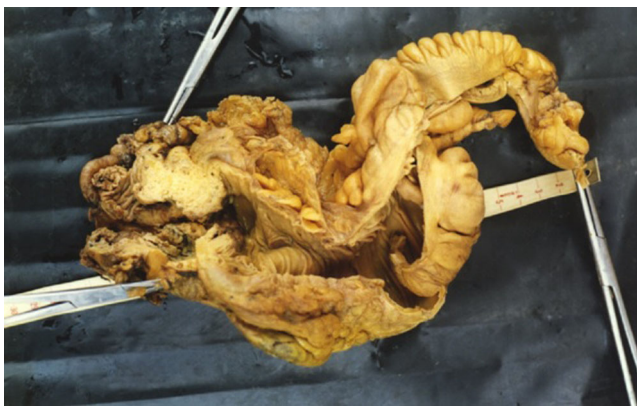
Objective: Colon cancer ranks second in the world population. This is the second cancer in terms of frequency in women and third in men. The KRAS mutations on codons 12 and 13 were observed in 40 % of metastatic colorectal cancer.
Method: Our sample includes 361 cases of which 41 are metastatic.The distribution by sex found a male predominance.The extreme age as for males are between 26–86 years old, 80 and 34 years for females. Detection of KRAS is done on fixed and paraffin-embedded tissues. KRAS genetic research was performed on 35 cases of metastatic colorectal cancer.
Results: Tissue specimens were the subject of a KRAS mutation research at codon 12 and 13 of exon 2. Ten cases had the following mutations: Six at codon 12: C.35G> T p.G12V; C.34G> T p.G12C; C.35G> T, p.G12V; C.35G> C, p.G12A; C.35G> T p.G12V; C.34G> T p.G12C. Four at codon 13; C.38G> A, p.G13D; C.38G> A, p.G13D; C.38G> A, p.G13D; C.38G> A, p.G13D. Twenty three showed no wild mutation and only two cases have been canceled for improper mounting reasons and insufficient amount of DNA
Conclusion: Oncology therapeutic response of a malignant tumour to treatment is increasingly dependent on the prediction of response before the starting of targeted therapy. Detection of KRAS status is currently an indispensable prerequisite to the use of cetuximab treatment especially for patients with metastatic colorectal cancer.

Macroscopic appearance of a malignant tumour of the colon:



PS-10-011

AR gene expression changes after epigenetic inhibitors treatment in normal and prostate cancer cell lines

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Objective: Androgen receptor (AR) plays an essential role in prostate cancer (CaP) progression. A castration-resistant prostate cancer (CRPC) is developed as a consequence of androgen deprivation therapy. Epigenetic regulation through DNA methylations and histone acetylation can affect androgen receptor signaling pathways. In some cases, in the CRPC a decrease expression of the AR gene due to DNA methylation silencing were shown. Our objective was to elucidate effects of DNA methyltransferase (5-Aza-2′-deoxycytidine, Aza-dC) and histone deacetylase (Sodium butyrate, NaB) inhibitors on expression of methylated AR gene in androgen-independent prostate cancer cells representing a CRPC model.
Method: Normal and androgen-independent prostate cancer cell lines were treated with Aza-dC, NaB and their combinations. The AR gene expression was determined at the cDNA level and using chromatin immunoprecipitation with following qPCR.
Results: In treated cells, restored AR gene expression was detected, which was accompanied with increased histone H4 acetylation upon co-treatment with the inhibitors.
Conclusion: Synergic/additive effect of the HDAC and DNA methylation inhibitors in cell model imitating the CRPC condition may contribute to influence the CRPC therapeutic strategy.

PS-10-012

An immunohistochemical and molecular study of MUC1 and MUC5AC in colorectal carcinoma genesis and progression in 135 cases

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Objective: Colonic mucins expression such as MUC1 and MUC5AC is altered in colorectal cancer. The aim of this study is to evaluate these two mucins involvement in 135 cases of colorectal carcinoma.
Method: We investigate MUC1 and MUC5AC expression and their implication in colorectal carcinogenesis using immunohistochemical and reverse transcriptase polymerase chain reaction (RT-PCR) analysis.
Results: MUC1 immunohistochemistry staining show high positivity in advanced tumour invasion stages pT3 and pT4 ($p = 0.003$) and lymph node metastasis ($p = 0.009$), while MUC5AC is considerably increased in precoce colorectal adenocarcinomas pT1 and pT2 ($p = 0.033$). Thereby, MUC1 and MUC5AC expressions are related inversely to tumour differentiation. RT-PCR amplification of MUC1 gene is correlated with both immunohistochemical profile ($p = 0.000$) and colonic localization ($p = 0.004$). Note that as for MUC5AC, the molecular results show no significance when compared with clinicopathologic features and immunohistochemical profile.
Conclusion: Our results suggest that the lack of Muc5AC staining versus positive mRNA expression in advanced colorectal carcinomas may be due to proteomic alteration such as hypermethylation. Conversely, we conclude that MUC1 expression is significantly associated with colorectal progression and may provide useful prognostic information for Tunisian patients with colorectal cancer.

PS-10-013

CCR5 Delta 32 implication in the carcinogenic process of the primitive colorectal adenocarcinomas among Tunisian patients

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Objective: Chemokines along with their receptors are heavily involved in many carcinogenesis processes such as colorectal cancer (CRC). This study aims to elucidate whether C-C chemokine receptor 5 gene (CCR5Δ32) polymorphism is related to CRC risk.
Method: CCR5 gene mutational status is analyzed, through a panel of 108 sporadic primitive CRC cases and 248 peripheral blood cases from healthy control subjects, using polymerase chain reaction (PCR) technique. The receptor expression is evaluated using immunohistochemistry performed on normal mucosa and tumours.
Results: The wild allele "wt" frequency in controls was 0.93 versus 0.97 in CRC cases, whereas rare allele "Δ32" frequency in controls was more recurrent at 0.07 as against 0.03 in colorectal carcinoma. No association was

observed between CCR5Δ32 variant and CRC clinicopathologiccriteria. Conversly, CCR5 wild type showed a significant risk of 4.13-fold (95 % CI = 1.42–11.09) to cause CRC compared to individuals carrying the mutated gene Δ32. Statistical analysis of CCR5Δ32 immunohistochemical profile and the different prognostic parameters showed no correlation. However, the wild allele expression displayed a significant association with tumour differentiation degree ($p \leq 0.001$) and non-mucinous carcinomas ($p \leq 0.001$).
Conclusion: We suggest that CCR5Δ32 may be a protective factor against CRC development.

PS-10-014
Differential expression of p63 isoforms: TAp63 and DeltaNp63 counterbalance in colorectal cancer among 63 Tunisian patients
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Objective: TP63 is a p53-related gene, is an important regulator of epithelial development, that contains two alternative promoters, which give rise to transcripts that encode proteins with (TAp63) or without (ΔNp63) an amino-transactivating domain.
Method: We examined the expression pattern of p63 in tumour tissues of CRC by immunohistochemistry, and by RT-PCR using isoform-specific primers to determine the variant distribution.
Results: Of 63 patients with CRC, 51 cases (81.0 %) showed positive mRNA expression for p63 while 12 cases (19.0 %) were negative. Analysis of colorectal carcinoma shows TAp63 to be the most widely expressed isoform (45/51), whilst ΔNp63 transcript expression is detected in 19 cases. We found that (88.2 %) of p63-positive subset express TAp63 ($p < 0.0001$). Of According to clinicopathological variables, no significant association was detected with TAp63 isoform through our statistical analyses except with well differentiated tumours ($p = 0.020$). However, ΔNp63 were found to be occurring in women patients ($p = 0.028$) and seemed to occur more frequently in the left colon ($p = 0.033$). For the immunoreactions we did not observe any correlation between p63 expression and clinicopathologic features because p63 was negatively expressed in the epithelial component in all cases examined.
Conclusion: Altogether, these results highlight the importance of Counterbalance among the different p63 isoforms during CRC progression.

PS-10-015
KRAS mutation testing in colorectal cancer: The convenience of using at least two methods
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Objective: We have investigated whether availability of two or more methods (as opposed to just one) decreases the number of false negative results when determining KRAS mutation in colorectal carcinoma (CRC).
Method: 79 paraffin-embedded CRCs were evaluated for KRAS mutation using both KRAS 12/13/61 Strip Assay® (Vienna Lab) and Therascreen® KRAS Pyro Kit (Qiagen). Discordant results were resolved by Sanger sequencing.
Results: Of the 79 CRCs, both methods showed KRAS mutation in 39 cases and wild-type KRAS in 37 cases. The remaining 3 cases showed discordant results: in the first case KRAS mutation was detected only with the more sensitive Strip Assay® (tumour cell percentage in the sample was low even after macrodissection); in the second case KRAS mutatation was detected only with Therascreen® (Sanger sequencing showed a Gly 12 duplication, which is not covered by Strip Assay®); in the third case KRAS mutation was detected only with Therascreen® (it analyzes a shorter amplicon than Strip Assay®, a significant advantage with poor-quality DNA).
Conclusion: The various methods for KRAS mutation detection have different advantages and limitations. Availability of more than one method and its selection depending on the sample characteristics could prevent false negative results and resolve doubtful cases.

PS-10-016
The cartridge-based express method for detection of cervical pathology
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Objective: High-risk human papillomavirus (HR-HPV) is the main etiological factor in development of cervical cancer. The aim of our study was to compare the results of HPV testing using GeneXpert HPV and Cobas on cytological material with cervical pathology. Both methods detect 14 types of high risk HPV. Xpert HPV is cartridge-based random-access platform, where testing can be completed in 1 h.
Method: Liquid-based cytology (B&D, TriPath) of 80 women, p16(INK4A)/Ki67 double immunocyto-histochemical staining (CINtec PLUS Cytology Kit), Xpert HPV, Cobas testing were performed. All methods were compared with biopsies (histology).
Results: HPV DNA testing results were obtained in 78 samples (22 H-SIL, 21L-SIL, 17 ASC-US, 18NILM) and were matched in 77 of 78 cases (98,7 %), two samples were invalid. Cobas test was negative in one case L-SIL (histology CIN I), while Xpert was positive.
Conclusion: Xpert HPV is a rapid and reliable method for detecting HPV DNA high risk types in cytological samples and can be used not only in diagnosis but also in screening for precancer and cancer of the cervix.

PS-10-017
Quality assessment of HER2 testing: Results of a two years study through method optimization and standardization in Albania
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Objective: Preanalytical variation produces a range of artifacts on examination results. Consequences of those variations are loss of confidence on the results, false negative/positive, and possibly the expense of repeating an examination. Considering the importance of IHC and SISH examination in clinical diagnosis, as a need arises it's standardization and routine involvement in the laboratory of pathological anatomy at University Hospital Center "Mother Teresa".
Method: We collected samples monthly and correlated HER2 gene status with IHC scores. 60 patients with Ad.Ca of gastrointestinal tract, who were proved as HER2 (2+) were taken in exam. HER2 gene amplification for these patients was assessed by silver in situ hybridization method (SISH) with Ventana BenchmarkXT.
Results: From 38 patients analyzed with SISH method, 45 % (17) of them showed problems and were unable to be interpreted. Among the problems encountered included the presence of black/red haze, presence of peripheral signal, poor staining, lack of signal etc. Discrepancies were mostly seen in tumours with intra-tumoural heterogeneity of HER2 amplification.
Conclusion: Routine HER2 tests, such as IHC and SISH, are subject of preanalytical variation, and validation is important to improve standardization. To limit preanalytical variation, its sources must be identified, the effects documented, and measures devised to eliminate its sources. Equivocal IHC and borderline SISH cases are difficult to interpret, even for highly experienced and validated laboratories, highlighting the need for quality-control procedures.

PS-10-018

High microsatellite instability in human colon cancer is associated with wild-Type p53 and unmethylated MLH1

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Objective: Colorectal cancers with high levels of microsatellite instability (MSI-H) are generally associated with aberrant methylation of hMLH1 promoter and wild type p53 gene. In the current study, we aimed to investigate the association between MSI status, with p53 mutation and hMLH1 methylation pattern in a cohort of Tunisian sporadic colorectal cancer.
Method: The MSI status was analyzed by microfluid-based on-chip electrophoresis. The p53 alteration was investigated by PCR and sequencing. The hMLH1 promoter gene methylation was determined by methylation-specific PCR.
Results: Statistical analysis show that of the 150 colorectal cancers 57 % were MSS, 28 % were MSI-L and 15 % were MSI-H. Most of the MSS/MSI-L (74 %) cancers were p53 mutated, while 26 % MSI-H cancers were p53 wild type ($p < 0.001$). Note that however the MSI status hMLH1 promoter remained unmethylated.
Conclusion: In colorectal cancer, p53 mutation is associated with MSI-H. This result provides a possible explanation for the paucity of p53 mutations in colon cancers with microsatellite instability. The relative correlation of MLHh1 promotor hypermethylation for the MSI status is similar to that reported for several study.

PS-10-019

Topoisomerase I and tyrosyl-DNA phosphodiesterase 1 activities are upregulated and correlate in non-small cell lung cancer tissue

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Objective: Chemotherapeutic drugs of the camptothecin family exert their anticancer effect by inhibiting the enzyme topoisomerase I (TOP1). This effect can be counteracted by tyrosyl-DNA phosphodiesterase 1 (TDP1). Therefore, this study was conducted to determine to what extent the enzymatic activities of TDP1 and TOP1 are increased in non-small cell lung cancer (NSCLC), and if the activities correlate in tumour and non-tumour tissue.
Method: Two biosensors previously used for measuring enzymatic activity in extract from cell lines were validated for use in cryosections and subsequently used for measurement of TDP1 and TOP1 activities in cryosections from paired tumour and non-tumour NSCLC tissue.
Results: Both TDP1 and TOP1 activities were upregulated in the tumour compared to the non-tumour tissue (20/20 and 14/17 patients, respectively). Furthermore, a correlation was observed between TDP1 activity and tumour percentage and between TDP1 and TOP1 activity in both types of tissue. An even stronger correlation was observed when comparing the changes in TOPI and TDP1 activities (change = activity in the tumour tissue / activity in the non-tumour tissue).
Conclusion: TDP1 and TOP1 activities are upregulated and correlate in NSCLC tissue, suggesting that chemotherapeutic treatment with camptothecin derivatives could be useful in NSCLC if combined with a TDP1 inhibitor.

PS-10-020

Simultaneous detection of HER2 protein overexpression and HER2 gene amplification in gastric cancer biopsy specimens using the gene-protein assay

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Objective: Gastric cancer (GC) represents a serious global health care problem with more than 900,000 newly diagnosed patients and 700,000 deaths per year. The median survival is only 8–10 months and 5-year survival rate is only 7 %. The status of HER2 protein/gene represents an important biomarker for targeted therapy.
Method: In the period Nov 2013–March 2015 we used a new method known as "gene-protein" assay (GPA) to examine 193 diagnostic biopsies of GC patients with aim to identify cases with positive HER2 status. In selected cases, we used a separate immunohistochemical analysis (IHC) of HER2 protein expression as well.
Results: 80 % (155/193) of patients showed negative HER2 protein/gene status. HER2 gene amplification was identified in 16 % (31/193) of patients, however, up nearly 1/3 of these cases lacked expression of HER2 protein. In 4 % the HER2 protein/gene status could not be identified due to insufficiency of GC cells.
Conclusion: GC often shows incomplete membrane staining and heterogeneity (focal staining) of HER2 protein IHC expression and of gene amplification examination caused by intratumoral heterogeneity. From this point of view, the method GPA is very suitable method to distinguish patients who may benefit from targeted therapy.

PS-10-021

Gastric carcinoma CDH1 genetic variants associated with survival of patients

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Objective: Due to the phenotypic and molecular diversity of gastric cancer (GC), it is a challenge to determine a patient's prognosis. Several CDH1 germline variants of the invasion suppressor E-cadherin are present in early onset of GC, but the pathogenetic significance of most of them are largely unknown. We aimed to find prognostic markers related to CDH1 variants of patient with GC.
Method: We collected 124 GC samples from patients at CRO (2009–2014), IRCCS in Italy. We analyzed the germline CDH1 sequence variants and compared them with patients survival. We used log-rank test and Kaplan-Meier method to asses survival. Helicobacter pylori infection and pathological data from samples were used as covariable factors.
Results: CDH1 missense mutations spans through the entire CDH1 coding regions and a mutation that affects the precursor region of the protein, a region that is normally cleaved to generate the mature protein, were associated with disease-specific survival times of 9 patients with GC patients (hazard ratio = 0.22; 95 % CI: 0.003 to 0.398, $P = 0.06$). The mutation of the precursor region was both associated with disease survival and histological HP infection.
Conclusion: Missense mutations of CDH1 codying regions and mutation of the precursor region are associated with outcomes of patients with GC. The prognostic accuracy of the CDH1 mutation would be validated in a further series. We proposed to test CDH1 mutations as a tool to stratify patients for therapeutic decisions.

PS-10-023

Global DNA methylation status of multiple myeloma patients compared with DNA methyltransferase expressions

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Objective: DNA methyltransferases DNMT1, DNMT3a and DNMT3b play important role in epigenetic regulation, which is involved in pathogenesis of monoclonal gammopathies. The aim of our study was to analyze the expression of these DNA methyltransferases and to compare it with the global methylation status of patients.

Method: DNA was obtained from unsorted cell population in bone-marrow aspirates of 30 patients with multiple myeloma (MM) or monoclonal gammopathy of undetermined significance. MethylFlashTM methylated DNA quantification kit was used for the colorimetric detection of the global methylation status. After reverse transcription of the isolated RNA, the cDNA was used for DNMT1, DNMT3a and DNMT3b express analysis by the real-time PCR.
Results: The percentage of methylated DNA varied between 0, 5 and 3 % in the examined group, which is not distinctly different from physiological state (5-methylcytosine constitutes app. 1,5 % of human genomic DNA). Increased DNMT3a and/or DNMT3b expressions corresponded with higher percentage of methylated DNA in some individual cases.
Conclusion: Our pilot study results suggest positive correlation between DNMT3a and/or DNMT3b expressions and the level of de novo methylation in the global methylation status. A cohort enlargement might bring useful information with respect to the activity of MM. Supported by IGA MZ CR NT14393 and LF_2015_008.

PS-10-024

Synchronous serous peritoneal carcinoma and infiltrating mucinous appendicular adenocarcinoma: Immunohistochemical and molecular study

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Objective: Molecular studies in poor cellular material can help in daily diagnosis.
Method: Case Report: 67 years old woman had increased CA125, CA53, normal CEA and ascites with peritoneal carcinomatosis. Laparoscopic exploration with biopsies demonstrated mucinous perforated appendicular tumour with extra-appendicular acellular mucin and serous carcinoma peritoneal implants with characteristic immunoprofile. KRAS mutation studies were done in both components suggesting the presence of synchronous carcinoma. Patient received neoadjuvant chemotherapy and cytorreduction surgery. Final histology showed infiltrating appendicular mucinous adenocarcinoma and peritoneal infiltrating serous carcinoma. Focally, both components were admixed. Immunohistochemistry and molecular studies confirmed existence of 2 carcinomas.
Results: Immunohistochemstry: Mucinous adenocaricnoma was positive for: CK20,CK7,CA125,CEA,CDX2 and P53. Negative for ER/PR,WT1 and PAX8. Serous carcinoma was positive for CK7,CA125,ER/PR,WT1, PAX8 and negative for CK20,CEA,CDX2,P53. Molecular studies: KRAS mutation (G12D) was found in acellular mucin and mucinous adenocarcinoma and was WT in serous carcinoma. BRAF was WT everywhere and we found LOH OF 18q and 17p in mucinous adenocarcinoma but not in serous carcinoma.
Conclusion: Different immuno and molecular profiles provided a proper diagnosis of two independent neoplasms. We emphasize the finding of mutations in the acellular mucin demonstrating the value of molecular analysis.

PS-10-025

Assessment of a new FISH hybridization buffer that enables fast-track: Single shift FISH results

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Objective: A typical FISH assay requires an average of 2 days to complete once the specimen is affixed to a slide, mainly due to an overnight hybridization step. Generally, there is a need to improve laboratory workflow, and decrease turn-around time to results which facilitates rapid results for doctors and patients. To that end, a new fast working Vysis Hybridization Buffer has been developed to facilitate single shift FISH results.
Method: Ten FISH probes were formulated in either fast working Vysis Hybridization Buffer or Vysis LSI/WCP Hybridization Buffer. Probes were applied to cytological or FFPE specimens adhered to glass slides by standard cytogenetic techniques. Probes in fast working Vysis Hybridization Buffer were hybridized 1 to 2 h and probes in Vysis LSI/WCP Hybridization Buffer were hybridized 16 h.
Results: The overall time to result that yielded optimal hybridization quality in fast working Vysis Hybridization Buffer ranged from 3 to 6 h whereas in Vysis LSI/WCP Hybridization Buffer it ranged from 17 to 20 h for cytological and FFPE specimens, respectively. Hybridizations were evaluated for probe signal intensity, specificity, background and overall quality using a 1 to 5 scale. A target was considered passing when the overall quality score was ≥3. Passing results were observed for all ten probes when hybridized in both buffers.
Conclusion: The new, innovative fast working Vysis Hybridization Buffer demonstrated the ability to complete FISH hybridizations within a single work shift (on average <6 h) by using a 2 h hybridization for all specimen types, reducing overall assay time to 3 to 6 h from the standard 17 to 20 h.

PS-10-026

NKX6.3 controls gastric differentiation and inhibits gastric carcinogenesis

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Objective: We investigate whether the NKX6.3 gene plays a role in the gastric carcinogenesis.
Method: We analyzed mutations, epigenetic alterations, DNA copy number change, and mRNA and protein expression of NKX6.3 in 35 gastric carcinomas. Stable AGSNKX6.3 and MKN1NKX6.3 cells expressing NKX6.3 were used to investigate the molecular basis underlying NKX6.3 function in cell proliferation, differentiation, and death.
Results: Absence of the NKX6.3 protein expression was observed in 88.2 % of gastric carcinomas, while no mutation and hypermethylation of the NKX6.3 gene were detected. Interestingly, DNA copy number and mRNA transcript expression of NKX6.3 were significantly decreased in gastric cancers and showed a positive correlation in both non-cancerous gastric mucosa and cancer tissues ($P < 0.05$). In addition, ChIP followed by DNA sequencing demonstrated that NKX6.3 modulates a repertoire of target genes, some of which are clearly implicated in regulation of cell cycle progression, differentiation and death. Furthermore, we were able to determine the binding site of NKX6.3 in the upstream sequences of GKN1. Expression of NKX6.3 was sufficient to inhibit cell proliferation and induce apoptosis in GKN1-dependent and -independent manners.
Conclusion: NKX6.3 controls the fate of gastric mucosal epithelial cells and functions as a gastric tumour suppressor.

PS-10-027

A cost efficient method for diagnosis, prognosis and therapy in neuroendocrine tumours

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Objective: Neuroendocrine tumours (NETs) are epithelial neoplasms that have different behavior from indolent tumours to clinically aggressive, poorly differentiated carcinomas. The objective of the study was to investigate small cell and poorly differentiated lung carcinomas in order to

identify an alternative, cost efficient, method for the immunohistochemical testing by performing a qRT-PCR reaction.
Method: RNA was extracted and processed according to protocols (Qiagen). c-DNA was tested by qRT-PCR using our customized array which included 18 genes of interest, two reference genes, a control for genomic DNA contamination, two reverse transcription controls and a control for amplification efficiency.
Results: In the case of small cell carcinoma of the 18 genes studied, 16 were overexpressed, a gene was downregulated (GRPR) and a gene expression showed unchanged (CCND1). For poorly differentiated lung carcinoma genes were overexpressed five (GAST, VGF, MKI67, TYMS, GRPR), 2 genes showed unchanged expression (SSTR2 and mTOR), while the remaining 11 genes were downregulated.
Conclusion: Our study focused on a novel approach in the diagnostic of NET both on the basis of the clinical, prognostic and therapeutic response and from a more technical and economical point of view (time management and cost vs benefit). The study was supported by Project RENET-PN-II-PT-PCCA-2011-3.2.0623 91/20012 and Project PERSOTHER - SMIS-567CSNR: 549/12.024.

PS-10-028
KRAS - BRAF interrelationships in colorectal cancer: Correlation with DNA Methylation
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Objective: Colorectal cancer (CRC) is a major public health problem being the third leading cause of mortality by cancer. Mutational activation of KRAS and BRAF gene and methylation of CpG islands play an important role in colorectal cancer progression.
Method: We studied tumour fragments from 30 patients with CRC and determined mutation status of KRAS and BRAF gene and methylation levels of DNA.
Results: The analysis revealed increased levels of DNA methylation in the tumour tissue compared with normal colon mucosa for 21 genes studied, except CDH1 gene (p = 1.8 E-6); we obtained similar results in the case of tumour tissue versus peritumoral tissue (p = 0.0006). Regarding the mutational status of the KRAS and BRAF gene, significant differences were observed between the tumour tissue with the mutation and the wild type, identifying high levels of methylation for all genes in tumour tissue with the mutation, except RUNX3 gene.
Conclusion: Identification of KRAS and BRAF gene mutations and DNA methylation levels is a sensitive and specific marker for both the establishment of a molecular classification and for diagnosis and prognosis in CRC. This work was supported by POSDRU/159/1.5/S/133391 and POSCCE173/2010

PS-10-029
MicroRNA signature in colorectal carcinoma
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Objective: Dysregulation of miRNAs may represent a diagnostic and prognostic biomarker in colorectal carcinoma. MicroRNAs are small non-coding RNA molecules of 21–25 nucleotides complementary to a partial sequences of one or more messenger RNA molecules. Because of this partial complementarity, miRNA molecules can alter mRNA activity involved in the regulation of cellular development, differentiation, proliferation and apoptosis.
Method: In our study we used fresh-frozen fixed in RNA later and FFPE specimens of colorectal tumours. We conducted a comparative study tumoural versus peritumoral tissue.
Results: We selected 24 samples (18 tumoural, 6 peritumoral) which were studied using Human Cancer Pathway Finder miRNA PCR Array. Analysis of the results was performed using the software "Free miRNA PCR Array Data Analysis", peritumoral tissue group representing the reference group. We identified 2 overexpressed miARNs (miR-373-3p, miR-203a), and 7 downregulated (miR-378a-3p, miR-132-3p, miR-138-5p, miR-124-3p, miR-144-3p, miR-215, miR-39-3p).
Conclusion: Dysregulation of miRNAs in CRC represent an important additional molecular prognostic marker, with implications in early detection and therapy and thus is a promising candidate in the better stratification of CRC patients. This work was supported by POSDRU/159/1.5/S/133391 and POSCCE 173/2010.

PS-10-030
Parallel Fluorescence in Situ Hybridisation (FISH) and Immunohistochemistry (IHC) for the detection of the ALK translocation in Non-small Cell Lung Cancer (NSCLC): The Birmingham experience
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Objective: A subset of patients with NSCLC and rearrangement of the ALK gene gain dramatic benefit from crizotinib treatment. There is still controversy over the best method for ALK testing.
Method: This series included all 3317 requests for NSCLC ALK testing received by our service in 2013-2014. Parallel FISH and IHC tests were performed for each case using the validated Vysis Abbott break apart FISH probes and the Ventana D5F3 antibody on the Ventana XT platform.
Results: 2973 cases were successfully tested with both methods. Of these 95 (3.2 %) were FISH+. Patients with ALK positive tumours were younger than those with ALK negative tumours (mean 63 and 69 years respectively; $p < 0.001$). IHC had a sensitivity of 73.7 % and a specificity of 99.9 % compared with FISH. There were 23 IHC-/FISH+ tumours and only 2 IHC+/FISH- tumours.
Conclusion: This is the largest series of ALK testing in lung cancer using parallel IHC and FISH yet described. The overall rate of ALK positivity is concordant with previous studies. Before IHC is introduced as a prescreening or surrogate for FISH the clinical significance of IHC-/FISH+ cases needs to be determined. We are now trying to obtain data about response to crizotinib for the IHC-/FISH+ cases in this series.

PS-10-031
Prevalence of germline mutations in genes engaged in DNA damage repair by homologous recombination in patients with triple-negative and hereditary non-triple-negative breast cancers
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Objective: To assess the prevalence of germline mutations in genes engaged in the repair of DNA double-strand breaks by homologous recombination (HR) in patients with triple-negative breast cancer (TNBC) and hereditary non-triple-negative breast cancer (Hn-TNBC). Tumours deficient in this type of DNA damage repair are known to be especially sensitive to DNA cross-linking agents and to PARP inhibitors.
Method: Genetic testing was performed for 36 common germline mutations in BRCA1/2, CHEK2, NBN, ATM, PALB2, BARD1, and RAD51D, in 202 consecutive patients with TNBC and Hn-TNBC.

Results: Altogether 22.2 % of patients in the triple-negative group carried mutations in genes involved in DNA repair, while 22.7 % of patients in the Hn-TNBC group carried such mutations. Mutations in BRCA1 were most frequent in patients with TNBC (18.4 %), and mutations in CHEK2 were most frequent in patients with Hn-TNBC (15.9 %). In addition, in the triple-negative group, mutations in CHEK2, NBN, and ATM (3.8 % combined) were found, while mutations in BRCA1, NBN, and PALB2 (6.8 % combined) were identified in the Hn-TNBC group.
Conclusion: Identifying mutations in genes engaged in DNA damage repair by HR other than BRCA1/2 can substantially increase the proportion of patients with TNBC and Hn-TNBC who may be eligible for therapy using PARP inhibitors and platinum drugs.

PS-10-032
Modulation of eukaryotic translation initiation factor expression in colorectal carcinoma by cytostatic and targeted medication as demonstrated in xenograft models
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Objective: Therapy of advanced stage colorectal carcinoma (CRC) includes both cytotoxic and targeted agents. Mutations of the targets and/or in proteins downstream of the targets may lead to therapeutic resistance. The eukaryotic translation initiation factors (eIFs) are functionally linked to putative therapeutic targets of the MAPK and the mTOR pathways. The study aimed at analyzing the influence of therapeutic cancer drugs on the expression of eIFs and members of the mTOR pathway.
Method: Xenografts in nude mice derived from 14 different surgical CRC specimens were treated with a panel of cytotoxic and targeted drugs. Western Blot and qRT-PCR for most eIF subunits and mTOR pathway members were performed. Untreated xenografts and non-neoplastic tissue served as controls. Statistical analysis was performed accordingly.
Results: Western Blot and qRT-PCR analysis of all treated xenograft tumours revealed a significant up-regulation of eIF subunits 2α, 3a, 3b, 3j, 4b, 4g and 5 and also a higher expression of mTOR, phospho-PTEN and PTEN compared to control ($p < 0.01$).
Conclusion: Our findings suggest that expression of eIFs and the RTK/PI3K/AKT-mTOR cascade in CRC can be modulated by cytotoxic and biological medication. In addition, eIFs themselves may be potential therapeutic targets.

PS-10-033
KRAS and NRAS mutations in metastatic Colorectal Cancer (CRCm) analyzed by pyrosequencing
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Objective: Around 50 % patients with metastatic colorectal cancer (CRCm) harbor KRAS mutations in exon 2 and do not benefit from anti-epidermal growth factor receptor (EGFR). Other activating RAS mutations are now established as negative predictive biomarkers for anti-EGFR therapy. Additional mutations in exons 3 and 4 of KRAS together with mutations in the same exons of NRAS have been detected in around 15 % of patients in different series. We determine the mutational status of 80 consecutive cases of CRCm, to observe the prevalence of different mutations in these exons.
Method: Pyrosequencing was performed using PyroMark Q24 with therascreen PyroKits (KRAS, NRAS, RAS extension) (Qiagen) on DNA extracted from FFPE tumour samples. To analyze RAS extension codons, a simultaneous known wild-type sample was performed in every run, and differences >10 % with wild-type sample in peak height were considered positive.
Results: 36 % of different mutations were detected in exon 2 (codons 12/13) of KRAS. An additional 14 % showed other mutations: KRAS (p.Q61H, $n = 1$; p.A59T, $n = 1$; p.A146T, $n = 4$); NRAS (p.G12C, $n = 1$; p.G12S, $n = 1$; p.G13R, $n = 2$; p.Q61L, $n = 1$).
Conclusion: Studying mutations other than exon 2 of KRAS allows us to detect 14 % additional patients who do not respond to anti-EGFR therapy.

PS-10-034
Preclinical investigation of new iron-oxide nanosystems-towards theranostic in cancer
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Objective: Develop a preclinical study on new nanostructures for theranostics in dispersed peritoneal microtumors.
Method: We used new iron oxide nanoparticles with L-DOPA-functionalized surface for improving nanoparticle disperssion in physiologic media. Nanostructures were intraperitoneally administered to C57BL/6 mice (100 mg/kg b.w.), and mice were thereafter housed in metabolic cages in controlled environmental conditions. Animals were sacrificed by cervical dislocation at various moments after nanostructures inoculation, and we studied the histopathological changes in various organs.
Results: Intraperitoneal administration of L-DOPA-conditioned nanoparticles to C57BL/6 mice induced the following histologic changes: a) persistent decrease of blood lymphocytes and platelets counts, along with the increase of eosinophil percentage (possible allergic reaction); b) dystrophic alterations in the renal parenchyma; c) regenerative alterations in liver parenchyma; d) vascular hyperemia in the brain tissue.
Conclusion: Our data suggest that L-DOPA-conditioned nanoparticles, administered intraperitoneally, have an acceptable toxicological profile. If loaded with anti-tumour drugs, they might be promising candidates for simultaneous imaging and cytotoxic therapy of dispersed microtumors in the peritoneum. This paper is partly supported by the Sectorial Operational Program Human Resources Development (SOPHRD), financed by the European Social Fund and the Romanian Government under the contract number POSDRU 141531.

PS-10-036
Genetic heterogeneity of colorectal carcinoma in NGS analysis: A complication for molecular diagnosis?
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Objective: Genetic analysis of colorectal carcinomas by next generation sequencing (NGS) is becoming a routine method in modern pathology. Tumour heterogeneity might be a confounding factor for these analyses, especially if it does not result in morphologically distinct tumour subtypes. The objective of this study was to determine if genetic heterogeneity exists in morphologically identical areas of the same colorectal carcinoma, and if this molecular heterogeneity can potentially influence the accurate genetic analysis of colorectal carcinoma.
Method: Six morphologically homogeneous colorectal tumours classified as invasive with spreading to regional lymph nodes were included in the study. In each case, DNA was extracted from four tumour areas by manual micro-dissection. Mutation analysis was performed using the Ion Torrent Comprehensive Cancer Panel.

Results: The analysis of the coding sequence of 409 cancer related genes in multiple areas of histologically homogeneous tumours revealed a total of 30 somatic mutations. In five of the cases all variations of mutated allele frequencies could be explained by different tumour cell content of the analyzed tissue areas. However, in one case a mutation of the FANC D2 gene was present in allele frequencies inconsistent with tumour cell content and distinct from other mutations in the four tumour areas. A mutation specific pyrosequencing assay confirmed this result, suggesting the presence of a tumour subclone harboring the mutation.
Conclusion: Genetic heterogeneity of morphologically homogeneous colorectal carcinoma is a rare event. Unusual frequencies of mutated alleles, which do not match the estimated tumour content of the sampled areas, could be explained by subclonal genetic heterogeneity.

PS-10-038
IDH1 reactivity and mosaic IDH1 or IDH2 somatic mutations in solitary enchondroma and enchondromatosis
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Objective: Somatic mutations in the IDH1 and IDH2 genes occur in most enchondromas. Next Generation Sequencing (NGS) may allow detection of even low-level mosaic mutation rates. IDH1 immunohistochemistry and NGS results are compared.
Method: IDH1 R132H reactivity (Clone H09, Dianova) was assessed in 8 enchondromas from 6 patients. Tumours were multiple in three patients, in the setting of enchondromatosis. NGS was performed on DNA extracted from paraffin blocks using the Ion AmpliSeq™ Cancer Hotspot Panel v2. Tumour content was close to 100 %.
Results: IDH1 reactivity, and IDH1 or IDH2 mutations were seen in all tumours. NGS showed concordant results in the two patients with paired tumours. A majority of tumours harbored IDH1 mutations (p.R132C in 3 tumours from 2 patients; p.R132L, p.R132G, and p.R132H mutations in one tumour each). An IDH2 mutation (p.R172S) was identified in the 2 tumours from one patient with Ollier disease. Heterozygous mutation rates varied between 14 % (indicative of mutations in 28 % of the cells), and 45 %. Interestingly, strong IDH1 R132H reactivity was seen in the 2 tumours harboring an IDH2 mutation.
Conclusion: This study confirms that IDH1 or IDH2 mutations occur in a mosaic fashion in enchondromas. IHC was found to display cross-reactivity.

Tuesday, 8 September 2015, 09.30 – 10.30, Restaurant
PS-11 Poster Session Dermatopathology

PS-11-001
Chondroid Syringomas: A clinicopathological analysis
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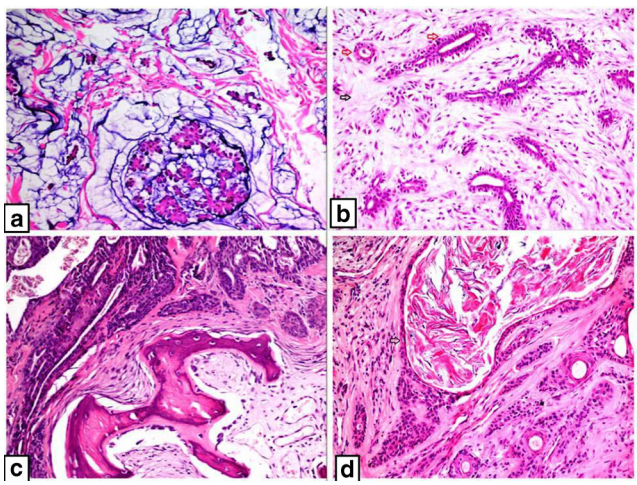
Objective: Chondroid syringoma is a rare benign skin adnexal tumour composed of both epithelial and mesenchymal components, and is known as a cutaneous mixed tumour. Their clinical pre-diagnoses are generally incorrect, and an exact diagnosis can only be made with histopathological investigations. The aim of this study was to determine the clinicopathological findings of the cases diagnosed with chondroid syringoma.
Method: In this study, over the period from January 2008 to March 2014, a total of 2661 excised skin lesions were evaluated for the clinicopathological findings, and 15 cases were diagnosed with chondroid syringoma. Various parameters such as gender, mean age, tumour localization and immunohistochemical markers (pan-cytokeratin, vimentin, S-100 protein, CEA-(M) and p53 were examined.
Results: Of the15 cases diagnosed with chondroid syringoma, 10 (67 %) were male and 5 (33 %) were female. The mean age of the patients was 46 (range 11–80 years).The chondroid syringomas were positive for pan-cytokeratin (87 %), vimentin (100 %), S-100 protein (100 %), CEA-M (53 %) and p53 (80 %).
Conclusion: Chondroid syringomas should be included in the differential diagnosis of a slowly growing, nodular mass in the dermis. Definitive diagnosis of the tumour is made by histopathologic examination. Difficult cases may benefit from immunohistochemical examination.

Figure 1: a: Apocrine type tubular structures (arrow black) within a chondromyxoid stroma b: Eccrine type tubular (red arrow) structures within a chondromyxoid stroma (black arrow) c: Bone formation within a chondromyxoid stroma d: Epithelial nests, tubuloalv:



PS-11-002
IgG4-related disease with primary cutaneous manifestation: A report of 3 cases
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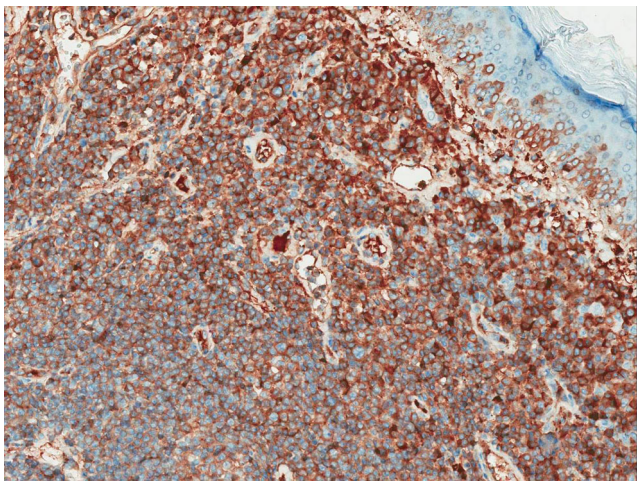
Objective: IgG4-related disease is a recently recognized fibro-inflammatory condition characterized by formation of tumour-like lesions with dense lymphoplasmacytic infiltrate rich in IgG4 plasma cells, storiform fibrosis and sometimes elevated serum IgG4 concentrations. Primary cutaneous manifestation in IgG4-related disease is uncommon and in virtually all cases represents a diagnostic dilemma.
Results: All cases were males (63, 37 and 39 years old; mean 46.3 ± 11.8), presented with a single slowly-growing painless well-

circumscribed reddish skin lesion (2 located on the lateral side of the trunk, and 1 on the forearm), irregular in shape. A size varied from 2.0 × 2.0 to 17.0 × 8.0 cm, all lesions were slightly elevated. Skin biopsy was performed in all cases. H&E stained slides microscopy revealed diffuse extensive lympho-plasmocytic infiltration of the papillary and reticular dermis, together with dermal fibrosis and edema. Immunohistochemical study with antibodies to IgG, IgG4, CD3, CD20, Kappa and Lambda was performed and revealed the elevated numbers of IgG and IgG4-positive plasma cells within the infiltrate (>30 positive cell per HPF) as well as lack of lymphatic cells clonality (equivalent Kappa and Lambda expression levels). Plasma IgG-4 level was elevated in 2 cases (not tested in 1 case).
Conclusion: IgG-4-related disease with primary cutaneous manifestation was diagnosed in all cases.

Cutaneous lympho-plasmatic infiltrate IgG4 expression, x200:



PS-11-003
Trend of malignant melanoma in Albania
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Objective: The aim of this study was to determine: 1- the incidence of malignant melanoma in albanian population from 2004-2013. 2- the most common subtype, and frequency according to sex and age.
Method: This was an retrospective study. We have analised all histopathological reports in the Department of Pathology in "Mother Teresa"-Hospital, in Tirana. Pearson and Spearman coefficent were used for statistical analysis.
Results: From 2003 to 2014 there were 196 cases of malignant melanoma (MM): 79 % cutaneous (n = 155), 14 % ocular (n = 27), 7 % metastasis (n = 14). There were 60 % (n = 117) males and 40 % (n = 79). Median age was 55.8 (SD 15) for males, and 50,6 (SD 18) for females. The most common subtype was nodular in 38 % of cases. Clinico-morphological correlation was 78 % (p < 0.005). The mean incidence rate for MM in Albania was 6,5 per 100,000 inhabitants.
Conclusion: The incidence of MM is increasing throughout the world and in Albania. The number of cases of metastatic melanoma has decreased while that of primary cutaneous melanoma is increased (new cases 17/2004 to 28/2013. There is a linear relationship between age and disease incidence (p < 0,042).

PS-11-004
Intra- and inter-tumour genetic heterogeneity of various morphological types of cutaneous melanoma
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Objective: BRAF and NRAS mutations are common in malignant melanoma, however their association with distinct morphological types of the disease has not been studied yet with sufficient level of comprehension. In addition, the issue of possible intra-tumour heterogeneity of driver mutations requires investigation.
Method: Mutation analysis for NRAS and BRAF was performed in 31 cases of malignant melanoma of different morphological subtypes (epithelioid, mixed (epithelioid and spindle cell), pure spindle cell or desmoplastic). Each tumour was sampled from 2 to 5 times depending on its size and morphology. In total 115 tissue spots were evaluable for mutational analysis.
Results: BRAF (V600E, V600K) mutations were detected in 7 of 10 epithelioid melanoma specimens and in 2 of 6 pure spindle cell melanomas, but in none of 9 desmoplastic or 6 mixed-histology tumours. NRAS (Q61L, Q61K, Q61R) mutations occurred in 4 of 6 mixed melanomas but were not detected in epithelioid, pure spindle cell or desmoplastic tumours. No instances of intra-tumour genetic heterogeneity were observed.
Conclusion: Melanomas with BRAF mutations usually present with epithelioid cell morphology, while NRAS mutations are characteristic for the tumours of mixed histology. In contrast to other common cutaneous melanoma subtypes, desmoplastic tumours do not carry BRAF and NRAS mutations. These findings suggest relationships between morphological and molecular portraits of melanoma.

PS-11-005
Syringocystadenoma Papilliferum in co-existence with Keratoacanthoma and Apocrine Nevus
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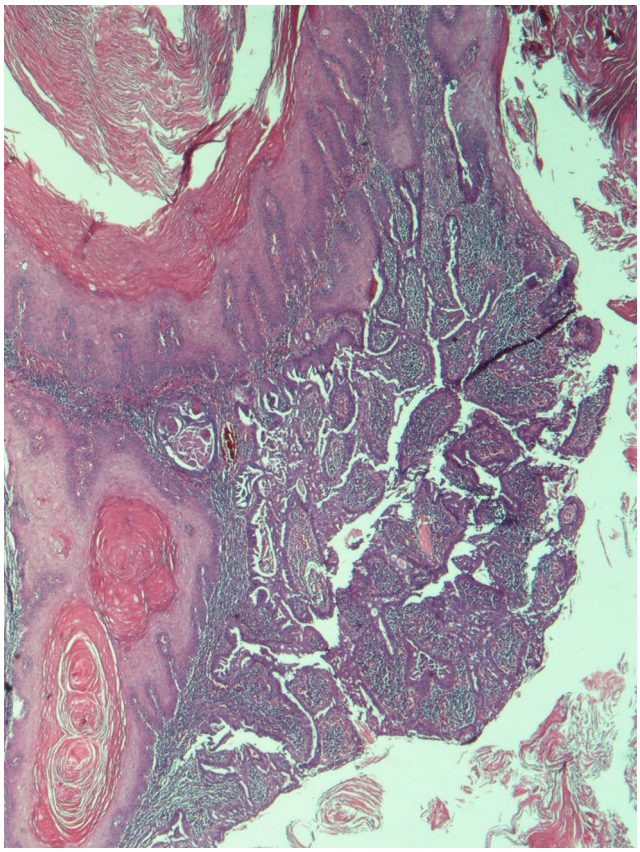
Objective: Syringocystadenoma papilliferum (SCAP) occurs singly or in association with other tumours, most commonly nevus sebaceous (of Jadassohn) (NS). Herein a unique case of SCAP coexisting with two different, other than NS, lesions is presented.
Method: A skin lesion clinically diagnosed as keratoderma was histologically examined. Immunohistochemical study was performed.
Results: Histologic examination revealed a crateroid epidermal lesion interpreted as a stable phase keratoacanthoma (KA), within which at least two focal areas of SCAP. A third underlying lesion was found compatible with an apocrine nevous (AN). No elements supporting nevus sebaceous (NS) could be found.
Conclusion: This case demonstrates that SCAP can arise without a NS background in adults in co-existence with benign or low-grade malignant squamous lesions of the type of KA and a background of an AN. It is postulated either that KA developed on a substrate of SCAP which developed from an AN or that both neoplasms arose synchronously during

the abnormal development of a folliculo-apocrine or a pilo-sebaceous unit. We report what we consider to be the first case, to our knowledge, of SCAP associated with KA and AN, without pre-existing NS.

KA and SCAP:



PS-11-006

Cutaneous lesions signaling a systemic diffuse large B-cell lymphoma

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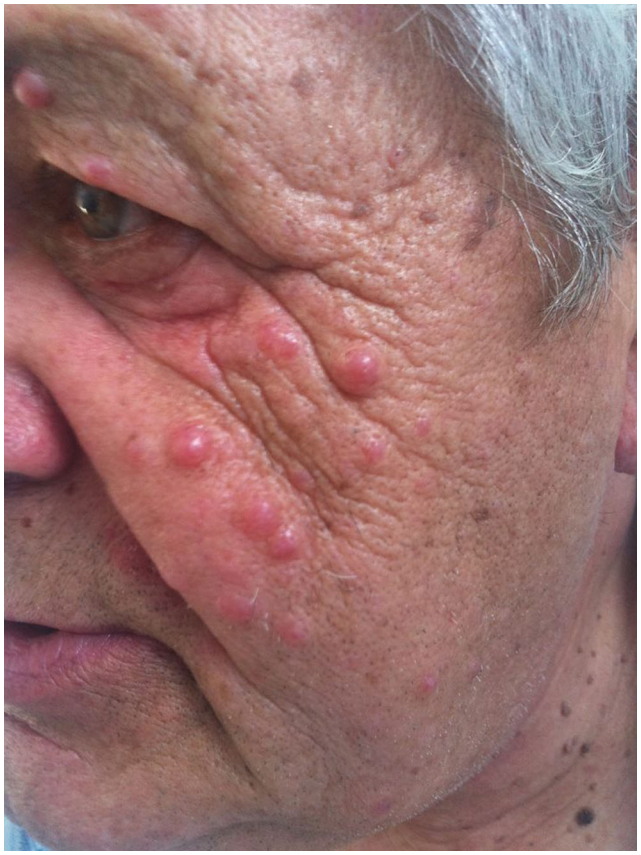
Objective: A systematic interdisciplinary monitoring of cutaneous hematological lesions is needed for a proper diagnosis to the patient.
Method: We present a case of a 67-year-old, male patient with erythematous, painful papular lesions, localized on the chest, face, and proximal extremities. They subsequently sporadically extended over the whole body. A cheek lesion was biopsied.
Results: The patient first presented to the hospital in August 2008 for an auricular lesion. The skin biopsy was advocated as a primary cutaneous follicle center B-cell lymphoma. Further investigations showed multiple adenopathies and enlargement of Waldeyer's ring lymphoid tissue, the case being reclassified as systemic non-Hodgkin lymphoma with cutaneous involvement. Chemotherapy was applied. In November 2014, new skin lesions appeared. The HE stained slides showed heavy dermal infiltrate with grenz zone composed of atypical lymphocytes, with vesicular nuclei, and inconstant nucleolus, with perivascular, periadnexal and nodular distribution. Some histiocytes and eosinophils were admixed with tumoural lymphocytes. The immunohistochemistry was consistent with a cutaneous involvement of a diffuse large B-cell lymphoma, with CD20-positive cells.
Conclusion: We highlighted the importance of interdisciplinary approach in establishing the final correct diagnosis.

Multiple papular lesions on head and neck area:



PS-11-007

The immunohistochemical expression of p16, p62 and DEK allows to distinguish between nodal nevus and melanoma metastasis

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Objective: Nodal nevus is an important differential diagnosis of metastatic melanoma in a sentinel node specimen of melanoma. The aim of our study is to introduce new immunohistochemical markers that distinguish between nevus and melanoma in a sentinel node biopsy of melanoma.
Method: We have revised 19 lymphatic nodes of 15 patients with nodal nevi and 14 lymphatic nodes of 14 patients with melanoma metastases. A study using Hematoxylin-Eosin, Melan-A, p16, p62 and DEK of each biopsy specimen was performed.
Results: Melan-A was positive in 100 % of the biopsies. A nuclear expression of p16 was found in 84 % of nodal nevi and in 21 % of melanoma. p62 was positive in 10,5 % of lymph nodes with nevi and in 93 %

of cases of melanoma. DEK showed high expression in 5 % of nodal nevi and 86 % of metastatic melanoma.
Conclusion: Melan-A does not distinguish between nodal nevi and metastatic melanoma, although it helps to find melanocytes. We confirm the usefulness of p16 as an immunohistochemical marker of nodal nevi. We demonstrate for the first time that the nuclear expression of DEK and cytoplasmic expression of p62 allows the differential diagnosis between melanoma and nevus in a lymph node. We propose a diagnostic algorithm using these immunohistochemical markers.

PS-11-008
Histomorphological and immunohistochemical analysis of 39 Merkel cell carcinoma cases examined on tissue microarray
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Objective: Merkel cell carcinoma (MCC) is a rare neuroendocrine tumour of the skin, characterized by aggressive course and poor prognosis. Primary lesions are frequently localized in sun-damaged sites, tipically at the face, neck, or extremites. MCC affects mainly the elderly and immuncompromised patients, but there can be some exceptions.
Method: We collected 39 cases at the National Institute of Oncology Budapest, Hungary between 2000 and 2015. All of the cases were examined on Hematoxyline-Eosine-slides by the pattern of architecture and infiltration, including cell type (intermediate, small cell etc.). We examined all of the cases by a wide spectrum of immunhistochemical reactions, including some markers with prognostic significance using Tissue Microarray technology.
Results: In seven cases Merkel cell carcinoma was verified from lymph nodes metastasis, and the rest of the cases were diagnosed as primary skin tumour. The mean-age of the patients was 75 years, the youngest patient was 17 years old.
Conclusion: We have found that CK-19 immunhistochemistry has important role in the diagnosis of the CK-20 negative MCCs.

PS-11-009
Granular cell tumour: A case of metachronous occurrence in the breast skin and the scalp
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Objective: Granular cell tumour (GCT) is a relatively rare neoplasm, possibly originate from Schwann cells. Herein we presented a case of 36 year-old woman with metachronous granular cell tumours in the breast skin and the scalp. We aimed to define the clinical and histopathological features of GCT and discuss the differential diagnosis of benign form from malignant GCT.
Method: Excisional biopsies from the breast skin and scalp were examined histopathologically and immunohistochemically; clinical findings were investigated.
Results: The first lesion was located in the breast-skin which was excised. It was reported as granular cell tumour. Eighteen months later, the second lesion appeared in scalp. Second lesion had similar histological and immunohistochemical features like former lesion. Histologically no malignant criterion was defined in both tumours. Finally both of the tumours were accepted as benign GCT.
Conclusion: GCT is an uncommon neoplasm which may occur on many different parts of the body. Most of the GCTS are benign but clinically and radiologically they may mimic malignancy. Histopathological diagnosis is important to establish the true nature of the lesion. GCT is characteristically solitary but may be multifocal, simultaneously involving the skin, submucosa and viscera. GCT is usually benign; however local recurrence is common due to incomplete removal.

PS-11-010
Activation-Induced Deaminase (AID) gene expressions in Merkel cell carcinomas by immunohistochemical and molecular analysis
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Objective: Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine carcinoma of the skin. Merkel cell polyomavirus (MCPyV) is a polyomavirus that is monoclonally integrated into about 80 % of MCCs. Recent studies have demonstrated carcinogenic contribution of activation-induced deaminase (AID), a DNA mutator, in some inflammation-related carcinomas. We analyzed whether AID is associated with virus-related carcinogenesis in MCCs.
Method: Immunohistochemical expressions for AID, NF-κB and Pax5 were analyzed using H-score in 20 MCPyV-positive, 10 MCPyV-negative and metastatic MCCs. Quantitative RT-PCR for AID mRNA will be also performed.
Results: AID expression (H-score); MCPyV-positive MCCs <MCPyV-negative MCCs ($p = 0.049$), and pure MCCs > combined tumour components ($p = 0.016$). NF-κB expression; MCPyV-positive MCCs >MCPyV-negative MCCs ($p = 0.028$), and pure MCCs < metastatic MCCs ($P = 0.004$). High H-score of Pax5 expression was observed in both MCC subgroups, but there was no significant difference.
Conclusion: AID expression in MCPyV-positive MCCs may be up-regulated by not only MCPyV-induced NF-κB but Pax5 expression, whereas unexpected higher AID expression in MCPyV-negative MCCs will be explained with not only Pax5 but other unknown strong inducers. Silencing factor data on AID expression is also important. MCPyV may contribute to AID induction but there must be more potent AID inducers in MCCs.

PS-11-011
Incidence of melanoma in melanotic tumours
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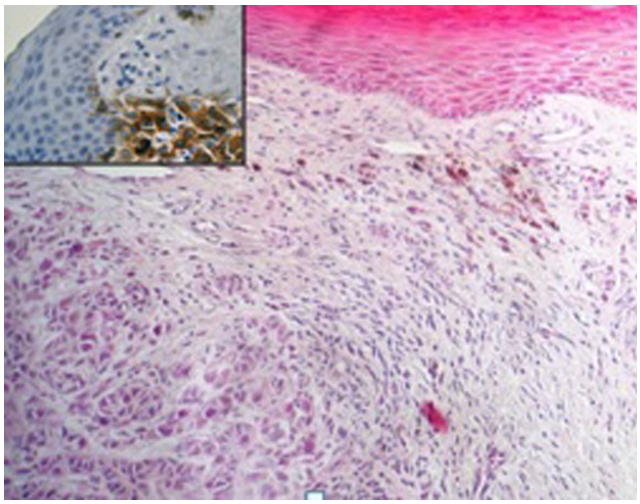
Objective: The aim of our work is to study the pathological aspects and histological prognosis of melanoma through a retrospective study about melanic tumours.
Method: Our study focused on 207 samples collected at the department of Pathology Constantine. CHU extending over a period of 5 years from January 2008 to December 2012.The macroscopic resection specimens should be thin sections of 4 micron thickness are performed and stained with hematoxylin and eosin. Immunostaining with anti PS100 and anti Melan A is always performed.
Results: During the 05 years we have collected only 19 malignant tumours (9.18 %), while our country is very sunny with predominant type 3 and 4 phototype skin. The rest is mild in nature, dominated mainly by skin nevus. A male predominance is noted, the sex ratio was therefore 1M / 0, 72W. The age of our patients varies between 06 and 85 years with a mean age of 61.62 in women and 55.2 in men. In our series, the nodular form (10.78 %) is the most common, followed by SSM and acro-lentiginale

form (10.52 %) with a Breslow index of> 4 mm and Clark level varies between IV and V on more than half of our patients.
Conclusion: The incidence of melanoma is increasing in fair-skinned populations which must impose a prevention against prolonged sunlight. Moreover, it has great potential metastatic hence the interest to seek the mutation in the BRAF gene, which is an indication of supervision in the metastatic progression of the disease.

Nodular melanoma: HMB45 positive:



PS-11-012
Cutaneous CMV infection in an HIV patient
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Objective: The Cytomegalovirus (CMV) belongs to the b-subgroup of the Herpes virus family. CMV infection is common and although in healthy patients CMV infection is usually asymptomatic, in immunosuppressed and especially in those with acquired immunodeficiency syndrome it can be seriously lifethreading. Cutaneous manifestations of CMV infection are rare. We report a case of a 27-year-old man with acquired immunodeficiency syndrome under treatment, who developed fever and a large skin ulcer at his intergluteal fold. A biopsy from the ulcer borders was taken.
Method: A dermal biopsy with the umderlying epidermal surface 0.2 cm max diameter and 0.3 cm max thickness, without any evident macroscopically lesion, was received in our laboratory.
Results: Microscopically we observed epidermal hyperplasia and ulceration and at the dermis chronic and acute inflammatory infiltrate with a small number of eosinophilis. We also observed enlarged, irregularly shaped endothelial and interstitial cells that contain large cytoplasmic and nuclear inclusions. The nuclear inclusions were large, single, eosinophilic, round to oval, and surrounded by a clear halo. The cytoplasmic inclusions tend to be multiple, granular, irregular, and basophilic. Immunohistochemically the cells stained positive for CMV.
Conclusion: Patients with generalized CMV infection have high mortality, but isolated cutaneous manifestations have a very good prognosis.

PS-11-013
Malignant Melanoma (MM) arising in the intradermal portion of small dermal congenital nevus: Report of two cases
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Objective: The chances of a congenital nevus undergoing malignant transformation are greater than those of an acquired and directly related to the size. In adults with congenital nevi, malignant transformation of the intradermal portion of the nevus occurs in less than 1 % of cases. We report two melanoma cases arising in small dermal congenital nevus, a 77-year-old man with scalp nodule and a 67-year-old woman with preauricular nodule. Both patients observed change in size within the last 6 months. There were no other suspicious pigmented lesions or history of melanoma.
Method: We received a grayish skin nodule measured 1.4 cm and a gray skin nodule measured 0.9 cm respectively.
Results: Microscopically in both cases we observed a small dermal congenital nevus with a well-defined nodule in the reticular dermis composed of nests and discohesive epithelioid melanocytes with nuclear pleomorphism, high mitotic activity (7/mm2 and 10/mm2 respectively), and stained immunopositive for S-100 protein, HMB-45, Melan A, Cyclin D1. There was no evidence of an epidermal component or vascular/lymphatic invasion.
Conclusion: These expansile nodules are reffered to in literature as variant of minimal deviation melanoma or nevoid melanoma. Future investigation will have to prove if they have a better prognosis than other melanomas of equal thickness.

PS-11-014
Malignant Melanoma (MM) and Basal Cell Carcinoma (BCC): A case report of a collision tumour
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Objective: To present a MM and BCC collision tumour in an 87 year old female patient. Malignant cutaneous tumours comprising of melanocytes and keratinocytes are uncommon and have been describes as MM with either BCC or squamous cell carcinoma.
Method: The patient presented to our hospital with an elevated, white to brownish red cutaneous lesion of the scalp, measuring 4 × 1.9 cm and surgical excision was carried out. The lesion was examined to our department using hematoxylin and eosin slides, as well as immunohistochemical techniques.
Results: The histological and immunohistochemical examination of the lesion showed two separate, adjacent and well demarcated neoplasms, within close proximity of each other maintaining distinct boundaries. The first neoplasm was a BCC, positive for CKAE1/AE3 and SMA. The second and larger of the two neoplasms was a nodular MM, positive for S100 protein, MART1, and HMB45 and negative for CKAE1/AE3. Ulceration was apparent. The melanoma component had high mitotic activity (12 mitoses/mm2), Breslow thickness 1.5 cm and Clark level V.
Conclusion: MM can coexist with a BCC as a collision, combined, colonized or biphenotypic tumour, from which the most common type is a collision tumour.

PS-11-015
Different expression patterns of Protein Arginine Methyltransferases 1 and 6 suggest distinct roles in the progression of cutaneous Squamous Cell Carcinoma (SCC)
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Objective: Protein arginine methyltransferases 1 and 6 (PRMT1 and PRMT6) are post-translational modifiers involved in regulation of gene transcription and cell proliferation.
Method: Immunohistochemical staining for PRMT1 and PRMT6 proteins was performed on tissue microarray blocks constructed from 168 cases of cutaneous SCC (58 well-, 55 moderately-, and 55 poorly-

differentiated SCC). Evaluation of PRMT1 and PRMT6 expression was assessed in three ways: a) semi-quantitative analysis of expression level (number of positive cells in tumour); b) distribution of positive cells in tumour islands; c) intensity of immunostaining. Expression of PRMT1 and PRMT6 was analyzed in relation to tumour level of differentiation, diameter and microscopically determined thickness, as prognostic factors of SCC.
Results: Poorly differentiated tumours had low intensity of PRMT1 immunostaining ($p = 0.001$), low expression level ($p = 0.04$), and diffuse distribution of positive cells ($p < 0.001$). In poorly differentiated SCCs intensity of PRMT6 immunostaining and expression level were high ($p < 0.001$), and positive cells were arranged in diffuse distribution ($p < 0.001$). No association was found with tumour diameter. Tumour thinner than 6 mm had high expression level of PRMT6 ($p = 0.042$) and diffuse distribution of positive-cells ($p = 0.034$).
Conclusion: Our immunohistochemical analysis suggests possible downregulation of PRMT1 and overexpression of PRMT6 during progression of SCC.

PS-11-016
Digital image analysis of melanocytic proliferation can reduce false-negative melanoma diagnoses
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Objective: To evaluate if digital melanocytic proliferation quantification can reduce false-negative melanoma diagnoses.
Method: 10 formalin-fixed and paraffin-embedded melanocytic skin tumours were included. The lesions were initially diagnosed as benign, but the development of subsequent metastases resulted in revised, malignant diagnoses. The tumours were stained with the MART1/Ki-67 immunohistochemical double stain. Whole slide images were scanned and quantified automatically by digital image analysis. MART1/Ki-67 indices were evaluated in four regions of interest: (I) Global dermal area index (proportion between nuclear area of proliferating melanocytic cells and tumour area), (II) hotspot dermal area index (proportion between nuclear area of proliferating melanocytic cells and tumour area in hotspot), (III) global dermal proportion of melanocytic cells in proliferation, and (IV) dermal hotspot proportion of melanocytic cells in proliferation.
Results: Using previously validated cut-off values to distinguish benign nevi from melanomas (I) classified 10/10 tumours as malignant, (II) classified 8/10 tumours as malignant, (III) classified 8/10 tumours as malignant and (IV) classified 9/10 tumours as malignant.
Conclusion: The application of digital image analysis of dermal melanocytic proliferation in routine diagnostics may alert the examiner and thus, hopefully, reduce false-negative melanoma diagnoses.

PS-11-018
A rare case of congenital Langerhans cell histiocytosis
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Objective: The Hashimoto-Pritzker variant of Langerhans cell histiocytosis is an extremely rare congenital disease. The aim of this study was to emphasize the importance of recognizing the clinicopathological, immunophenotypic and prognostic features of this disease and to discuss differential diagnoses.
Method: In 2012, a case of Hashimoto-Pritzker histiocytosis was diagnosed in our department. Relevant clinical data and microscopic slides were retrospectively reviewed.
Results: We report a case of a 2-day-old boy born at term who presented with multiple skin lesions on the trunk, limbs and face. These lesions consisted of violaceous papules and nodules with hemorrhagic crust. Histopathological exam of the skin biopsy specimen revealed a dermal infiltrate with predominance of medium-sized, histiocytic cells with dense eosinophilic cytoplasm. These cells had eccentric reniform nuclei resembling coffee beans. Immunohistochemical stains were positive for CD1a, which confirmed the presence of langerhans cells. Cerebromedullary magnetic resonance imaging was normal. A second evaluation at age 2 months showed a complete and spontaneous resolution of the lesion. The clinical, histological and immunohistochemical results were consistent with Hashimoto-Pritzker histiocytosis.
Conclusion: Hashimoto-Pritzker histiocytosis is a rare disease with a favorable prognosis. Nevertheless, a multidisciplinary follow-up is necessary since recurrence is reported in 5–10 % of all cases.

PS-11-019
A regional panorama of melanomas
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*Tepecik Training and Research Center, Dept. of Pathology, Izmir, Turkey

Objective: We aimed to describe the characteristics of malignant melanomas (MM) in pathology laboratory of İzmir Tepecik Hospital during 2008–2013.
Method: Fifty-six patients with cutaneous invasive melanomas were evaluated retrospectively. Demographic, clinical and pathological data were extracted and analyzed.
Results: This study consisted of 32 males (57.1 %) and 24 females (42.9 %) with a mean age of 61.9 ± 16.7 years (24–86 years). The most common subtype ($N = 27$, 48.2 %) was superficial spreading MM in both genders. Only 10 patients (17.9 %) have early stage of diseases (Clark 1 and 2), while 15 cases (26.8 %) were Clark III, 26 (46.4 %) were Clark IV and 5 (8.9 %) were Clark V. The mean diameter of tumours was 14 ± 8.7 mm (1.4–40 mm). The most common location was body in males, while it was face and body in females. Similarly females (mean = 63.9 ± 17.5 years) were older than males (mean = 60.4 ± 16.1 years).
Conclusion: In the present study, a realistic comprehensive picture of cutaneous malign melanomas in a central hospital has been provided. In addition, we discussed how clinical and histopathological features of melanoma differ between men and women according to the current literature.

PS-11-020
Composite haemangioendothelioma development after several decades of hemangioma existence
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Objective: The composite haemangioendothelioma is mentioned in the 4th Edition of the "WHO Classification of Tumours of Soft Tissue and Bone" (2013) as a very rare tumour, with only 28 cases published in the English language literature. The aim of this study was to report a new observation of such lesion.
Method: A 52-year-old man was presented with a past medical history of an inherent mass on the shoulder which has been slowly growing during last months up to 1 cm in diameter. Clinically, this lesion was diagnosed as a fibroma and surgically excised. Histological and immunohistochemical studies were performed.
Results: In the surgical specimen the haemangioma with different patterns was revealed. It was presented as a poor circumscribed nodular mass (measuring 0.9 cm in diameter) centered in the dermis. The histological examination discovered a complex admixture of various distinct vascular components. There were areas of predominantly papillary intralymphatic angioendothelioma (70 %), retiform haemangioendothelioma (20 %),

glomeruloid haemangioma (approximately 7 %), cavernous and capillary haemangioma (approximately 3 %). Myxoid and hyaline degeneration of the tumour stroma was a common feature. Fibrinoid changes with multiple thrombi were focally evident. Endothelial atypia was mild while the mitotic activity ranged from 1 to 30 % in areas with high cellularity. The tumour cells showed positive immunohistochemical staining with CD31, CD34, VWF, vimentin.
Conclusion: This case demonstrates that a composite hemangioendothelioma can arise in the inherent vascular lesions after several decades of benign behavior. It is regarded as a low-grade malignant vascular tumour, with significant potential for local recurrence. Thus, the recommended treatment is wide surgical excision.

PS-11-021
A comparative study of Cobas® 4800 BRAFV600 mutation test and Immunohistochemistry anti-BRAFV600E for the detection of BRAFV600E mutation in melanoma samples
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Objective: The emergence of target therapies aimed to the mutated BRAFV600 protein showed an improvement on survival of patients with advanced melanoma. An antibody against the BRAFV600E mutated protein was recently developed. Since immunohistochemistry is a routine technique used by most hospitals, the anti-BRAFV600E antibody could be an efficient tool for the identification of BRAFV600E mutation in paraffin samples. Herein, we have compared the methods cobas® 4800 BRAFV600 Mutation Test and immunohistochemistry for the detection of BRAFV600E mutation in melanoma samples.
Method: A total of 182 melanoma samples were analyzed for the detection of BRAF mutation through cobas® and anti-BRAFV600E immunohistochemistry. Discrepant cases were also analyzed by Sanger sequencing.
Results: From the 182 cases examined, 161 cases showed equivalent results between the two methods and 21 cases showed discrepant results. Fourteen discrepant cases were mutated by anti-BRAFV600E immunohistochemistry, but not mutated by cobas® test. Sequencing of these cases confirmed the V600E mutation in 11 cases. Seven discrepant cases were mutated by cobas® test, but stained negative with anti-BRAFV600E immunohistochemistry. Sequencing of these cases identified the V600K mutation in 5 cases.
Conclusion: The immunohistochemistry is an effective tool for the diagnosis of BRAFV600E mutation in melanoma tumours.

PS-11-022
A case of pyodermia fistulans sinifica (fox den disease) in 62 years old man
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Objective: Pyodermia Fistulans Sinifica (PFS) or Fox den disease (FDD) is a rare inflammatory skin lesion in the group of Hidradenitis Supurativa (HS). PFS is characterized by formation of epithelialized fistulous tracts, subdermal abscesses and scarification. The axillary, inguinal, genital and perineal areas are most commonly affected. Systemic complications may appear as: amyloidosis, anemia, heart, renal failure, etc.
Results: We present a case of PFS in the left gluteal region of 62 years old man. On the base of the specific clinical demonstration, gross and microscopic findings, the lesion was diagnosed as PFS, also referred to FDD. Pathology was found only in the gluteal region. No others areas were affected.
Conclusion: In differential diagnosis were excluded nodular acne, tuberculosis, leprosy and furunculosis. No signs of secondary lymphedema were discovered. The patient had no any complications as anemia, amyloidosis, heart or renal failure. The clinical, morphological and therapeutic aspects of PFS and HS are discussed.

PS-11-023
Higher CADM1 expression and lower MAL expression in Merkel Cell Carcinomas (MCCs) are associated with MCPyV-negative MCCs and unfavorable outcome
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Objective: Merkel cell carcinoma (MCC) is a clinically aggressive neuroendocrine skin cancer; 80 % of cases are associated with Merkel cell polyomavirus (MCPyV). MCPyV-positive and -negative MCCs possess different morphological features and exhibit different prognoses. To the best of our knowledge, this is the first study investigating the association of prognosis or MCPyV infection in MCCs with CADM1/DAL-1/MPP3 tripartite complex or MAL expression.
Method: Immunohistochemistry and hypermethylation of CADM1, DAL-1, and MAL were performed using H-score, MSP, and statistics, respectively, in 26 MCPyV-positive and 15 -negative MCCs.
Results: Higher CADM1 expression was associated with worse overall survival (OS) and MCC-specific survival (DSS). Higher MAL expression was significantly associated with favorable OS but not DSS. Univariate Cox regression analysis showed that advanced age (HR 8.249, $p = 0.007$) and high CADM1 expression (HR 5.214, $p = 0.012$) were unfavorable, whereas the presence of MCPyV (HR 0.043, $p < 0.001$) and lower MAL expression (HR 0.273, $p = 0.018$) were favorable OS parameters. Hypermethylation of CADM1, DAL-1, and MAL promoters was detected in 1/18, 15/27, and 1/13 cases, respectively.
Conclusion: MCPyV-negative MCCs expressed higher CADM1 and lower MAL than MCPyV-positive MCCs. CADM1 overexpression and MAL underexpression in MCCs were related to unfavorable outcomes.

PS-11-025
Decorative and cosmetic tattoos: Clinicopathological findings in a series of 23 cases
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Objective: Due to the increasing popularity of tattoos, pathologists often have to deal with their histopathological manifestations, not uncommonly in the absence of pertinent clinical information. Familiarity with the reaction patterns associated with tattoos is therefore paramount for the successful diagnosis of these ever more common events.
Method: Biopsy cases reported as "Reaction to tattoo" were retrieved from the files of HUGTiP and Anatomopatològic Diagnòstic Àrea, Barcelona. Twenty-three cases were identified and microscopically reviewed.
Results: Histological findings were grouped into six patterns, some of which concurred in the same case. The six reaction patterns were the following: lichenoid, granulomatous, pseudolymphomatous, spongiotic, fibrosing and keratoacanthomatoma-like pseudoepitheliomatous hyperplasia.
Conclusion: In addition to the patterns identified in this work, infections, keratoacanthoma-type squamous cell carcinomas and a variety of inflammatory reactions have been described in association with tattoos. Thus, in the presence of unexplained histopathological findings in a skin biopsy, a diligent search for pigment and clinical information may lead to the correct diagnosis.

PS-11-026

Papular xanthoma: Report of a case and review of literature

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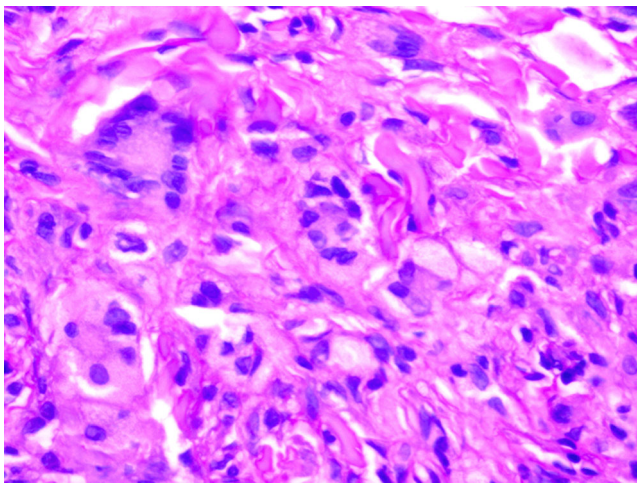
Objective: Papular xanthoma (PX) is one of several clinicopathologic variants of normolipemic cutaneous non-Langerhans cell histiocytoses with a lipid profile within normal range. The objective is to present a case of a patient with papular xanthoma and review of literature.

Method: The medical record was reviewed and the material was evaluated in the pathology department for preparation of the case report and a review of the literature on this topic was performed.

Results: A 2 years old, male patient that presented since he was 5 months old a widespread dermatosis that involved the face and arms, characterized by erythematous yellowish, flat, raised papules, with defined edges and chronic evolution. A punch biopsy was taken and in the different sections of the tissue the presence of Xanthomatous cells with vacuolated cytoplasm and with Touton-type giant cells and few lymphocytes were observed at the level of the upper and mid dermis. Immunohistochemical staining was performed for CD 68, which was positive in the tumoural cells, and negative for CD 1a; and the diagnosis of papular xanthoma (PX) were performed.

Conclusion: The Papular xanthoma is a cutaneous condition that is a rare form of non-X histiocytosis. That can be diagnosed based on the clinical and histological features. The PX can occur at any age but usually appears in childhood or after adolescence, it predominates in men and usually presents as a single lesion, its disseminated presentation is still rare.



PS-11-027

Primary Merkel Cell Carcinoma (MCC) involving the lower limbs: Report of 4 cases

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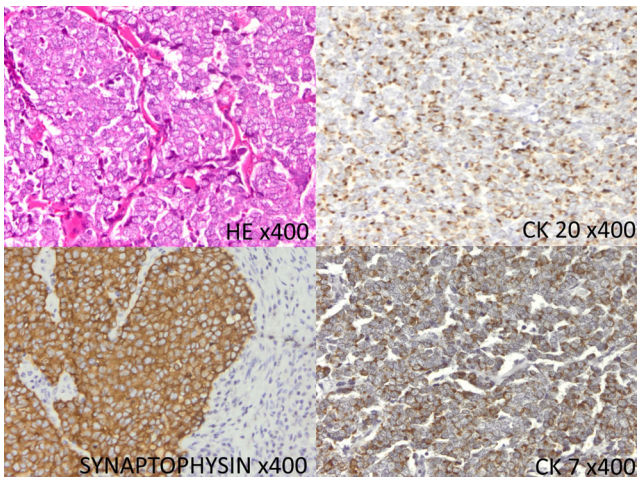
Objective: Merkel cell carcinoma (MCC) is a rare, rapidly growing, highly malignant neuroendocrine carcinoma of the skin. It presents as asymptomatic, red-to-purple nodule in the sun exposed areas of fair skin elderly individuals, hence the predilection for the head and neck region.

Method: We analyzed the clinical records and histopathologic data from 4 cases of MCC involving the lower limbs from a total of 13 MCCs diagnosed in our department since 2003.

Results: The group included 3 females and one male, 66–88 years old, with fast growing, reddish cutaneous tumours involving upper tigh (3 cases) and lower leg (1 case). Morphological examination revealed aspects of neuroendocrine carcinoma, nodular/trabecullar aggregations of small-to-medium monomorphous cells with scanty cytoplasm, "salt-and-pepper" nuclei and frequent mitoses. Immunohistochemical profile demonstrated paranuclear dot-like pattern of positivity for CK20, focal CK7 positivity for one case; TTF-1 and CD99 were negative; no other cases of MCC (with head and neck and forearm location) were positive for CK7. Differential diagnosis includes metastatic neuroendocrine carcinoma (mainly MCC or pulmonary small-cell carcinoma), melanoma or Ewing sarcoma.

Conclusion: Primary MCCs involving the lower limbs are rare. CK7 positivity may be a peculiar finding of these turmours.

Immunohistochemical stains:



PS-11-028

Melanoma cells are responsible for pseudohyperplasia of epidermis in nodular melanoma

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Objective: Similarly to other tumours, the intercellular interactions are crucial for biological properties of melanoma microenvironment. This study is focused on the influence of the tumour melanocytes on the differentiation pattern of normal keratinocytes.

Method: 100 samples of nodular melanoma removed during radical melanoma resection were analyzed by routine histology and immunohistochemistry. The data were compared with in vitro model, where we co-cultured normal keratinocytes with melanoma cells, neonatal melanocytes and neural crest stem cells (NCSC). Transcriptional analysis of those models was carried out on the whole genome level by using Illumina, microarrays.

Results: In the pseudohyperplastic epithelium, aberrant suprabasal expression of keratin 14 (K14) was detected. In vitro melanoma cells and NCSC were able to influence expression of K14, K19, K8 and vimentin in co-cultured keratinocytes. We detected cytokines and growth factors such as FGF2, CXCL1, IL8 and VEGFA, which seem to participate in this activity of the melanoma cell to the keratinocytes, by transcriptional analysis.

Conclusion: Melanoma-epidermal interactions result in maintenance of low differentiation pattern of keratinocytes in vivo as well as in vitro. This interaction further highlights the role of the intercellular interactions in melanoma. This study was supported by the Grant Agency of the Czech Republic, project no.304/12/1333.

PS-11-029

Eccrine Syringofibtoadenoma (ESFA): Discussion a case

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Abstract: Eccrine syringofibroadenoma (ESFA) is a rare, benign, adnexal neoplasm. We report the case of a 33-year-old man who had presented as a solitary nodule in base of right foot. Tumour size was 0,8 × 1,8 × 1,5. Histologic examination revealed a proliferation of anastomosing strands, cords, and columns of monomorphous epithelial cells that harbor eccrine duct formations embedded in a fibrovascular stroma. Epithelial cells are PAS positive.

PS-11-030

Eccrine sweat gland carcinoma of the skin: A case report

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Objective: Eccrine sweat gland carcinoma is a rare malignancy with a high metastatic potential seen more commonly in elderly patients. Solid organ metastases, lymph nodes metastases, and local recurrence are observed in 10–20 % of cases.
Method: We report a case of recurrent and metastaticum eccrine sweat gland carcinoma 9 months after confirmed histologic tumour clearance by narrow-margin excision without regional lymphadenectomy.
Results: Our patient was a 65-year-old female with nodular skin lesion at the posterior side of neck, 35 mm in size. In July 2014, a wide surgical excision was performed, and after histopathological examination, tumour was diagnosed as Spiradenocylindroma eccrinum cutis cum carcinoma ductale eccrinum invasivum cutis. Immunohistochemistry revealed positive reactions for CK7, EMA and CEA and negativity for TTF1. Lymph nodes were not enlarged. On physical examination distant metastasis were excluded. In March 2015, three local recurrences were observed, largest of which was 20 mm with central ulceration. Recurrence was confirmed on microscopic examination. Multislice computed tomography of thorax showed multiple metastases in the lungs.
Conclusion: Eccrine sweat gland carcinoma may occur de novo or developing from a pre-existing lesion, as a solitary lesion with non characteristic macroscopic appearance. The presentation of this case shows an extremely aggressive behavior carcinoma of adnexal origin.

PS-11-031

A hyperactive lesion of Borderline Lepromatous Leprosy: Case report in a pregnant woman

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Objective: Leprosy is a contagious chronic granulomatous infection caused by Mycobacterium leprae, uncommon in Europe. The spectrum of its lesions is related with the immunological status of the individual.
Method: We report a case of a 36-year-old pregnant woman from Paraguay who presented with pruritic papules, misdiagnosed of polymorphic eruption of pregnancy. The Dermatology service performed skin biopsies of upper back, flank, and leg.
Results: The histopathological study of the upper back and flank biopsies shows small dermal collections of macrophages with perivascular, perineural and periappendageal distribution, with few lymphocytes. In the cytoplasm of many of these macrophages there are eosinophilic masses of organisms intensely positive with Job-fitte technique. The leg biopsy shows in dermis a dense population of spindle-shaped cells that resembles a fibrohistiocytic tumour, with small collections of foamy macrophages. With Job-fitte there are numerous intracytoplasmic bacilli. These spindle-shaped cells are Factor 13a positive and S-100 negative. The patient was diagnosed with borderline-lepromatous leprosy.
Conclusion: Hyperactive lepromatous leprosy can occur during pregnancy as a reactional state of immunological instability in patients without previous leprosy diagnose. These histioid lesions are reported in literature as Factor 13a positive/S-100 negative, and histologically may be misdiagnosed as a fibrohistiocytic tumour.

PS-11-032

Low level laser therapy (810 nm) in oral lichen planus: Immunohistochemical study

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Objective: Oral lichen planus (OLP) is autoimmune disease that leads to destruction of epithelium cells of oral mucosa. Despite the antigen is unknown, activation of T-lymphocytes occurs. The conventional corticosteroid therapy is the first choice of treatment but it is often associated with side effects and new therapeutic strategies are in focus of the investigators. The low level laser therapy (LLLT) is new therapeutic ability for OLP patients. The aim of the study was to detect and compare the expression of the proliferative (p63) and tumour-suppressor (p53) markers in OLP patient's biopsy before and after LLLT.
Method: The biopsies from ten OLP patients (7 women and 3 men) were immunohistochemically analyzed for expression of examined markers. The biotin streptavidin peroxidase method was used. The expression of markers was measured using semiquantitative scale
Results: The results of the study showed that in the keratinocytes the p63 expression was nuclear diffuse and not changed whereas the levels of p53 protein decreased after LLLT. The interactions between these two proteins are important for proliferation and differentiation of the stratified epithelium.
Conclusion: The present study demonstrates that LLLT recover the oral mucosa probably maintaining the proliferation of the basal epithelium layer combined with decreased apoptosis induction. Acknowledgments: Grant 03/2014 from Medical University-Plovdiv

PS-11-033

Skin metastasis of atypical carcinoid tumour: How easy is it with no history info?

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Objective: Carcinoid tumours are derived from neuroendocrine cells and are commonly located in the bronchopulmonary and gastrointestinal tract. Less than 50 cases of cutaneous metastasis have been reported.
Method: A 62-year-old female presented with a painless, solitary, rapidly enlarging tumour on the left temporal area that was completely resected.
Results: Grossly, it was a cutaneous, fragile, ulcerated nodule (2.5 × 2.2 × 1.5 cm). Microscopically, the tumour had a diffuse and focally organoid growth, infiltrating the dermis, subcutis and skeletal muscle, involving focally the epidermis. The tumour cells were medium-sized, with round-ovoid, small, uniform nuclei, finely dispersed chromatin, inconspicuous nucleoli, and scanty cytoplasm. There was extensive apoptosis, necrosis and moderate mitotic activity. The differential diagnosis included amelanotic melanoma and Merkel cell carcinoma. Pending the immunohistochemistry, the patient's medical records were reviewed. She had breast carcinoma 16 years ago and atypical carcinoid tumour of inferior mediastinum 5 years ago, with liver, pancreatic, omental and bile cystic duct metastases (24 and 6 months ago). On immunohistochemistry, the neoplastic cells were positive for synaptophysin/chromogranin (3+), TTF-1 (1+), CK8/18/CK7/AE3. Ki-67 index was ~40 %.

Conclusion: We present a rare case of metastatic atypical carcinoid tumour in the skin, a difficult diagnosis if this is the primary manifestation or if the patient's history is unknown.

PS-11-034

Rosacea and demodecosis under the mask of descriptive diagnosis in pathologists' practice

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Objective: Demodex folliculorum et brevis are obligate human ectoparasites found in or near the pilo-sebaceous units. The mites play a possible role in the induction of rosacea, a common chronic inflammatory dermatosis of the face. Demodecosis itself is characterized with an infestation by mites provoking varying degrees of local inflammation and immune response with no evidence of rosacea.
Method: We report 12 cases of rosacea and demodecosis being clinically and histologically misdiagnosed. Clinically these lesions were presented as an erythematous patch, papule or diffuse hyperemia of the face. The diagnosis was predominantly a basal cell carcinoma. Among other entities there were pigmented nevus, papilloma, mycosis, sarcoidosis and a single case diagnosed as a sarcoidosis or hygroma of the face. All of these lesions were surgically excised. The pathologic diagnosis invariably was descriptive of non-specific changes namely hyperkeratosis, elastosis and perivascular lymphohistiocytic infiltrates.
Results: There were 6 male and 6 female patients (age 27–84 years, mean age 55.25 years). The skin lesions histologically presented rosacea with Demodex mites ($n = 8$) and rosacea-like demodecosis ($n = 4$), the latter with no clinical reference to blushing and teleangioectasia. Overall, the histopathology was characterized by: (1) perivascular and perifollicular lymphohistiocytic infiltrates, occasionally with pustular or granulomatous changes; (2) excessive Demodex mites in follicular infundibula and pilo-sebaceous units and (3) teleangioectasia of superficial blood vessels.
Conclusion: Rosacea with Demodex mites and demodecosis should be considered in the differential diagnosis of dermatitis-like or even tumour-like eruptions of the face when there is a chronic inflammation and pieces of mites are seen in the pilo-sebaceous units.

PS-11-035

Eccrine porocarcinoma arising in a forearm poroma: A case report

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Objective: Eccrine porocarcinoma is a rare malignant sweat gland tumour, representing 0.005 to 0.01 % of all epithelial cutaneous neoplasms. We report a rare case of porocarcinoma developed on left forearm, with an expansive growth pattern and a wide variety of histological features.
Method: We present the case of a 65-year-old male with a left forearm tumour first noted 25 years before presentation. Histopathological and immunohistochemical examinations of resected specimen were performed.
Results: The resected tumour measured 3.6/3.5/1.8 cm. Histology revealed an ulcerated tumour composed of islands and downgrowths of broad anastomosing cords of basaloid and atypical squamoid cells with marked nuclear pleomorphism and proeminent nucleoli; ductal differentiation was evident and highlighted with CEA/EMA; areas of necrosis, squamous differentiation and bowenoid changes with bizarre multinucleated cells were found; the tumour had an expansive growth pattern with focal infiltrative aspects; atypical mitotic figures were numerous (10 mitoses/HPF). Also, large areas of tumour had histopathological appearance of classical poroma. Tumour cells stained intensely positive for p53 and ki67.
Conclusion: Porocarcinoma of the forearm arising in a long-standing poroma is an extremely rare event. Considering the fact that malignant features were identified in a limited part of the tumour, extensive sampling is recommended, especially in long-standing lesions.

PS-11-036

Demographic and clinicopathologic features of basal cell carcinoma in adults under 36 years of age: A 12 years (2003–2014) retrospective comparative study

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Objective: To analyze basal cell carcinoma (BCC) characteristics in young pacients (<36 years).
Method: We investigated 5601 BCC diagnosed in our department over a 12 year period (2003–2014). We identified two groups-group A (young patients, <36 years) - 62 cases and group B (older patients, ≥36 years) - 5539 cases. All cases from group A were independently revised by two pathologists in order to exclude basaloid proliferation such as trichoblastoma, trichoepitelioma, basaloid hamartoma; basaloid proliferations arising in Jaddashon nevi were excluded.
Results: BCCs were more common in females than in males in group A ($P = 0.042$); most frequent anatomic location in group A was head&neck region (55,77 %); there was an overall tendency towards decreasing head&neck location in group A comparing to group B ($P = 0.025$); main histological subtype in group A was nodular (51,51 %) similarly to group B (57,71 %); aggressive types of BCC(infiltrative, micronodular and metatypical variants) were less frequent in group A (14,52 %) than in group B (27,73 %): $P = 0.020$.
Conclusion: Our study support the idea that BCC in young individuals is a relatively rare finding; females are more frequently afflicted; there is a less pronounced tendency for this tumours to occur in sun-exposed areas. Also, these lesions may present better prognosis considering the less frequent occurrence of aggressive morphological type.

PS-11-038

Cystic panfolliculoma: A report of 3 cases

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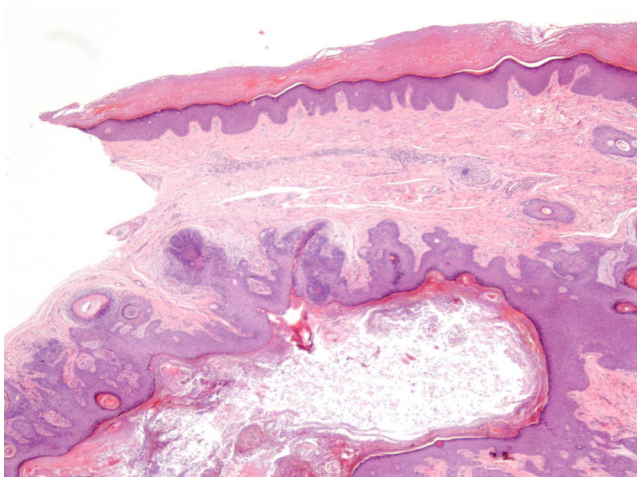
Objective: Panfolliculoma is a rare follicular neoplasm with differentiation towards upper and lower segments of the hair follicle. It has a benign behavior and morphological features similar to tricoblastoma but with an advanced follicular differentiation.
Method: We report a 58-year-old man with a papular lesion on nose's dorsum; a 54-year-old man with a cystic lesion on a temple; and a 67-year-old man with a cystic lesion on his right upper lip. Nodulectomies were performed with subsequent studies through microscopy with HE staining.
Results: The first patient presented a pearled lesion (6 mm) clinically suspected to be a basal cell carcinoma. The second patient showed a cystic keratosical lesion (6 mm) with an abraded area on its surface. An epidermal cyst was suspected. The third patient presented a hemispherical papule (3 mm), suspecting an intradermal nevus. Under the microscope, the lesions correspond to cystic lesions. They show protrusions from cysts' wall, with differentiation towards infundibulum, isthmus, bulb and follicular papillae. The diagnosis was "cystic" panfolliculoma.
Conclusion: Panfolliculoma is a rare lesion presented as a nodule or mass, clinically similar to a basal cell carcinoma, tricoephitelioma and epidermal cyst. Differential histopahology diagnosis must include: cystic trichoblastoma, tricofolliculoma and acanthoma of the hair follicle sheath.

Lesion with cystic dermic architecture:



PS-11-039
Investigation for the role of trauma in an Asian series of Acral Melanoma
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Objective: Exploration of the relationship between the recently implicated trauma/pressure in the aetiopathogenesis of acral melanoma by evaluation of haemosiderin dermal/intratumoral pattern deposition with respect to pressure versus non-pressure location and histologic subtype.
Method: Retrospective 10 year data retrieval. Perls' staining assessment away from surgical sites.
Results: Of 237 melanoma cases, 83 were acral (35 %), with a M:F ratio of 0.9:1. Of 62 cases, 80.6 % were feet (50/62), and 19.4 % (12/62) hands. Overall, 53 % were acral lentiginous (AL), 32 % nodular, 2 % superficial spreading (SS), 11 % in-situ, and 2 % desmoplastic subtypes. Apart from a single negative desmoplastic case, dermal haemosiderin deposition was seen within 13/32 AL, 10/20 nodular, 1/2 SS and 3/7 in-situ types. Intratumoral staining present in 15/32 AL and 9/20 nodular subtypes.
Conclusion: A high incidence of acral melanoma in Singapore (35 %), associated with significant dermal haemosiderin deposition, ranging from 41 to 50 % of cases, whether specifically designated as 'pressure sites' or not. In the feet, 46 % pressure sites were positive, compared with 56 % non-pressure, and 30 % subungual. No significant differences were seen between intratumoral staining in AL (47 %) or nodular tumours (45 %), or dermal haemosiderin in AL (41 %) versus nodular tumours (50 %). The high incidence of haemosiderin deposition observed, possibly indicates propensity to trauma, but no particular distinction between pressure, as opposed to non-pressure sites.

PS-11-040
Cutaneous leiomyosarcoma: A case report
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Objective: Report a rare case of cutaneous leiomyosarcoma.
Method: Patient 54 years old, referred for dermoid tumour of the outer thigh. The biopsy performed concluded dermatofibrosarcoma protuberans. The skin resection piece is the seat of a tumour 05 cm long, of whitish. An immunohistochemical study using: CD34, smooth muscle actin and H-caldesmon was performed.
Results: Microscopic examination shows a dermal proliferation infiltrating the hypodermis. The tumour is composed of interlacing bundles of elongated spindle-shaped cells with eosinophilic cytoplasm and blunt-ended nuclei. These have atypia and more than 2 mitoses per 10 fields. Immunohistochemistry shows diffuse expression of tumour cells to smooth muscle actin and h-Caldesmone. The CD 34 is negative. The diagnosis was a cutaneous leiomyosarcoma low grade.
Conclusion: Cutaneous leiomyosarcoma is a rare tumour; few cases have been reported in the literature. This is a low-grade sarcoma with a better prognosis than its equivalent in other locations.

PS-11-041
Cutaneous leiomyosarcoma / Atypical intradermal smooth muscle tumour: A case report and review of the literature
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Objective: Cutaneous leiomyosarcomas are uncommon lesions derived from the arrector pili muscle. They occur in adults with a predilection for the lower legs. They occasionally recur but they do not seem to have potential for metastases.
Method: A 77 year old female presented with a nodule in the lower leg.
Results: A dermal tumour that extends focally in a number of areas into the subcutaneous tissue is observed. It consists of bundles of spindle-shaped cells that have features of smooth muscle. There is variable but not very prominent cytological atypia as demonstrated by enlargement of nuclei with hyperchromatism. Mitotic figures can be found and the overall mitotic count is about 4/10HPF. Necrosis is not a feature. We believe that the lesion represents a cutaneous leiomyosarcoma. A wider excision was performed. The biopsy was performed 3 years ago and no recurrence or metastases have been identified so far.
Conclusion: Cutaneous leiomyosarcomas when confined to the dermis or showing minimal subcutaneous involvement show almost no risk for metastasis. The risk of recurrence is very low when the tumour is excised. The term "atypical intradermal smooth muscle neoplasm" was introduced by Kraft S and Fletcher CD in 2011 as being more appropriate.

PS-11-042
Keratoacanthoma with perineural invasion: A case report and review of the literature
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Objective: Keratoacanthomas with perineural invasion usually occur on the central face, involving the nose and the peri-oral area. They do not seem to behave in an aggressive manner but complete excision and very close follow up is indicated.
Method: We report a case of a 58 year old female presented 3 years ago with a nodule on the nose of 4 months duration. The patient suffers from aplastic anemia.
Results: A fairly large symmetrical squamoproliferative lesion connected to the epidermis and neighboring hair follicles is observed. It is associated with inflammation that tends to be prominent in some areas. Tumour lobules are glassy and keratinocytes are fairly bland which indicates a lesion that is quite mature. Mitotic activity is not high.A striking feature however, is the presence of a deeper component that is associated with prominent perineural invasion and this extends close to the cartilage.We believe that this represents a keratoacanthoma with extensive perineural invasion. No recurrence has been identified so far.
Conclusion: Keratoacanthomas with perineural invasion are distinctive lesions that should be differentiated from squamous cell carcinoma. Their recognition is of great importance in order to avoid overtreatment of the patient.

PS-11-043

Sarcomatoid carcinoma of the skin: A case report

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Objective: Sarcomatoid carcinomas of the skin are uncommon and their derivation is challenging.
Method: A 44-year-old woman presented with a crateriform ulcerated, rapidly growing tumour on her left thigh, 1.3 cm in greatest dimension.
Results: Light Microscopy: The tumour was composed of spindle cells with marked nuclear atypia and pleomorphism. Multinucleated tumour giant cells were observed, necrosis was prominent and mitoses numerous. No glandular formation or other conspicuous cell arrangement was observed. Immunohistochemistry: CKAE1/AE3, CAM5.2, CK7, vimentin, p16 diffusely positive, EMA, SMA, CD163, p53, D2-40 focally positive, CK20, CK3412, p63, HMB45, desmin negative. Diagnosis: Primary sarcomatoid carcinoma of the skin, probably of eccrine derivation. A benign adnexal tumour or foci of well differentiated carcinoma were not found and this was attributed to the fact that the lesion was deeply ulcerated and partially necrotic.
Conclusion: The differential diagnosis of spindle cell tumours of the skin includes sarcomatoid carcinomas e.g. squamous cell carcinomas, melanoma, atypical fibroxanthoma, sarcomas as well as metastatic tumours. The positive p16 and D2-40 staining favors a primary cutaneous carcinoma, probably of eccrine derivation.

PS-11-045

Angiolymphoid hyperplasia with eosinophilia

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Objective: Angiolymphoid hyperplasia with eosinophilia (ALHE) is a rare, benign vasoproliferative disease of undetermined origin. It is characterized by pink-red papulonodular lesions located mainly on the forehead, scalp and periauricular region.
Method: An 36 -old female attended our plastic surgery clinic with complaint of a gradually increasing painless swelling in the left temporal (auricular) region of 10 year's duration. She had similar type of scalp swelling on the same side 9 years ago. She got operated in a general hospital. The histopathology report came as reactive hyperplasia. On clinical examination there was no evidence of lymphadenopathy. The left temporal (auricular) region showed conglomerate and different sizes tumour mass.
Results: Gross examination revealed brown, papulonodules measuring of 0.5–0.8 cm. Histopathologic features are vascular proliferations, plump endothelial cells which protrude into the lumen and eosinophilic and lymphocytic infiltration.
Conclusion: ALHE causes a therapeutic dilemma because of frequent resistance to treatment.

PS-11-046

The presence of dendritic cells in regressed and non-regressed melanoma

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Objective: From all possible ways of evolution of melanoma, the most intriguing is spontaneous regression (complete/partial disappearance of tumoural cells replaced by inflammatory infiltrate, melanophages, fibrosis and tortuous vessels). We studied the presence of dendritic cells in inflammatory infiltrate in regressed and non-regressed areas of melanoma.
Method: We performed a retrospective study of 60 consecutive cases of melanoma, 30 of them with tumour regression. Distribution and frequency of dendritic cells were evaluated by imunohistochemical stains (CD1a, Langerin, CD21, S100).
Results: Dendritic cells are most frequent in the regressed areas, comparing with non-regressed ones and peritumoral inflammatory infiltrate. In regressed areas, dendritic cells have a predominant nodular pattern (19 cases), followed by diffuse isolate pattern (8) and with mixt pattern (diffuse and nodular) (3 cases). In melanoma without regression, most cases presented a diffuse pattern of dendritic cells distribution.
Conclusion: Significant increase of the number of dendritic cells, as well as their particular distribution in areas of regression indicates that they are involved in regression mechanisms and have potential prognostic value for melanoma patients. Cioplea, Nedelcu and Zurac have equal contribution. This work was partially supported by project 190/2014/PN-II-PT-PCCA-2013-4-1407 and by SOPHRD contract POSDRU/159/1.5/S/137390.

PS-11-047

Cutaneous ciliated cyst of the gluteal region

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Objective: Cutaneous ciliated cyst is an exceedingly rare benign lesion, that is lined by a simple cuboidal to columnar ciliated epithelium.It seen typically on lower extremity in females in the second or third decade of life.They have been widely regarded as Müllerian heterotopias because of the morphological similarity of the cyst lining cells to the epithelium of fallopian tubes.
Results: We reported a case of an 19-year-old female presented with painless swelling, over gluteal region since 1 years. On examination soft swelling was noted. Surgical removal of the cyst was carried out under local anesthesia. Grossly, specimen was 4 × 2 × 0,5 cm in size and an multiloculated cyst was identified.Light microscopy revealed a cyst in the deep dermis, which was predominantly lined by single layer of ciliated cuboidal to columnar cells without mucous cells. In some areas the epithelium showed stratification and squamous metaplasia. The cyst wall was thin, fibrocollagenous without any inflammatory infiltrate. On immunohistochemical staining, the lining epithelial cells showed strong membrane positivity for pancytokeratin and strong nuclear positivity for estrogen receptor (ER) and progesterone receptor (PR).
Conclusion: Surgical removal under local anesthesia is the recommended treatment for cutaneous ciliated cyst.The recurrence has not been reported in the literature.

PS-11-048

Steatocystoma multiplex: In different localizations of six patients

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Objective: Steatocystoma multiplex (SM) is a hamartomatous malformation of the pilosebaceous consisting of dermal cysts filled with a sebum-like material. SM lesions are typically located in areas with sebaceous follicles, although atypical presentations involving sites lacking sebaceous follicles have exceptionally been described. The lesions are usually asymptomatic.
Results: We reviewed retrospectively of six histologically diagnosed SM observed in our department in the 2009–2015, evaluating the kinds of lesions and their locations. Two patients were female and four patients were male. These lesions located in neck, conjuctiva, face, frontal region and axillar area. Histopathological examination of skin showed presence

of cystic formation with sebaceous gland on its wall in the dermis and typical stratified squamous epithelium that showed its stratum corneum wavy shaped, refractile and strongly eosinophilic located in the cystic wall.
Conclusion: Lesions are most commonly found on the chest and proximal extremities although other sites are also described such as: axillae, vulva, central area of the chest, and inguinal region (common in women). Other regions like face and scalp are rare to be found. Our patients range from 30 to 50 years old, female / male ratio is 2/4, which is the most common locations were within the region in the literature.

PS-11-049
Cutanous lymphadenoma: A case report
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Objective: Cutaneous lymphadenoma is a rare benign tumour. About 57 cases were reported in literature under various names, like benign lymphoepithelial tumour and adamantinoid trichoblastoma. Our aim is to study the clinico-pathological features of this misleading tumour.
Method: A 40 years old male patient presented with a temporal solid reddish nodule. It was clinically suspicious for a basal cell carcinoma and subsequently excised. Macroscopic examination showed a well circumscribed nodule, 1 cm in diameter. Microscopic examination showed a well limited intradermal epithelial proliferation, composed of rounded lobules of basaloid cells with peripheral palissading, embedded in a fibrous stroma. There was an intense infiltrate of small mature lymphocytes and histiocytes within the nodules. A hair differentiation was noted in few places. At immunohistochemistry, lobule's inflammatory cells were mostly stained by CD3, scattered cells were stained by CD20 and CD30.
Results: Diagnosis: Cutaneous lymphadenoma.
Conclusion: Cutaneous lymphadenoma is an uncommon epithelial neoplasm. Although it is benign, its recognition is important as it resembles clinically and histologically the far more common and locally destructive basal cell carcinoma. Histological differential diagnosis includes also syringoma, dermal thymus, and lymphoepithelioma-like carcinoma of the skin. Simple surgical excision is sufficient for treatment.

PS-11-050
Pathological features of basal cell carcinoma on non-sun-exposed areas
P.-I. Stinga*, C. Popp, R. Andrei, A. Bastian, L. Nichita, M. Busca, V. Mageriu, D. Michire-Stefana, C. Salavastru, F. Staniceanu, S. Zurac
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Objective: Basal cell carcinoma (BCC) is a heterogeneous group of malignant proliferations, mostly related to UV exposure. However, some of BCC's are arising in areas with minimal or no exposure. We studied particular histological features of these BCC.
Method: This study included a cohort of 150 consecutive cases histopathologically diagnosed as BCC. Non-sun-related BCCs were considered those cases simultaneously fulfilling two criteria: 1. tumours occurred in areas where patients denied sun exposure; 2. no dermal actinic damage was identified on microscopic examination.
Results: 26 cases (17.33 %) were non-sun-related BCCs. They occurred mostly on the trunk and upper limbs without sex preference. Several features were identified (younger age at diagnosis (65.7 versus 70.1), larger tumour diameter (1.27 versus 1.11 cm), higher frequency of complete excision (73 versus 65 %) and lower incidence of ulceration (53.8 versus 55.2 %)) but no statistical significant differences were recorded. Superficial type was more frequent in non-sun-related BCCs than sun-related counterpart (26.9 versus 1.6 %, $p = 0.0037$). Also lesser depth of invasion was recorded in non-sun-related BCC (0.8 mm versus 3.2 mm, $p = 0.0003$).
Conclusion: Non-sun-related BCC are less invasive tumours with less aggressive pattern and may have a better prognosis.

PS-11-052
Merkel Cell Carcinoma (MCC): In search of prognostic features of a tumour with a dismal prognosis
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Objective: Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine skin carcinoma with poorly understood prognostic features. We evaluated the prognostic value of morphologic characteristics in primary MCC with and without divergent differentiation (DD).
Method: We reviewed 30 MCCs, clinical data and morphologic features: necrosis, mitotic count (MC), cell size, lymphovascular invasion (LVI), regional (LN) and distant metastases. We compared DD cases with pure MCCs.
Results: Mean age was 78 years, 19 were sun-exposed. Overall survival (OS) was 27 months. Pure MCCs were predominant in sun-exposed areas ($n = 18$). Small-cell-sized tumours($n = 3$) had LVI, LN+, a mean MC = 16/mm2 with an OS of 7 months. Two patients with unexposed tumours had 55 and 58 years, LN+ at presentation and an OS of 15 months. Three cases had DD (squamous and sarcomatous component in two, the latter in an unexposed location). The mean age was 82 years, the OS was 20 months and all had recurrence. Morphologically they were large-cell-sized, had LVI and a MC>42/mm2. None of the pure cases had these three features.
Conclusion: No single or combined feature predicts survival. Our data suggest that small-cell-sized and non-sun-exposed pure MCCs in younger patients represent more aggressive forms. Moreover, DDMCC morphologic features may correlate with recurrence and a poorer prognosis.

PS-11-053
Prognostic value of serum and tissue matrix metalloproteinase 1 in melanoma
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Objective: To correlate matrix metalloproteinases (MMPs) expression in serum and tumour tissue in melanoma patients.
Method: We investigated 47 patients with melanoma for seric and tissue presence of MMP1, 2, 3 and 9. Serum samples were investigated using multi-plex technology (BP-Pro-Hu-MMP Panel 9-Plex/BioRad); MMP1, MMP2, MMP3 and MMP9 immunohistochemical expression on tumour tissue were assed using a semiquantitaty scale with 0-to-3 level of positivity.
Results: Serum MMP1 and MMP9 stand out of the normal ranges for patients diagnozed in stage III and IV (stage IV patients have double serum MMP1 levels; stage III-IV patients have double serum MMP9 levels). For serum MMP2, no statistical differences was recorded, irrespective of stage. MMPs expression in tumour tissue followed a tendency towards increased expression of MMP1, MMP2, MMP3 and MMP9 for higher pT levels but no significant statistical differences were recorded except for MMP1 ($P = 0.047$). Also, studying MMPs dynamics correlated with tumour expression, each individual patient with increased seric MMPs associates bad outcome.
Conclusion: Our study showed overall increased expression of MMP1 correlated with increased seric level in advanced tumours; moreover, increased seric levels of MMPs in dynamic correlates with increased

tumour expression and bad prognosis. All authors equally contributed. Partially supported by project 190/2014 PN-II-PT-PCCA-2013-4-1407 and POSDRU/159/1.5/S/137390.

PS-11-054

The rhabdomyomatous mesenchymal hamartoma: A rare skin lesion

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Objective: The rhabdomyomatous mesenchymal hamartoma (RMH) is a rare congenital dermal lesion with propensity for head&neck region, occurring as single or multiple cutaneous lesions, often polypoid, typically on the midline. It presents striated muscle fibers with a haphazard distribution, in a matrix of mesenchymal elements (adipose, connective, nervous, vascular elements). It appears due to a deficient migration of the mesenchymal elements of the second branchial arch during embriogenesis, thus, the patients must be carefully investigated for other congenital diseases.
Method: We present the case of a middle aged man with an upper lip tumour.
Results: Its gross appearance is of a polypoid, skin covered, elastic papule, with a reddish section. Microscopic examination revealed a dermal tumour composed of mature striated muscle perpendicularly to the skin, penetrating into the underlying dermis, mixed with smooth muscle bundles, adipose and nervous elements in a myxoid stroma with scant fibroblasts and small blood vessels, without atypia.
Conclusion: Although due to its microscopic features, RMH is easily diagnosed, only few cases have been reported, mainly in children, only four adult presentations being reported to-date. Its clinical significance is mainly of cosmetic importance, but proper diagnosis is important because it may associate congenital anomalies. Zurac and Pop have equal contribution.

PS-11-056

Merkel Cell Carcinoma (MCC): In search of prognostic features of a tumour with a dismal prognosis

B. Pena*, V. Henriques
*IPOLFG, EPE, Serviço de Anatomia Patológica, Lisboa, Portugal

Objective: Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine skin carcinoma with poorly understood prognostic features. We evaluated the prognostic value of morphologic characteristics in primary MCC with and without divergent differentiation (DD).
Method: We reviewed 30 MCCs, clinical data and morphologic features: necrosis, mitotic count (MC), cell size, lymphovascular invasion (LVI), regional (LN) and distant metastases. We compared DD cases with pure MCCs.
Results: Mean age was 78 years, 19 were sun-exposed. Overall survival (OS) was 27 months. Pure MCCs were predominant in sun-exposed areas (n = 18). Small-cell-sized tumours(n = 3) had LVI, LN+, a mean MC = 16/mm2 with an OS of 7 months. Two patients with unexposed tumours had 55 and 58 years, LN+ at presentation and an OS of 15 months. Three cases had DD (squamous and sarcomatous component in two, the latter in an unexposed location). The mean age was 82 years, the OS was 20 months and all had recurrence. Morphologically they were large-cell-sized, had LVI and a MC>42/mm2. None of the pure cases had these three features.
Conclusion: No single or combined feature predicts survival. Our data suggest that small-cell-sized and non-sun-exposed pure MCCs in younger patients represent more aggressive forms. Moreover, DDMCC morphologic features may correlate with recurrence and a poorer prognosis.

PS-11-057

Histopathological prognostic parameters of cutaneous melanoma in central Serbia: Thick, ulcerated with bimodal pT distribution

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Objective: To analyze histopathological characteristics of cutaneous melanoma in central Serbia over the 14-year period (2001–2014).
Method: Analysis of data obtained during examination of primary melanoma specimens at the Institute of Pathology, Faculty of Medicine in Belgrade.
Results: A total of 909 patients (426 males and 483 females), mean age 56.7 years were included in the study. Mean Breslow thickness was 3.6 mm (range 0.15–41 mm), showing almost no changes over the observed period. Clark I (in situ) melanomas represented 15.3 % of all cases with the increase from 7.1 % (2001–2007) to 18.2 % (2008–2014). pT1 melanomas were diagnosed in 31 % of patients, increasing from 29.5 %, during the 2001–2007 period, to 34.5 % from 2008 to 2014. pT4 lesions were found in 30.9 % of patients, remaining almost unchanged over the observed period. Ulceration was present in 37.4 % of all cases, increasing from 35.5 % (2001–2007) to 38.8 % (2008–2014). Females presented more often than males with in situ/pT1 lesions (50.9 and 37.4 %, respectively) and less often with the pT4 melanomas (19.5 and 30.3 %, respectively).
Conclusion: Cutaneous melanomas in central Serbia are thick, ulcerated, with bimodal pT distribution and stable, high share of pT4 tumours despite the increase in percentage of in situ and pT1 lesions.

PS-11-059

Benign nevus with nerve sheath differentiation

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Objective: The authors report a case of a benign nevus with nerve sheath differentiation and points out the importance of the immonuhistochimestry in this particular differentiation.
Method: A 74 year old woman presented with lump on the right elbow. The lump was removed and examined in the Histopathology department of Salah Azaiez carcinologic institute.
Results: Histological examination showed a well circumscribed dermal lesion partly consisting of nests of melanocytes and partly of spindle shaped cells with elongated and wavy nuclei, suggestive of a nerve sheath tumour. There was no atypia and no mitoses. Immunohistochemistry showed that both the nevus cells and the spindled cells in the nerve sheath tumour-like area were positive for melaninA, S100, EMA, CD34 and negative for Desmin and SMA.
Conclusion: The intimate mingling and merging of the nevus cells and the spindle-shaped cells suggest that this is a single lesion corresponding to a benign intradermal nevus with nerve sheath differentiation. The immunohistochemistry results shows a mixture of S-100, EMA and CD34 positive cells is reminiscent of the cell population seen in a neurofibroma, comprising Schwannian, perineurial and intraneural fibroblastic differentiation.

PS-11-060

Cutaneous presentation of ALK-positive anaplastic large cell lymphoma following insect bite in an adult patient

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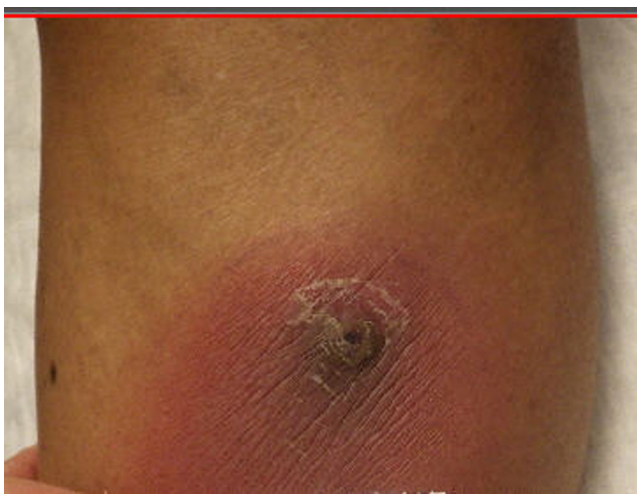
Objective: Insect bites are a possible triggering event in cutaneous ALK+ anaplastic large cell lymphoma (ALK+ ALCL). Reported as rare and exclusively in children, the initial skin biopsies consistently appear

reactive, which causes significant delays in diagnosis. We report a case in an adult patient.
Method: A 65 year-old woman presented with a 'bug bite/sting' on the right lower extremity of 1 week duration. The lesion was singular, purplish and pustular with surrounding erythema. The wound subsequently advanced despite antibiotic, debridement and compression therapies. Multiple skin biopsies were interpreted as mixed granulomatous inflammation supporting a clinical impression of pyoderma gangrenosum. She developed progressive muscle weakness, shortness of breath, fever, and right groin lymphadenopathy.
Results: Lymph node excisional biopsy revealed partial effacement by histiocyte-rich necrotic large cell collections with wreath-like nuclei expressing CD30, ALK, and a T-cell phenotype. Molecular cytogenetic studies showed an unbalanced rearrangement of the ALK locus with retention of the 3′-ALK region. Retrospective skin biopsy immunostains revealed a histologically occult CD30, ALK+ neoplastic cell population.
Conclusion: We report the first adult case of the rare cutaneous presentation of ALK+ ALCL following insect bite previously reported in children. Familiarity with this histologically occult entity is essential for a timely diagnosis.

Clinical photo lesion right lower extremity:



PS-11-061
Cutaneous Leishmaniasis
Y. Sahin*, B. Lebe
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Objective: To report the case of 'Cutaneous Leishmaniasis' because it might cause difficulties in differential diagnosis and its prevalence is increasing apart from endemic regions.
Method: A 48-year-old male patient was admitted to a dermatology clinic due to nodular lesions on upper and lower extremities for 7 months. Excisional biopsy performed at another clinic was reported as diffusely infiltrated tumoural lesion in dermis. Parafin embedded tissue sections were consulted to our department and in Hematoxylin-Eosin stained sections non-caseating granulomatous inflammation as nodular pattern in dermis was observed. In dermis, macrophages that phagocyted multiple small basophilic microorganisms, epitheloid histiocytes, Langhans type multinucleated giant cells, plasma cells and lymphocytes are demonstrated. Basophilic microorganism were also revealed by Giemsa histochemistry and dermal histiocytic cells were positive by CD68 immunohistochemistry.
Results: With these findings, the case was diagnosed as 'granulomatous dermatitis compatible with Cutaneous Leishmaniasis'.
Conclusion: In cases with granulamotous dermatitis, 'Cutaneous Leishmaniasis' should be considered in differential diagnosis even in non-endemic regions.

Tuesday, 8 September 2015, 09.30–10.30, Restaurant
PS-12 Poster Session Digestive Diseases Pathology II: Lower gastrointestinal tract

PS-12-001
Assessment of the density of Wilms Tumour Protein 1 (WT-1) positive microvessels in stage IIA colon cancer: Is there any prognostic significance?
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Objective: To investigate the potential prognostic value of Wilms Tumour protein-1 (WT-1) expression in patients affected by pTNM stage IIA colon cancer (CC).
Method: The immunohistochemical expression of WT-1 was analyzed in the cancer cells as well as in the tumour vessels in a cohort of 50 pTNM stage IIA CC, subdivided into two groups on the basis of their disease progression.
Results: WT-1 staining was found in the neoplastic cells of 38 % CC and showed no correlation with the various clinico-pathological parameters. On the other hand, WT-1 immuno-reactivity was evidenced in the tumour vessels of all but two cases, with a variable number and density of stained vessels. WT-1 microvessel density (MVD) was significantly higher in stage IIA CC with recurrences compared to non-recurring tumours and it was a significant negative, though not independent, predictor of shorter disease-free interval.
Conclusion: Our findings suggest that WT-1 MVD may be useful to discriminate high risk patients with stage IIA CC who may benefit from adjuvant treatment. In addition, WT-1 expression in the tumour vessels may represent a target for novel therapies aimed at reducing tumour blood supply in stage IIA CC.

PS-12-002
Loss of tapasin enables the tumour to elude CD8+ T-cell defense in colorectal cancer
L. Sokol*, V. Kölzer, E. Karamitopoulou, I. Zlobec, A. Lugli, T. Rau
*Universität Bern, Inst. für Pathologie, Switzerland

Objective: Tapasin is a crucial component of the MHC-I antigen presentation pathway, which is a prerequisite for the initiation of the CTL antitumoral response. The aim of this study was to test whether tapasin expression can promote CD8+ cytotoxic T lymphocytes (CTL) infiltration of colorectal cancer (CRC) and thus influence overall survival.
Method: A next-generation tissue microarray of 198 CRC patients with full clinicopathological information was included in this study. TMA slides were immunostained for tapasin, MHC-I and CD8. Marker expression was analyzed with immune cell infiltration, patient survival and TNM-staging.
Results: Tapasin expression in CRC was positively correlated with the surface expression of MHC-I (OR:2.22, $p = 0.008$, 95 %CI:1.24–4.0). Tapasin loss strongly correlated with venous invasion (AUC:0.682, OR:0.37, $p = 0.002$, 95 %CI:0.2 0.69), lymphatic invasion (AUC:0.62, OR:0.5; $p = 0.005$, 95 %CI:0.3–0.8), distant metastasis (AUC:0.727, OR:0.35, $p = 0.004$, 95 %CI:0.17–0.71), and the absence of CTL infiltration (AUC:0.729, OR:5.4, $p < 0.001$, 95 % CI:2.6–11). Furthermore, tapasin expression was significantly associated with favorable overall survival ($p = 0.004$, HR:0.6, 95 %CI:0.42–0.85).

Conclusion: Loss of tapasin is a marker of tumour progression. In CRC, it can facilitate immune evasion by downregulating MHC-I antigen presentation and thus evading immune recognition and destruction by CD8+ CTLs.

PS-12-003

MSI and p53 in the polypoid colon adenomas with high grade dysplasia - the preliminary results

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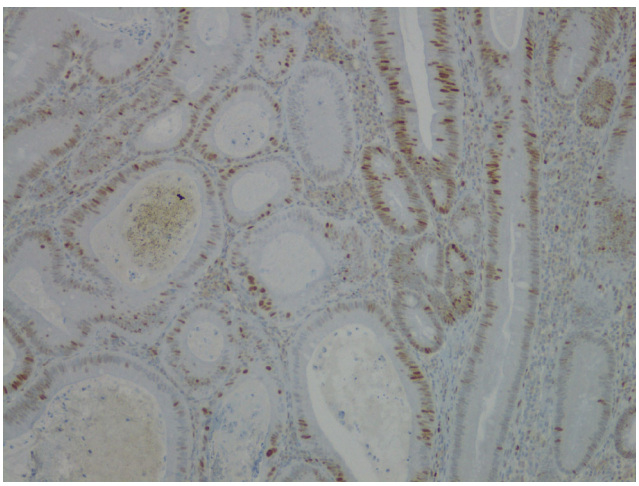
Objective: The paradigm presented by Vogelstein in 1990 about sequence adenoma-carcinoma is still unquestionable but the main role of APC mutations is complementing day by day. As such, the purposes of the study were stated: an analysis of MSI and TP53 in the polypoid colon adenomas.
Method: 104 polypoid colon adenomas with high grade epithelial dysplasia were included to the research. Typical immunohistochemical procedures were performed with use the monoclonal antibodies p53, MLH1, MSH2, MSH6 and PMS2, respectively.
Results: The p53 overexpression has been stated in 17 % of low grade dysplasia parts of polyps in contrast to 39 % in high grade dysplasia. Here, have been shown 3,8 % frequency of MSH-6 and 1 % of MSH-2. We have not noted MLH-2 mutation and PMS-2 is still under evaluation. A clear heterogeneity of the MSH-6 has been a feature in 24 % of the cases. What is interesting, each case of MSI was located at left-side colon.
Conclusion: These results indicate MSI pathway as an additional sporadic mutation in left-sided polypoid adenomas. It confirms a significance of the previous studies' results in area of the necessity of molecular profiling an each case of colorectal cancer.

The heterogeneity of MSH-6:



PS-12-004

Artificial matrix-free co-culture spheroids of human colonic adenocarcinoma cells and normal colonic fibroblasts promote tumourigenicity in nude mice

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Objective: The local stromal compartments surrounding carcinoma play essential roles in tumour development. Fibroblasts are one of the important stromal cells in the progression of many carcinomas. In this study we investigated the role of normal colonic fibroblasts (NCFs) in the tumourigenicity of colonic adenocarcinoma cells (CACs).
Method: We used three-dimensional (3D) co-culture spheroids of the CACs and NCFs. The 3D co-culture spheroids were formed using an artificial matrix-free forced aggregation technique by a rotary orbital shaker. The spheroids were characterized by transmission electron microscope. Assays of CAC invasion using matrigel and tumorigenicity in nude mice to examine the effect of NCFs on CACs invasive behavior and tumorigenicity were performed using the 3D spheroids.
Results: The 3D co-culture spheroids showed the traits of the interaction between CACs and NCFs in vivo. The mono-cultivation of CACs did not form into densely packed 3D spheroids, whereas co-cultivation of the CACs and NCFs resulted 3D spheroids. The 3D co-culture spheroids seeded on the extracellular matrix using matrigel increased the invasion of CACs compared to CACs alone or together with NCFs in suspension. Injection of the 3D spheroids statistically generated more frequently and progressively growing tumours in nude mice compared to the CACs alone or together with NCFs in suspension.
Conclusion: We demonstrated our novel 3D co-culture spheroids with an in vivo like condition. Our findings provide evidence of that the interaction between CACs and NCFs were essential to lead the cancer cells to tumorigenesis and tumour propagation.

PS-12-006

MCP-1 -2518G polymorphism is associated with high expression of gelatinase B (MMP-9) but not with gelatinase A (MMP-2) in Tunisian patients with colorectal cancer

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Objective: The purpose of this study was to investigate the impact of MCP-1, MMP-2 and MMP-9 genes polymorphisms on the susceptibility of colorectal cancer (CRC). Next, we investigated whether there were relationships between MCP-1 A2518G polymorphism and the pattern of MMP-2 and MMP9 expression.
Method: MCP-1 A2518G, MMP-9 C1562T and MMP-2 C1306T polymorphisms were determined using restriction fragment length polymorphism method and expression of MMP-9 and MMP-2 were determined using reverse transcriptase polymerase chain reaction.
Results: There is a significant difference in the distribution of MMP-9 genotypic frequencies in patients compared to control subjects ($p = 0.001$). For-1306 C/T MMP-2 gene polymorphism, there was no significant association between −1306C/T MMP-2 gene variant and CRC. Interestingly, combined analyses of MCP1A2518G and MMP-9 (−1562C/T) polymorphism showed a significant association ($p = 0.007$). We next examined the presence or absence of statistically significant correlations among MCP1A2518G and MMP9 mRNA expression. High expression of MMP9 was significantly higher in patients with at least one mutated G allele of MCP-1 gene. However no significant association was found between MCP-1 gene variant and the pattern of MMP-2 expression.
Conclusion: Our data indicate that MCP-1 polymorphism was correlated with the overexpression of MMP-9 which are associated with increased risk of CRC in Tunisian population.

PS-12-007

Interlaboratory variability in the histological grading of colorectal adenocarcinomas in a nationwide cohort

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Objective: Differentiation grade of colorectal adenocarcinoma is important for therapy selection. Poor differentiation (PD) is a contraindication for local therapy and, in stage II colon cancer, an indication for adjuvant chemotherapy. We analyzed the interlaboratory variability in histological grading of colorectal adenocarcinomas in daily practice.
Method: Using the Dutch Pathology Registry (PALGA), all synoptically reported adenocarcinomas resected between 2010 and 2013 were identified. The percentage of adenocarcinomas with PD was determined, and clinico-pathological factors associated with PD were investigated. We compared percentages of PD in a subgroup of 22 laboratories that had ≥ 50 synoptically reported adenocarcinomas. Univariable logistic regression analyses were performed.
Results: We included 16,419 adenocarcinomas (15,986 patients) of which 11.1 % showed PD. Female gender, advanced age, right-sided localisation, tumour size, and T-stage were associated with PD. The percentage of PD adenocarcinomas varied from 7.0 to 18.5 % between 22 laboratories. Three laboratories graded significantly less and three laboratories significantly more PD than a reference laboratory. Over the years, laboratories that were aberrant varied. No laboratory was aberrant throughout the whole study period.
Conclusion: We observed considerable interlaboratory variation in grading, but this was not consistent throughout the study period. Multivariable analyses are needed to further investigate the variation in grading.

PS-12-008
Elastofibromatous polyps of the sigmoid colon and rectum: Report of two cases

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Objective: Elastofibromatous changes of the gastrointestinal tract are rare benign, often polyp-forming lesions, characterized microscopically by an excessive accumulation of elastic fibers in the submucosa, mimicking amyloid deposit. We herein report two cases of elastofibromatous polyps of the sigmoid colon and rectum, that presented to our department in a period of 15 years.
Method: Case 1: A 30-year-old male patient with a 13 mm pediculated polyp of the sigmoid colon. Case 2: A 47-year-old female patient with a 3 mm rectal polyp.
Results: Microscopic examination showed, in both cases, an unremarkable colorectal mucosa and a dense eosinophilic amorphous deposit involving the muscularis mucosae and the submucosa, associated, in Case 2, with thick-walled submucosal blood vessels. This eosinophilic material stained negatively with Congo Red and positively with elastic stain (Verhoeff). The diagnoses of fibroelastosis and angioelastosis were retained in Case 1 and Case 2 respectively.
Conclusion: Elastofibromatous changes of the gastrointestinal tract are rare benign lesions. Depending on the histological pattern, they are classified as fibroelastosis, angioelastosis or elastofibroma. Although the pathogenesis remains unclear, they are considered to represent degenerative changes. On H&E stain, these lesions may be mistaken for amyloidosis. However, once one is aware that they exist, they can be easily identified.

PS-12-009
Cyclooxygenase-2 expression in colorectal adenomas and carcinomas: Immunohistochemical study of 50 cases

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Objective: Cycloxygenase-2 (COX-2) is a key enzyme in arachidonic acid metabolism which is supposed to take part in colorectal carcinoma carcinogenesis but its specific role is still to be validated. The aim of this study is to analyze expression of COX-2 protein in colorectal adenomas and carcinomas using immunohistochemistry.
Method: A total of 50 endoscopic and surgical specimens of colorectal neoplasms −26 adenomas and 24 carcinomas - were studied. The results from the immunohistochemistry procedure were categorized based on their percentage −0, 1–25, 26–50 %, 51–75 and 76–100 % - and intensity −0, 1+, 2+ and 3+, and then summarized as a score from 0 to 7.
Results: There is a significant difference in COX-2 expression between carcinomas and adenomas ($p < 0.01$). Adenomas tend to be negative for the marker - only four of them showed focal positivity (score ≤4). Carcinomas are positive with variable score except for one case.
Conclusion: COX-2 is a marker which occurrence could be associated with adenoma-carcinoma transition in colorectal neoplasms. Its correlation with pathological features and biological behavior needs further investigation since the results from our and other studies in this field remain contradictory.

PS-12-010
An unusual case of medullary carcinoma of the colon

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Objective: The morphologic characteristics of colorectal medullary carcinoma (MC) have been extensively described but not its immunohistochemical profile. A case of MC is presented with emphasis on immunophenotype.
Method: A 79 year-old female patient presented with obstructive ileus and underwent emergency colectomy. We received a specimen of right colectomy. At the cecum a large (8.5 cm), ulcerated tumour was found. Twenty-five lymph nodes were found.
Results: Sections from the tumour showed a carcinoma consisting of cells with "neuroendocrine" features organized in nests and trabecular formations. Large areas of necrosis and abundant mitoses were found. There was no mucin production. At the periphery of the carcinoma there was dense inflammation. The neoplastic cells showed the following immunophenotype: CK8/18+, EMA+, CEA+, calretinin+, CK5/6-, CK7-, CK20-, CDX2-, MUC1-, MUC2-, chromogranin-, synaptophysin-, CD56-, HMB45-, CA125-, vimentin-, HepPar1-. The neoplastic cells were positive for MSH2 and MSH6 and negative for PMS2 and MLH1. All lymph nodes were free of metastasis. The diagnosis of MC (pT3pN0) of the colon was reached.
Conclusion: MC of the colon usually shares common morphologic characteristics with neuroendocrine carcinoma. An immunohistochemical panel including neuroendocrine markers, MMR proteins markers, CDX2 and calretinin seems to help establishing a correct diagnosis.

PS-12-011
Diffuse nodular lymphoid hyperplasia

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Objective: Diffuse nodular lymphoid hyperplasia, is a rare disease of unknown etiology characterized by the presence of numerous visible mucosal nodules with or without germinal centers, measuring up to, and rarely exceeding 0,5 cm in diameter. These may involve the entire small intestine, the large intestine, or both. The etiology is unknown. A male 35 years old presented with rectal bleeding underwent colonoscopy and biopsies were taken from terminal ileum, right and left colon.

Method: Colonoscopy showed multiple small polyps with diameter 0.2 cm. covering the whole length of the large intestine and terminal ileum.
Results: Microscopically these lesions consisted of normal lymphoid nodules. There were no other pathological findings. Diagnosis was compatible with benign, diffuse, colonic, nodular lymphoid hyperplasia in conjunction with immunohistochemical study against L-26, CD79a, CD-3, CD-5, bcl-2, CD-23, CD-10 and Cyclin-D1 and clinical information.
Conclusion: Diffuse nodular lymphoid hyperplasia often associates with congenital or acquired, late onset hypogammaglobulinemia and isolated IgA deficiency. Presenting symptoms may be recurrent sinopulmonary infections accompanied by diarrhea, steatorrhea and giardiasis or other diseases from pernicious anemia to sarcoidosis and arthritis. Older patients without a detectable immunodeficiency are in risk for developing malignancies such as small intestinal lymphoma, particularly of the mucosa-associated lymphoid tissue (MALT) type.

PS-12-012
Colorectal adenocarcinoma with heterotopic bone
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Objective: Heterotopic bone is rarely found in colorectal carcinoma with low incidence of 0,4 %. We report a case of a 75-years old male presenting with constipation, vomiting and abdominal, i.e. acute abdomen, due to large bowel obstruction. He underwent urgent surgical operation.
Method: The received material was a total colectomy with egsophytic tumour in the sigmoid colon, measuring 4 cm in length, with proximal dilatation of 16 cm in diameter. Standard tissue samples were embedded in paraffin blocks and Hematoxylin-Eosin and imunohistochemical stainings were made.
Results: Histological analysis showed poorly differentiated adenocarcinoma Stage IVA. We found abundant desmoplastic stroma, partly hyalinised, with deposition of osteoid and focal formation of well-defined osseous islands of various shapes and sizes, with evident osteoblasts arranged as osteoplasts, with focally formed Haversian canals. Immunohistochemical staining showed CK18(+), Vimentin(-) signal for tumour cells, and Vimentin(+) signal for the osteoid, Osteopontin(+) signal for osteoblasts and osteoid.
Conclusion: Pathogenesis is unclear, but there are theories describing fibroblast metaplasia into osteoblasts or production of BMP-2 and FGF-2 by tumour cells, inducing bone formation. The finding of osseous metaplasia in colorectal carcinoma does not change the prognosis, although is very important to differentiate this entity from carcinosarcoma, that have poor prognosis.

PS-12-014
Evaluation of extramural tumour deposits in colorectal carcinoma
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Objective: The aim of this study was to use immunohistochemical staining to estimate the tumour deposits nature in colorectal carcinoma.
Method: Colorectal carcinomas were selected from 50 histologically analyzed tumours with tumour deposits in peritumoural zones or with distant tumour deposits. Six parts of primary tumours and fat tissue were analyzed. Two hundred seventy six slides were examinated. A mean of ten blocks were sampled for each tumour. Staining for Neuron Specific Enolase and Smooth Muscle Actin to identify perineural invasion or angioinvasion were used.
Results: Our results show that tumour deposits observed in 21 % were peritumoural, 19 % tumour deposits were associated with angioinvasion, 10 % tumour deposits were associated with perineural invasion, 8 % tumour deposits were associated with lymph nodes. True tumour deposits without association with any histology structures were evident in 42 % of cases. Different types of tumour deposits were met in all cases, more then three types in 16 %.
Conclusion: Our findings suggest the role of adjunct techniques to evaluate the carcinoma invasion in paracolon fat tissue, to find perineural invasion or angioinvasion and identify true tumour deposits. Tumour deposits are heterogenic group with different subtypes. Tumour deposits can be used as prognostic indicator for colorectal carcinomas associated with metastatic potential.

PS-12-015
The clinicomorphological risk factors analysis in early stages of colorectal carcinoma
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Objective: Tumour staging is the most important prognostic predictor for clinical outcome in colorectal adenocarcinoma (CRC). We aimed to assess the clinicopathologic factors in patients with early stage (pT1-T2) versus advanced CRC.
Method: We performed a multivariate analysis in patients with CRC who underwent radical resections in Timisoara County Hospital from 2010 to 2013. Associations between tumour stage (pT1-T2 vs. pT3-T4) and tumour grade, nodal status (LNM), as well as the presence of lymphovascular invasion (LVI) were analyzed using the Fischer's exact test.
Results: We identified 539 cases of CRC. The incidence of CRC increased with age, with a slight predominance in males (323 cases, 60 %). 15 % of the cases were stage pT1-T2, 85 % pT3-T4. Five percent of all the cases were well-differentiated (G1), 95 % moderately (G2) and poorly (G3) differentiated CRC. In multivariate analysis low differentiation (p = 0,0178, OR = 2,793), LVI (p < 0,0001, OR = 10,92) and LNM (p < 0,0001, OR = 5,631) were significantly related to depth of invasion.
Conclusion: LVI, LNM and tumour grade are independent risk factors in pT1-T2 CRC. Due to the subjective nature of some of the elements assessed and the controversy in colorectal pathology reporting we need standardized examination protocol and reporting.

PS-12-016
Metastatic Mixed Mdenoneuroendocrine Carcinomas (MANECs) of the colorectum: Two cases
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Objective: MANECs of the colorectum, as defined by WHO-Digestive/ 2010, are exceedingly rare tumours with approximately 100 well-documented cases in the literature.
Method: Herein we report two cases with subsequent and simultaneous metastases respectively.
Results: A 61-year-old man was submitted to surgery for a rectal tumour microscopically characterized after the excision as MANEC. A year after the initial surgery, he presented with a scalp lesion histopathologically consistent with metastasis from the neuroendocrine component of his previous carcinoma. The patient died 4-months after the diagnosis of metastatic disease. The second case is about a 45-year-old man who underwent surgical biopsy due to mediastinal lymphadenopathy. Microscopic examination was consistent with lymph node metastasis of a large-cell neuroendocrine carcinoma of unknown primary site. Immunohistochemical co-expression of CD-X2 and CK20 along with absence of TTF-1 immunoreactivity suggested gastrointestinal tract investigation which revealed a MANEC of the descending colon. No follow-up is available up to date. Both colon tumours consisted of a well-

differentiated adenocarcinoma component, noninvasive beyond muscularis mucosa (intramucosal) and with no positive lymph nodes.
Conclusion: Our cases support the impression that, concerning MANE Cs, patient outcome is based mainly on the neuroendocrine component. The optimal management of MANECs is largely unknown, due to the rarity and incomplete classification of these neoplasms.

PS-12-017
Somatostatin receptors in ileal mucosa in Inflammatory Bowel Disease (IBD)
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Objective: Somatostatin (SMS) is a major anti-inflammatory neuropeptide, which could influence bowel homeostasis, immunologic and morphologic changes in patients with inflammatory bowel disease (IBD).
Method: Our research includes ileal biopsies from 42 patients: 16 patients with Crohn`s disease (CD), 14 patients with IBD unclassified (IBDU) and 12 patients as a control group. To determine neuroendocrine changes in IBD patients, immunohistochemical staining of ileal biopsies with SMS Receptor type 2 (SSTR-2) antibody was performed. The number of SSTR2-positively stained cells was counted per 100 enterocytes.
Results: Three different staining patterns were observed: membranous, cytoplasmic and membranous-cytoplasmic. The amount of positive cells with membranous staining was 1 ± 1 in patients with CD, 2 ± 1 in controls and 3 ± 2 in patients with IBDU. Cytoplasmic staining was observed in 1 ± 2 cells in the CD group; 2 ± 1 in controls and 3 ± 1,5 in IBDU group. The number of membranous-cytoplasmic SSTR2+ cells was 5 ± 3 in CD patients, 3 ± 1 in controls and 2 ± 3 in patients with IBDU.
Conclusion: Our data illustrate that the number of SSTR+ cells with a membranous-cytoplasmic staining pattern is elevated in patients with CD while all three staining patterns are elevated in IBDU when compared with controls. This is additional evidence for the participation of somatostatin in IBD pathogenesis.

PS-12-018
Elevation of intraepithelial lymphocytes as additional diagnostic criteria for ileitis in Inflammatory Bowel Disease (IBD)
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Objective: The etiology of inflammatory bowel diseases (IBD) remains largely unknown, but it is thought that the interaction between the immune system and changes of the intestinal flora might play a big role in the pathogenesis. This is why it is possible to use changes in immune system as an additional criterion for diagnosis in IBD.
Method: Our research includes ileal biopsies from 50: 18 patients with CD, 11 patients with IBD unclassified (IBDU) and 21 patients with normal mucosa, they were chosen as control group. We performed an immunohisrochemical (IHC) examination of ileal biopsies with antibodies directed against CD3. The number of CD3 positively stained intraepithelial lymphocytes (IEL) was counted per 100 epithelial cells, covering a villus.
Results: Mean number of intraepithelial lymphocytes (IEL) in patients with CD was 39,5 ± 11. Patients with IBDU had 46 ± 13 positive stained cells. In the control group the number of IEL comprised 29 ± 6 cells.
Conclusion: Our data show that number of IEL in ileum biopsies is relatively higher in patients with CD and IBDU comparing to normal ileal mucosa. This also shows that CD3 IHC-staining could be used as additional diagnostic criterion in IBD.

PS-12-019
Detection of cytomegalovirus by immunohistochemistry in colectomy pieces made for severe acute colitis in the context of chronic Inflammatory Bowel Disease (IBD)
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Objective: We propose to discuss the pathogenesis of Cytomegalovirus (CMV) in colitis, the CMV's role in disease severity, and the approach to diagnosis and management.
Method: It was an immunohistochemical study of 37 samples of patients with chronic inflammatory bowel disease (CIBD) collected in our department over a period of 10 years using the anti-CMV antibodies.
Results: The average age of patients was 38 years. Twenty-three patients were with Crohn disease (CD) (62 %), 12 patients with Ulcerative Colitis (UC) (33 %) and 2 patients with Indeterminate Colitis (CI) (5 %). Twenty-nine cases had deep ulcers and 8 cases had superficial ulcers. Our study shows that 3 cases among 37 expressed CMV. Among these three cases, 1 case was CI and 2 cases were UC. The CMV inclusions were generally present in areas of ulceration which shows large cells with an intranuclear inclusion in appearance of "owl eye" characteristic of CMV infections. The absence of ulceration does not exclude CMV infection.
Conclusion: Immunohistochemistry is an available method to detect CMV compared to other expensive techniques (PCR, ELISA ...). It must be included in the assessment of patients with CIBD to guide surgeons to do biopsies at ulcerations before deciding to achieving colectomy.

PS-12-021
The role of pathological assessment of Endoscopic Submucosal Dissection (ESD) specimens in superficial malignant Colo-rectal (CR) tumours
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Objective: ESD is a new resection technique for superficial CR tumours not amenable to snare resection. This method may avoid resective surgery, providing lymph node involvement risk factors can be evaluated. This is in contrast to standard endoscopic mucosal resection, where fragmentation precludes adequate pathological evaluation. This study explores pathological results and clinical follow-up among CR-ESD treated patients.
Method: Between 2006 and 2014, 192 CR-ESDs were performed at St-Luc Hospital. Lesion location, TNM classification, grade, surface area, lateral margins, and width and depth of sub-mucosal invasion were prospectively recorded. Endoscopic and clinical outcomes were also observed.
Results: We found low and high grade dysplasia, and adenocarcinoma in 51 (26.6 %), 74 (38.5 %) and 67 (34.9 %), respectively. Twenty-two (11.5 %) lesions were pT1. Of these, 16 (72.7 %) were pT1sm1 and 6 (27.2 %) were pT1sm2/3. Subsequent surgery was indicated for 6/16 (37.5 %) pT1sm1 and all pT1sm2/3. No surgeries showed residual carcinoma (pT0 N0). In the remaining 10/16 pT1sm1 (62.5 %), follow-up did not reveal recurrence.
Conclusion: In this large series of CR lesions treated with ESD, specimen integrity allowed us to make clear diagnoses and clinical decisions. This approach avoided resective surgery in the pT1sm1 tumour subgroup of patients without pejorative factors.

PS-12-022
Immunohistochemical investigation of prognostic factors in colon adenocarcinoma
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Objective: Of investigation was to identify morphologic prognostic factors for colon adenocarcinoma.
Method: 776 patients with colon adenocarcinoma (mean age 57,6) were included. Receptors for chemokine (CCR10, CXCR4), stem cell marker (ALDH1), ki-67, MSH2, MSH6, MLH1, PMS2 assessed by immunohistochemistry.
Results: Low proliferation level (Ki-67<30 %) and expression of CXCR4 were more frequently revealed in disseminated cancer (IV stage) compared to localized (II stage), $p = 0{,}002$. Relapse-free survival rate in patients with primary II stage with Ki-67>70 % and CXCR4<30 % was more than 5 years in 75 % of cases and in 25 % cases median was 16, 5 month. Cases with CXCR4>70 % and Ki-67<30 % had 5 years relapse-free survival rate 32 and in 68 % cases median was 7 month. In 9 % of cases immunohistochemical study of MSH2, MSH6, PMS2, MLH1 expression prevented incorrect evaluation of cancer grade.
Conclusion: Immunohistochemical assessment of CXCR4, Ki-67, MSH2, MSH6, PMS2, MLH1 can be useful prognostic tool for patients with colon adenocarcinoma.

PS-12-023
Adenocarcinoma ex goblit cell carcinoid, signet ring cell type: A rare case
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Objective: Goblet cell carcinoid (GCC) is a mixed glandular-neuroendocrine neoplasm that seems to represent a seperate entity, distinct from both classic carcinoids and denovo appendiceal adenocarcinomas. They display a spectrum of histologic features and possess the potential to transform to an adenocarcinoma phenotype of either signet ring cell or poorly differentiated types.
Method: A 40 years old man was admitted to our hospital with a right iliac fossa abdominal pain.
Results: Blood investigations and radiologic findings were consistent with an acute apppendicitis and an appendiectomy performed. Histopathologic examination revealed transmural infiltration of the appendiaceal wall by mucin containing goblet-shaped epithelial cells arranged in round or oval clusters in a background of acut appendicitis. Some parts of the tumour showed partial loss of goblet cell clusters with disorganized arrangement of atypical tumour cells and a predominant signet ring cell feature associated desmoplastic stromal reaction. Immunohistochemically tumour cells were positive for CK7, CK20, CDX2, focally positive for chromogranin, synaptophysin and p53. Final diagnosis was adenocarcinoma ex GCC, signet ring cell type.
Conclusion: GCC is a rare tumour with a distinctive histologic appearance and variable biologic behavior. Careful evaluation of the morphologic features and appropriate pathologic classification are important for clinical management and prediction of management.

PS-12-024
Colonic polipoid ganglioneuroma: Case report
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Objective: Ganglioneuromas are rare benign peripheral neuroblastic tumours characterized by hyperplasia of ganglion cells, nerve fibers and supporting cells. They are very uncommon in the colon.
Method: A 49 years old woman was admitted to gastroenterology clinic for routin screening. A colonoscopy revealed one polyp in the colon measuring 5 mm in largest diameter. The polyp was removed with hot biopsy forceps.
Results: Histopathologic evaluation of polyp displayed displaced colonic crypts with underlying proliferation of ganglion and spindled schwan cells within the lamina propria. The polyp reacted positively to neuron spesific enolase stain and S-100 stain.
Conclusion: We describe a case of solitary polypoid ganglioneuroma of the descending colon incidentally discovered in a patient.

PS-12-025
Adenosquamous carcinoma of the rectum
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Objective: Adenosquamous carcinoma of the colon and proximal rectum is rare neoplasm with an incidence of less than %0,2. We present a rare case of adenosquamous carcinoma of the rectum.
Method: A 71-year-old man presented with intermittent rectal bleeding. Colonoscopy revealed ulcerative lobulated mass 10 cm from anal verge that was biopsied. Pathologic analysis of biopsy specimen revealed an adenocarcinoma. Abdominal CT revealed asymmetric wall thickening of upper rectum, which has ill defined margins with perirectal fat tissue. Low anterior resection was performed.
Results: Macroscopically, the tumour was 8 cm. It was described as infiltrative yellow-white, gray mass with areas of necrosis. Microscopically the tumour exhibited a biphasic malignant growth identified as moderately differentiated adenocarcinoma and poorly differentiated squamous cell carcinoma. Thirty percent of tumour cells were positive for CK5/6.
Conclusion: Adenosquamous carcinoma of the rectum is a rare and aggressive tumour characterized by coexisting of malignant glandular and squamous components. It has higher metastatic rate and worse prognosis than conventional adenocarcinoma. Early detection and radical operation with other available therapeutic modalities may improve clinical outcome.

PS-12-027
Could APOE E4 isoform be a protective factor in colorectal cancer?
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Objective: Apolipoprotein E (APOE) gene variants influence the enterohepatic metabolism of cholesterol and bile acids. Some APOE polymorphisms have been associated with the decrease of cholesterol absorption in colon and with the increase of excretion secondary bile acids. These factors revealed to have an important role in colorectal cancer (CRC) development. This study aimed to investigate the association between APOE common isoforms and CRC.
Method: FFPE non-tumoural colonic mucosa of 100 CRC biopsies was compared with blood samples of 100 healthy controls as a case-control study. APOE polymorphisms (E2/E3/E4) were genotyped by PCR-SSP, through commercially available kits.
Results: APOE E2E2 isoform was associated with CRC prevalence (10 vs 0 %; $P < 0.001$), while the remaining isoforms were correlated with CRC absence. In contrast, APOE E4E4 genotype were only present in control subjects (0 vs 8 %; $P < 0.005$).
Conclusion: These findings provided insight into the potential role APOE polymorphisms as risk factor for CRC whose dysregulation is associated with higher levels of secondary bile acids production which correlates with increased risk for CRC. Moreover, E4 form of APOE could, somehow, inhibit these pathways being a CRC protective factor. These results suggest that APOE E2 and E4 genotypes can influence CRC risk.

PS-12-028

MTHFR C677T and A1298C polymorphisms are risk factors for colorectal cancer

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Objective: Genetic changes in MTHFR gene are associated with folate metabolism deregulation. This metabolism influences the synthesis of purines, the hypometylation of the global DNA and hypermethylation of tumour suppressor genes, which can be associated with colorectal cancer (CRC) risk. The aim of the study was to explore the association between common polymorphisms MTHFR (C677T and A1298C) and CRC prevalence.

Method: FFPE non-tumoural colonic mucosa of 100 CRC biopsies was compared with blood samples of 100 healthy controls as a case-control study. MTHFR common polymorphisms (C677T and A1298C) were genotyped by PCR-SSP, through commercially available kits.

Results: MTHFR 677TT (40 vs 21 %; $P < 0.005$; OR = 2.5; 95 % CI 1.3 to 4.7) and MTHFR 1298CC (42 vs 22 %; $P < 0.005$; OR = 2.6; 95 % CI 1.4 to 4.8) mutated genotype were linked to CRC prevalence, while the remaining genotypes were associated with CRC absence.

Conclusion: Mutated genotypes have been associated to low activity of the enzyme, consequently decreasing the efficiency of folate metabolism. Deregulation of MTHFR gene seems to be associated with a decrease of MTHFR enzyme activity that leads folate downregulation and therefore to CRC predisposal. These findings provided insight into the potential pathogenesis of MTHFR common polymorphisms in CRC predisposal and prognostic.

PS-12-029

Mixed adenoneuroendocrine carcinoma arising from the anal mucosa: A rare case presentation

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Objective: The term mixed adenoneuroendocrine carcinoma was introduced by the WHO in 2010 referring to a neoplasm with dual adenocarcinomatous and neuroendocrine differentiation, each component representing at least 30 % of the tumour.

Method: Our case was diagnosed in a 68-years-old female as a polypoid lesion of the anal region measuring 1,2 cm in diameter and was surgically excised and sent for histopathological examination.

Results: Histopathology examination revealed cords, and islands of large cells with large round nucleus and abundant cytoplasm. Glandular structures amounting to more than 30 % of the tumour and amidst pools of extracellular mucin(PAS+). Immunohistochemical examination revealed CK8/18, CK7, CK20, Chromogranin were strongly positive and focal positivity for Synaptophysin. Ki67 proliferation index was >20 %. The diagnosis was MANEC of the anal region, poorly differentiated.

Conclusion: Due to the rarity of this tumour, few aspects are known about its histogenesis, with most of the authors admitting its origin in a multipotent stem cell with bidirectional differentiation, opposite to collision tumour, in which a separate origin of the two components is supposed. Clarifying this hypothesis could help identify of the proper therapeutic management of these rare, highly malignant tumours, similar to that of ordinary adenocarcinomas or for neuroendocrine tumours.

PS-12-030

Retrorectal epidermoid cyst: A rare case presentation

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Objective: Retrorectal epidermoid cyst is one of the developmental cysts which arise from remnants of embryonic tissues. Because of the rarity of these tumours in adults, the differential diagnosis is very difficult before surgery.

Method: A 32-year-old woman presented with a cystic lesion 3,2 cm, adhered to the posterior wall of the rectum, but complete resection was possible and was performed.

Results: Histological study revealed that the epithelium of this cyst wall consisted of keratinized, stratified squamous cells without atypia. According to these pathological findings, this tumour was diagnosed as an epidermoid cyst. Immunohistochemical studies using CEA, antigen antibody were performed and was strong positive in the stratified squamous epithelium.

Conclusion: Retrorectal cysts in adults are rare and in most cases are congenital. Anatomical, developmental cysts are described between the anterior sacrum side and posterior wall of the rectum. They occur in young women in a female/male ratio of 3:1. Chronic infection occurs in 30–50 % of developmental cysts and are source of a perianal abscess or a draining sinus. Malignant degeneration, estimated at about 7 % and met after 30 years of evolution has been reported for enteric cysts. Histopathological types commonly found as adenocarcinomas or squamous cell carcinomas.

PS-12-031

Interlaboratory variability in the grading of dysplasia in a nationwide cohort of colorectal adenomas

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Objective: Although high-grade dysplasia (HGD) is a risk factor for malignant transformation and future development of adenomas/carcinomas, it is not incorporated in Dutch colonoscopy surveillance guidelines, partly due to high interobserver variability. We analyzed interlaboratory variability in grading dysplasia in daily practice.

Method: Using the Dutch Pathology Registry (PALGA), all in 2013 synoptically reported classic adenomas were identified. Percentages of adenomas with HGD were determined for biopsies and polypectomies separately, and clinico-pathological factors associated with HGD were investigated. We compared percentages of HGD in a subgroup of 21 laboratories, and performed univariable and multivariable logistic regression analyses.

Results: Pathology reports of 21,145 colonoscopies (20,332 patients) were identified. HGD was diagnosed in 2.6 % of 21,544 adenomas from biopsies, and varied from 0 to 11.8 % between 21 laboratories. On 10,980 adenomas from polypectomies, HGD was diagnosed in 9.6 %, and it varied from 2.2 to 35.3 %. On multivariable analysis, four laboratories were outliers; three with a higher frequency of HGD and one had not diagnosed HGD on biopsies at all.

Conclusion: We observed considerable interlaboratory variation in grading dysplasia, only partly explained by differences in casemix.

It is important to find ways to standardize grading to enable incorporation of degree of dysplasia in Dutch colonoscopy surveillance guidelines.

PS-12-032

Correlation between desmoplastic reaction and perineural invasion in colorectal cancer

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Objective: Desmoplastic reaction (DR) is characterized by stromal fibrosis and myofibroblastic proliferation. The complex signaling pathway between tumour and stromal cells is not illuminated yet. We investigated the relationship between prominent DR and other clinicopathological features in colorectal cancer.
Method: One hundred consequent cases diagnosed between 2006 and 2010 years, with available survival data were enrolled in the study and were reevaluated for presence of dense fibroblastic and mixed "fibroblastic-inflammatory" DR.
Results: The median age was 63 ± 14.7 years-old (range: 22–91), the female/male ratio was 45/55. Forty-eight of the cases were located in right colon, 84 % had T3, 63 % had (N1-N2), 36 % had perineural invasion (PNI) positive tumours. DR was pure fibroblastic in 27 % and mixed in 25 % of the cases. Overall 33 (91.7 %) of the cases with DR had PNI (p = 0,000,χ2) and 38 (73 %) had lymph node metastases (p = 0.032, χ2). Among the PNI positive group, 21 (77.8 %) had fibroblastic DR (p = 0, 000,χ2) and 59 % (n = 16) of them has died during the follow up (p = 0.022, χ2). No correlation was found between age, gender, location and tumour stage.
Conclusion: The significant correlation between fibroblastic DR and presence of PNI deserves further research for both understanding the crosstalk between tumour cells and tumoural microenviroment and for developing future targeted therapies.

PS-12-033

SMAD4 expression as a prognostic factor in colorectal cancer

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Objective: SMAD4 protein, encoded by SMAD4 on chromosome 18q21, is involved in mediating the TGF-β pathway. In colorectal cancer (CRC), SMAD4 has been associated with liver metastasis and decreased survival. We investigated whether SMAD4 loss correlated with survival outcomes.
Method: Immunohistochemistry was performed in TMA format for SMAD4 on 2722 consecutive CRC patients treated at our institution from 1998 to 2011. We analyzed the association between SMAD4 loss and survival and also calculated hazard ratios (HR) and 95 % confidence intervals (CI) for mortality using Cox regression, adjusting for age, gender, tumour grade, site and SMAD4 loss.
Results: Mean age at diagnosis was 71.49 years (range 17–103 years), and 1328 (48.4 %) were male. SMAD4 loss occurred in 300 (10.9 %) of tumours. On univariate analysis, SMAD4 loss was related to decreased survival in tumours of the transverse colon (p = 0.014). In a multivariate analysis, age (HR 1.04, 95 %CI 1.037–1.05, p < 0.0001), male gender(HR 1.36, 95 %CI 1.19–1.56, p < 0.0001), high tumour grade (HR 1.70, 95 %CI 1.45–2.00, p < 0.0001) and SMAD4 loss (HR 1.26, 95 %CI 1.03–1.55, p = 0.026) all predicted increased mortality.
Conclusion: We present weak evidence linking SMAD4 loss to decreased survival outcomes, possibly influenced by the site of tumour occurrence.

Table 1: Cox multivariate regression showing hazard ratios for mortality:

Variable	HR (95% CI), p-value
Age at diagnosis	1.04 (1.037 - 1.05), <0.0001
Gender	
Female	1.00
Male	1.36 (1.19 - 1.56), <0.0001
Grade	
Low grade	1.00
High grade	1.70 (1.45 – 2.00), <0.0001
SMAD4 status	
SMAD4 positive	1.00
SMAD4 loss	1.26 (1.03 – 1.55), 0.026

PS-12-035

Entropy in colon adenocarcinoma

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Objective: The prognostic value of the tumour stem cells and mathematical histological features including novel ones; tissue "entropy" and "complexity"; were evaluated in colon adenocarcinomas.
Method: Tumour, stroma and lumen were manually marked and recorded on microscopic digital images from 248 colon adenocarcinoma cases. Mean, maximum, minimum and variance of tumour/stroma proportion, entropy and complexity were calculated for the whole analyzed tumour area and invasive border separately. Sub-images with different sizes were formed in main images and all calculations were done for these sub-images of 8 × 8 and 16 × 16 pixels. Stem cell markers, CD133 and Lgr5 were evaluated by immunohistochemistry. The relation with prognosis was evaluated.
Results: Cox regression analysis revealed an increase of death risk of 1,02 fold for tumour/stroma proportion at the maximum group of 8 × 8 pixel images, 1,2 fold for tumour/stroma proportion at the mean group of 16 × 16 pixel images and 1,9 fold for entropy at the invasive tumour border. Recurrence risk increased 1,002 times for variance of tumour/stroma at 16 × 16 pixel images. There was no relation with stem cell markers and prognosis.
Conclusion: Entropy at the invasive border of colon adenocarcinomas may be a novel independent prognostic feature as well as tumour/stroma proportion at subimages.

PS-12-036

Colon adenocarcinoma developed from traditional serrated adenoma: Report of 6 cases

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Objective: Serrated polyps are relatively new group of premalignant lesions of the colon and rectum. Among all, traditional serrated adenoma (TSA) is the most rare and understudied type and has unique genetic profile and marked neoplastic potential, however a few cases of colon adenocarcinoma developed from TSA were described in the literature.
Method: We describe six cases of the colon adenocarcinoma developed from TSA.
Results: Patients' age was 47–76 years (mean age 60 years). Three of them were female (50 %), others were male. Only two patients presented with specific clinical symptoms (one with bowel obstruction, second - with blood in stool). In remaining cases the tumour was detected at colonoscopy performed on another occasion. In 4 cases tumour was located in the right side of the colon. In remaining cases - in sigmoid. Maximum diameter measured from 2,5 to 8 cm (mean 5,8 cm). On section tumours in all cases had polypoid appearance. Histological examination revealed carcinoma is situ in one case (17 %), well differentiated adenocarcinoma in three cases (50 %) and moderately differentiated adenocarcinoma in two cases (33 %).
Conclusion: Thus, colon adenocarcinoma developed from TSA is more common in older patients, has polypoid shape and is more often found in the right parts of the colon.

PS-12-037

Evaluation of the epigenetic pathway in primary and metastatic colorectal carcinomas

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Objective: DNMT1, DNMT2 and BMI1 are implicated in the regulation of protein expression through epigenetic modification of DNA/RNA. Even though, their expression in primary colorectal carcinomas has been studied before, the epigenetic heterogeneity between primary and metastatic carcinomas has not been assessed.
Method: We examined the expression of DNMT1, DNMT2 and BMI1 in 38 cases of primary colorectal carcinomas and their respective hepatic metastases using immunohistochemistry. Nuclear staining was evaluated for all markers. Cytoplasmic staining was additionally evaluated for DNMT2. The intensity of staining was graded in a scale of 1–3 and was multiplied by the % of positive cells.
Results: DNMT1 expression was higher in metastatic compared to primary tumours and in carcinomas compared to the adjacent non-neoplastic colonic epithelium ($p = 0.041$ and $p = 0.008$, respectively). Metastatic tumours had a trend for higher levels of BMI1 and nuclear DNMT2 expression compared to their primaries ($p = 0.060$ and $p = 0.054$, respectively). DNMT2 and BMI1 expression was higher in primary tumours compared to the non-neoplastic epithelium ($p < 0.001$).
Conclusion: Our results demonstrate that aberrations of the epigenetic pathway may be implicated in the metastatic potential of colorectal carcinomas. The heterogeneity between primary and metastatic tumours needs to be accounted for in the evaluation of potential therapeutic targets.

PS-12-038

Bone formation (osseous metaplasia) in a rectal inflammatory polyp: Case report

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Objective: Osseous metaplasia is rarely detected in the gastrointestinal tract, in benign tumours. Heterotopic osseous metaplasia is a relatively infrequent finding and is more commonly seen in degenerative and reparative conditions than in neoplasms. Most of the reported cases are associated with malignant lesions.
Method: We are reporting a rare case of an inflammatory polyp in a 31 years old male who came to our hospital because he noticed blood in the stools and pain during defecation.
Results: Colonoscopic examination revealed a solitary polypoid lesion located in the rectum. On pathologic gross examination, the polyp was a 57 × 23 × 20 mm fragment, gray-yellow mucosa covered and soft consistency. It was submitted in total for histopathological examination. Microscopically, H&E stained sections showed that polyp was composed of inflammatory granulation tissue with numerous capillaries and accumulations of neutrophilic granulocytes and lymphocytes. Fragments of well-formed bony spicules were also found.
Conclusion: Benign lesions with osseus metaplasia are often seen with a histological background of active chronic inflammation and/or ulceration. Different mechanisms have been suggested but the pathogenesis of osseous metaplasia still remains unknown.

PS-12-039

Adenosquamous carcinoma of the rectum: A case report of an unusual localization

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Objective: Adenosquamous carcinoma is a rare histological type of colorectal cancer (<0.1 % of all cases). We report a case of a rectal adenosquamous carcinoma, an even rarer entity.
Method: A 64-year-old female presented with a rectal mass, localized 5 cm above the anus. Endoscopic biopsy revealed squamous carcinoma with mixed morphology. Our differential included adenosquamous carcinoma. Chemoradiation was followed by abdominoperineal resection, left oophorectomy, cholecystectomy and partial resection of lateral pelvic wall.
Results: Grossly, we identified a vague mass (9.5 × 5.5 × 3.8 cm) located 1.8 cm above the dentate line, infiltrating the entire rectal wall. Histopathology revealed neoplastic cells with high grade glandular and squamous morphology, focal clear cell morphology and extracellular mucin. Immunohistochemically, glandular areas were positive for CK18, PAS-D and Alcian-Blue and squamous areas for CK5/CK14/p63. The diagnosis of high grade adenosquamous carcinoma was made with metastasis in pericolic lymph nodes, the left ovary and lateral pelvic wall.
Conclusion: This is one of the very few reported cases of rectal adenosquamous carcinoma, with a more aggressive clinical behavior than a rectal adenocarcinoma. As cell of origin, has been suggested ectopic squamous or reserve cells in the colonic mucosa or transformation of normal glandular or in situ adenocarcinoma cells into malignant squamous cells.

PS-12-040

Eosinophil granulocytes: Important modulators in ulcerative colitis

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Objective: Eosinophil granulocytes (EoG), important component of inflammatory infiltrate in ulcerative colitis (UC), are considered, by various studies, modulators of immune response and not only effectors of inflammation. We studied presence and distribution of EoG in UC to identify new data supporting this hypothesis.
Method: This study included 45 patients with UC, which were evaluated (clinically, endoscopically and microscopically) at the beginning of the study and 12 months later. Two fully-trained pathologists semi-qualitatively evaluated the number of EoG in lamina propria of colonic mucosa.

Results: The number of EoG predicted with high specificity (92 %) the risk of early relapse and was very significantly correlated with the risk of poor outcome ($p < 0.0001$). Also, EoG persisted in mesenchimal microenvironment after neutrophil granulocytes disappearance, this persistence being correlated with relapse ($p = 0.0194$).
Conclusion: These data indicate that EoG are playing an important role in colonic chronic inflammation, being as well modulators and effectors in UC lesion. Therefore their number should be routinely evaluated in all colonic mucosa samples from UC patients and included in treatment and surveillance decisions.

PS-12-041
Sigmoidectomy in a patient with chronic intestinal pseudo-obstruction due to inflammatory neuropathy (enteric ganglionitis) with high titres of circulating anti-Hu autoantibodies
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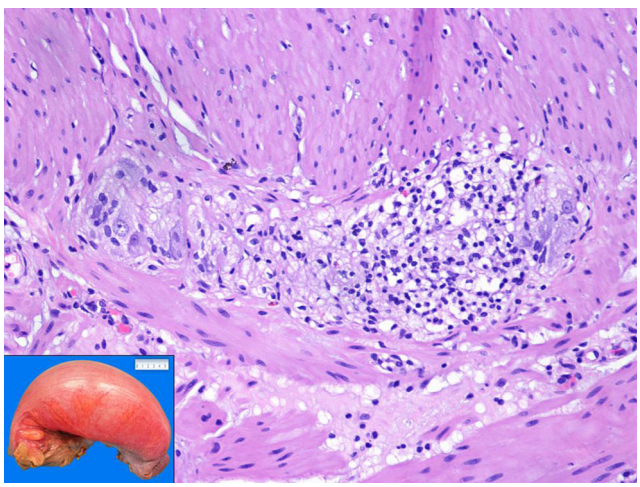
Objective: To report a case of inflammatory neuropathy with high titres of anti-Hu autoantibodies as cause of chronic intestinal pseudo-obstruction (CIPO).
Method: A 56 year old male presented with a 6-months history of severe sensory neuropathy, cerebellar involvement, stiff person syndrome, repeated episodes of intestinal obstruction and high titres of serum anti-Hu autoantibodies. Sigmoidectomy was performed with the suspicion of volvulus, not confirmed intraoperatively.
Results: The sigmoid specimen was markedly dilated. Microscopically, inflammatory infiltrates with lymphocytes and eosinophils were observed in the myenteric plexus, without hypoganglionosis. The muscular wall showed no fibrosis or vacuolization, and immunohistochemically retained its normal actin expression; CD-117 highlighted conserved interstitial cells of Cajal.
Conclusion: CIPO is characterized by failure of intestinal peristalsis in the absence of any mechanical obstruction. Three major forms exist with different pathologic finding: enteric visceral myopathies, neuropathies (inflammatory neuropathy and degenerative neuropathy) and mesenchymopathies (depletions/absence of interstitial of Cajal). Inflammatory neuropathy, which involves enteric ganglionitis, can be idiopathic or secondary to many different conditions, including circulating antineuronal antibodies (mainly anti-Hu) often as paraneoplastic syndrome. After 4 years of follow up and exhaustive study (CT,CT-PET, endoscopies,…) no tumour has been detected in our patient.

Macroscopically sigmoid specimen was markedly dilated. Detail of myenteric plexus with infiltrating lymphocytic, eosinophilic between the ganglion cells and neurons without obvious cellular destruction:



PS-12-042
Good's Syndrome and chronic diarrhea. A mimicker of Crohn's Disease with a challenging histopathological diagnosis
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Objective: Good's syndrome (GS) is the association of thymoma and hypogammaglobulinemia and is characterized by recurrent infections, diarrhea and other autoimmune manifestations. We report the gastrointestinal histopathological findings of a 54-year-old man with GS who developed chronic diarrhea.
Method: Gastrointestinal endoscopy studies showed pancolitis with ulcers intercalated with normal mucosa, and different histopathological lesions.
Results: The colon mucosa revealed chronic inflammation, ulcers, cryptitis, crypt abscesses and epithelioid granulomas, and the diagnosis of Crohn's disease was suggested. The ileocecal valve was positive for CMV and later became negative. In the subsequent biopsies the ileal mucosa showed blunt villi, intraepithelial lymphocytosis, frequent apoptotic bodies and absent plasma cells, resembling the changes of the Common Variable Immunodeficiency. In the sigmoid colon a pattern of Graft-versus-Host-type-colitis with striking apoptotic cells and atrophic glands with luminal debris, was observed. All findings were finally considered to be a gastrointestinal manifestation of the immunodeficiency.
Conclusion: The diarrhea in GS may be related to infectious pathogens, malabsorption, bacterial overgrowth or an autoimmune basis. Chronic inflammatory colitis similar to IBD has been described, but the association of IBD and GS is probably questionable. The histopathological findings can be quite variable in morphology, so the diagnosis may become a challenge, especially without clinical data.

PS-12-043
Superficial leiomyoma of the gastrointestinal tract with interstitial Cajal-like cells
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Objective: Some authors suggest common origin of all gastrointestinal stromal tumours from stem cells, which may show diverse differentiation. There are reports in which cells with a morphology of interstitial Cajal-like cells are found in deep leiomyomas. The aim of this study was to demonstrate CD117 positive cells in superficial gastrointestinal (GI) leiomyomas and to find other cells that would suggest diverse differentiation in histologically typical leiomyoma.
Method: We have analyzed 9 cases of superficial leiomyomas, received in our institutions as endoscopically or surgically obtained material. The tumour sections were immunohistochemicaly stained with CD117, CD34, NSE, S 100, α-S MA and desmin.
Results: There were one esophageal and 8 colonic superficial leiomyomas, 2 of which rectal. Histological analysis showed presence of stellate cells morphologically similar to the interstitial cells of Cajal. Immunohistochemical analysis showed that in addition to diffuse positivity for -SMA and desmin, all leiomyomas showed presence of CD117, CD34 and NSE positive cells between smooth muscle cells, while six of them showed presence of S-100 positive cells. The cells were found in different quantity, usually were scarce and diffusely scattered through the tumours without predilection site.
Conclusion: The presence of CD177, CD 34, S-100 and NSE positive cells in superficial leiomyomas may suggest a common origin of GI stromal tumours.

PS-12-044

CMV and acid-fast bacilli coinfection presenting as an ileo-caecal mass in a patient with supposed Crohn's Disease

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Objective: Cytomegalovirus (CMV) infection of the gastrointestinal tract presenting as a mass-like lesion is an extremely rare condition. Less than 50 cases were reported in literature to date. Association of CMV and acid-fast bacilli (AFB) is also very rare and usually occurs in immunosuppressed patients.
Method: We report the case of a 63-year-old man with a 15-year history of abdominal complaints and 5-year history of ileo-caecal Crohn's disease. In 2012 he presented with haemoptysis. Further investigation revealed basal bronchiectasis and tuberculous sequelae, negative bronchoalveolar lavage and Quantiferon Gold test. Recently he presented with a flare of ileo-caecal inflammation. Colonoscopy revealed an infiltrative and ulcerated ileo-caecal mass, which was biopsied.
Results: Microscopically, the biopsy showed ulcerative/erosive inflammation, with areas of necrotizing granulomas and viral cytopathic changes within stromal, endothelial and epithelial cells, characteristic of cytomegalovirus infection: enlarged cell size, enlarged and centrally located nuclei and nuclear inclusions. The infection was confirmed by positive nuclear CMV immunohistochemical stain. Ziehl Neelsen stain was also positive. The patient died 4 days after the histological report was issued.
Conclusion: Marked immunosuppression was associated with AFB and CMV infection in this patient. It's not clear whether this was an association of Crohn's with tuberculosis or tuberculosis interpreted as Crohn's disease.

PS-12-045

Comparative assessment of CD34 and Endoglin (CD105) positive tumour blood vessels from rectal cancer: Correlation with biological and histopathological parameters

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Objective: To compare CD34+ and CD105+ tumour blood vessels in intratumor (IT) and peritumor (PT) areas of rectal cancers and correlation with TNM staging and inflammation.
Method: Fifty cases of rectal cancer were immunohistochemically processed to highlight tumour blood vessels by using two endothelial markers CD34 and Endoglin (CD105). Comparative analysis of microvascular density (MVD) assessed by using these two markers was performed and MVD values were then correlated with biological and TNM staging parameters.
Results: A higher MVD was registered for both PT and IT areas compared with normal adjacent rectal mucosa. MVD-CD34-PT had a statistically significant correlation with T ($p = 0,004$) but not with N or M. MVD-CD-105 IT correlated with N ($p = 0,004$) and T factor ($p = 0,004$) while MVD-CD105-PT had no correlations with TNM parameters. Leukocytosis but not anemia correlated with MVD-CD105-IT ($p = 0,027$) and MVD-CD105-PT ($p = 0,011$). Tumour inflammatory infiltrate showed a significant correlation with MVD-CD34-PT but not with CD105-MVD.
Conclusion: Our study revealed the need of a differential evaluation of CD34 and CD105 tumour vessels for IT and PT areas. Correlations found between CD105-MVD, TNM parameters and leukocytosis sustain that differential evaluation of tumour vessels in rectal cancers may have a prognostic and therapeutic impact.

PS-12-046

Simultaneous presentation of rectal adenocarcinoma, hepatic neuroendocrine carcinoma and pancreatic non-Hodgkin lymphoma

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Objective: Multiorgan tumour involvement is condition usually leading to consideration of metastatic stage of tumour. Therefore histologic confirmation of each of them should be done whenever it is possible.
Method: Routine histologic and immunohistochemical examination.
Results: We present a case of a 52-year-old man initially diagnosed with well differentiated sigmoid adenocarcinoma (stage T3N2) and radiologically described liver metastases. Radiofrequent ablation of 21 metastatic liver tumours as well as resection of five more liver metastases were performed. However, immunohistochemical examination revealed liver metastases of serotonin producing well differentiated neuroendocrine carcinoma suggesting metastatic NETG2 with Ki-67 index of 2,5 %. Additional CT imaging revealed pancreatic mass measuring 30 mm leading to possible primary site of NETG2. Distal pancreatectomy and splenectomy were performed as well as rectum resection for recurrent colorectal adenocarcinoma. Surprisingly, after histological and immunochistochemical examination pancreatic mass appeared to be non-Hodgkin lymphoma of follicular type grade I. Immunoprofile of concurrent peripancreatic lymph node metastases of neuroendocrine carcinoma showed no CDX-2, TTF-1 and PAX-8 expression. To date, no primary site of neuroendocrine carcinoma was found.
Conclusion: To the best of our knowledge synchronous presentation of colorectal adenocarcinoma, hepatic neuroendocrine carcinoma and non-Hodgkin pancreatic lymphoma have not yet been reported.

PS-12-047

Clear Cell Carcinoma (CCC) arising from endometriosis of the rectum: A case report presenting in a patient with Lynch Syndrome (LS)

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Objective: Malignization of extra-ovarian endometriosis is extremely rare and associated with a specific histology such as endometrioid and CCC. LS patients have increased risk of developing colorectal cancer and other malignancies. Women with LS endometrium and ovary tumours present as sentinel at least as commonly as for colorectal cancer. We report a case of a woman with a clear cell carcinoma arising over endometriosis of the wall of rectum.
Method: We describe clinic-pathological features of a 49 years old woman presenting with a rectal neoplasm.
Results: On CT: thickness of the rectal wall. On endoscopic biopsies, is made a diagnosis of rectal adenocarcinoma. The histopathology of surgical resection shows a clear cell carcinoma arising on a endometriosis of rectum wall, evidencing a transition between endometriosis and CCC. The carcinoma-inmunoprofile was: CK7+, ER+, PgR+ /CK20-,CDX2-/MLH1-,PMS2-. Patient medical files shows a past hysterectomy due to leiomyomas and, 7 years ago, a right hemicolectomy due to a medullary carcinoma with MLH1-/PMS2- and fulfilling three of the Bethesda criteria.
Conclusion: Adenocarcinoma from endometriosis is rarely described at colon-rectum. Our patient fulfill three of the Bethesda criteria for LS, have a CCC histology, more closely related with LS, and present MLH1-,PMS2- on immunohistochemistry.

PS-12-048

Alpha-methyl-acyl-coenzyme: A racemase expression in hyperplastic polyps

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Objective: Hyperplastic polyps (HPs), considered previously harmless lesions, are currently regarded as pre-neoplastic lesions involved in serrated adenocarcinoma pathway. Few studies focused on α-methylacyl-

coenzyme A racemase (AMACR) expression in HPs. AMACR may allow identification of HPs that might progress to serrated sessile adenomas (SSAs). We aim to analyze AMACR expression in HPs in relation to their localisation.
Method: A series of 31 HP was recorded from 2008 to 2013. We evaluated AMACR immunostaining in crypt epithelial cells. Chi-squared test was used to evaluate the association between AMACR expression and HPs localization.
Results: AMACR expression was observed in 70 % of HPs. Fifty percent of HPs expressing AMACR were located in the left colon, 22.8 % in rectum and 27.2 % in right colon. The AMACR negative HPs were distal in 75 % of cases and proximal in 25 % of cases. No statistically different AMACR immunoexpression was detected among proximal and distal HPs ($p = 0.42$).
Conclusion: Recently published data find that although morphologically identical, HPs exhibit varying AMACR immunophenotype in relation to their location. Distal HPs were characterized by AMACR overexpression in contrast to proximal HPs, having higher risk to progress to SSAs. In our study, there was no correlation between AMACR expression and HPs localisation.

PS-12-049
Goblet cell carcinoid (adenocarcinoid) of appendix: Need for a reproducible histologic classification to predict the outcome
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Objective: Review of goblet cell carcinoid (GCC) in appendectomy specimens with emphasis on the reproducibility of current histopathologic classification.
Method: Records in the anatomic pathology information system were reviewed retrospectively for neuroendocrine tumour in all appendectomy specimens from 2005 through 2015. A total number of 3351 cases was retrieved. Neuroendocrine tumour was identified in 22 cases (0.6 %). Four of these (0.1 %) were diagnosed as GCC.
Results: Of the four cases, two were classified as type A (typical goblet cell carcinoid). In one patient the right hemicolectomy showed involvement of cecum, appendix, and ileocecal valve by tumour classified as type C (adenocarcinoma ex goblet cell carcinoid, poorly differentiated carcinoma type). The tumour of the fourth patient proved to be difficult to classify as type A or B (adenocarcinoma ex goblet cell carcinoid), and an expert who was consulted also found it challenging to classify.
Conclusion: GCC, an uncommon tumour almost exclusively found in the appendix, was first described in 1974. The aim of this study is to assess the practicality of the three-tiered histologic classification published by Tang et al. Considering the rarity of this tumour and the resulting lack of vast experience, even among experts, this classification, particularly the distinction between types A and B, appears not to be reproducible. The significance of separating types A and B based on some overlapping histomorphologic features is questioned. A two-tiered classification has been proposed by Wang et al. Application of a reproducible histologic classification or discovery of specific unfavorable biomarkers may help reliably predict the outcomes.

PS-12-050
Tumours of colon - are they always cancers?: Necrotic amoeboma in a healthy Scandinavian with no travel anamnesis
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Objective: We present a case of an intestinal tumour in a 58 years old Danish male, who was admitted to hospital with acute abdominal pain. He had no recent traveling history. Laparoscopy showed a normal appendix. However, a tumour in the ascending colon was found and a right hemicolectomy was performed. Gross examination showed ulcerations of the mucosa and tumour-like lesion in the caecal area. Further pathological examination showed deep ulcerations with undermined edges and massive inflammation and necrosis. Periodic acid Schiff (PAS)-positive amoebae trophozoites were identified, and the patient was diagnosed with and treated for amoebiasis.
Conclusion: Clinically suspected tumours of the GI-canal can in seldom instances reveal infectious disease when examined pathologically. Infections with entamoeba histolytica are very rare in otherwise healthy persons in our part of the world. Patients in developed countries working with sewage should be considered at risk of developing amoebiasis.

PS-12-051
Architectural distortion of colonic mucosa: A substitute for p53 and p21 immunostaining in routine screening for intraepithelial neoplasia in ulcerative colitis
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Objective: Ulcerative colitis (UC)-associated carcinogenesis driven by chronic inflammation is a rare feared complication of longstanding disease. Prevention of invasive carcinoma includes endoscopic and histologic periodic surveillance. p53 and p21 immunostaining can be used to monitor DNA damage induced by oxidative stress. This study tries to validate architectural distortion - an easily evaluable parameter on routine stains as marker of evolution towards intraepithelial neoplasia.
Method: We performed a prospective study on 45 patients with UC that underwent colonoscopy with multiple biopsies at the beginning of the study and 12 months later. Architectural distortion was semi-quantitatively evaluated by two independent pathologists. p53 and p21 were reported as percentage of epithelial and inflammatory cells.
Results: Only one case developed intraepithelial neoplasia during surveillance. On the other hand, architectural distortion was more severe in 89 % of patients, p21 expression increased from 7.33 to 10.67 % and p53 from 17 to 21 %. Architectural distortion correlated with p53 increase ($p = 0.0251$) and p21 ($p = 0.0035$).
Conclusion: Routine evaluation of architectural distortion is a good substitute for p21 and p53 immunostaining in surveillance for evolution towards intraepithelial neoplasia in UC, especially in compliant patients and in first decade of the disease.

PS-12-052
Histological examination of colonic mucosa from patients with clinical remission of ulcerative colitis
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Objective: To examine histological changes in the mucosa of patients with clinical remission of ulcerative colitis (UC).
Method: 25 patients with clinical remission of UC underwent colonoscopy with biopsy. The disease activity was determined using Ulcerative Colitis Endoscopic Index of Severity (UCEIS), for assessing histological activity of the UC used a Geboes score.
Results: 76 % patients (19 of 25) had UCEIS = 0 while in 24 % patients (6 of 25) UCEIS = 1. Histological examination revealed signs of disease activity (erosions, cryptitis, increased density of infiltrate) in 32 % patients (8 of 25). The number of eosinophilic leukocytes was increased in 44 % patients (11 of 25).
Conclusion: Increased eosinophil count often accompanied by other signs of lack of the mucosa healing. Confirmation of complete remission of the disease requires histological control for exclusion of the inflammation signs.

PS-12-053

Appendiceal adenocarcinoma developed in the setting of Crohn's Disease: A case report

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Objective: Colorectal and appendiceal malignancies are rarely encountered in Crohn's disease (CD). Here, appendiceal adenocarcinoma developed in the setting of CD is presented.
Method: 46-year-old male referred to clinic with epigastric pain and diarrhea. Physical examination was normal. Anamnesis revealed diagnosis of ulserative colitis, high and low grade displasia in caecum and colon. Colectomy was performed.
Results: Macroscopically, 1,8 × 0,6 cm mucosal swelling in ascending colon was detected. Appendiceal diameter was 2 cm at its proximal, wall was thickened and vascularity was prominent on serosa. Microscopically, adenocarcinoma with a diameter of 1,5 cm and subserosal invasion was seen in proximal appendix and appendix-caecum junction. High and low grade displasia were detected in neighboring areas. Nonnecrotizing granulomas across appendiceal wall and subserosa, linear lymphoid follicles, submucosal fibrosis, neuronal hyperplasia were seen. Other findings were chronic colitis, cript distortion, basal lymphoplasmacytosis and inflammatory pseudopolyps. No metastasis was detected in lymph nodes, however granulomas were present. Findings made us think of an invasive adenocarcinoma developing in the setting of CD.
Conclusion: There are few appendiceal adenocarcinoma cases associated with CD in the literature. Furthermore, macroscopic identification of malignancies that develop in CD are reported to be harder. Careful endoscopic examination and pathological sampling is suggested in CD cases.

PS-12-054

Mixed Neuroendocrine/squamous Cell Carcinoma (MNSC) of the rectum: Report of a case

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Objective: To describe a rare case of MNSC of the rectum.
Method: We describe a recent case from a 84-year-old female with a tumour submitted to abdominoperineal resection of the rectum and total mesorectal excision; no clinical evidence of distant metastases.
Results: The tumour disclosed a large cell component (60 %) admixed with a squamous component (40 %), invaded the mesorectum, and focally the surgical mesorectal margin; no evidence of any anal neoplasm; 38/40 lymph nodes with metastases, several with both components.The large cell component expressed synaptophysin, CAM5.2, and high Ki-67 index (80 %), whereas squamous component expressed AE1/AE3 and p63. Final diagnosis: MNSC of the rectum, pT3 N2b M0 R1.
Conclusion: The 2010 OMS classification of neuroendocrine neoplasms includes mixed neuroendocrine carcinomas that occur in different sites of the gastrointestinal tract. The non-neuroendocrine component may be an adenocarcinoma (MANEC) or, less frequently, a squamous carcinoma. MANEC occur more often in the stomach and colorectum; MNSC more often in the esophagus and anorectum. MNSC are aggressive neoplasms rarely reported in the rectum (a couple of published cases) that must be accurately diagnosed to allow the best management decision for patients harboring these tumours.

PS-12-056

DNA Mismatch Repair (MMR) protein expressions in colorectal medullary carcinomas

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Objective: DNA Mismatch repair (MMR) protein expression deficiency is closely related to high degree of Microsatellite instability (MSI-H) in colorectal cancers. Medullary carcinomas (MC) are especially common among MSI-H tumours.
Method: We searched immunoexpression of MLH-1, PMS-2, MSH-2 and MSH-6, in 7 MCs, in 43 poorly differentiated adenocarcinomas with MC-like areas and in randomly selected 100 tumours, including 8 mucinous and 92 well-to-moderately differentiated adenocarcinomas and correlated with other clinicopathological parameters by non-parametric tests ($\chi 2$).
Results: Three of the MC cases were female and the mean age was 62 ± 5.9 (Range:41–80 years). Tumours were located in right colon (5/7) ($p = 0.003$), showed prominent Crohn's-like aggregates (5/7) and tumour infiltrating lymphocytes (4/7) but less tumour budding (0/7) ($p = 0.07$) and dirty necrosis (0/7) ($p = 0.000$). MCs showed significantly higher MMR protein loss (85.7 %) when compared to poorly differentiated adenocarcinomas (48.6 %), adenocarcinoma with MC-like areas (33.3 %), mucinous (25 %), and well-to-moderately differentiated adenocarcinomas (17.4 %) ($p = 0.000$). Five cases (71.4 %) showed MLH1-PMS2 loss and was more frequent than other tumours ($p = 0.028$), while one case (14.3 %) showed MSH6-MSH2 loss.
Conclusion: MC is a distinct type of carcinoma that frequently associated with MMR protein loss. Further evaluation is needed to discriminate between sporadic MSI tumours and Lynch syndrome-associated tumours.

PS-12-057

Analysis of KRAS mutation heterogeneity between inner and peripheral areas of colorectal cancer

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Objective: KRAS mutation intratumor heterogeneity constitutes current clinical problem in targeted therapy of patients with colorectal cancer. We assessed KRAS mutations in tumour tissue excised from mucosa/submucosa and from the infiltrating outer (peripheral) border of the tumour.
Method: In 15 primary formalin fixed paraffin embedded colorectal cancers (one adenocarcinoma G1, 12 adenocarcinomas G2 and 2 adenocarcinomas G3) in which KRAS mutations were detected with PNAClamp™ KRAS Mutation Detection Kit (Panagene, Daejeon, Korea) using macrodissection, KRAS mutation testing was repeated in tumour tissue microdissected with the use of PALM MicroBeam (Zeiss) from two different areas (mucosa/submucosa versus outer peripheral area).
Results: PNAClamp™ detects 6 KRAS mutations in codon 12 and one mutation in codon 13. In all tumours examined KRAS mutation was detected in codon 12. There were no differences in the presence of KRAS mutations between microdissected tumour tissue from different areas examined.
Conclusion: A sensitive PNAClamp™ KRAS Mutation Detection Kit did not show mutation heterogeneity between microdissected tumour tissue from inner and peripheral areas of colorectal cancer.

Tuesday, 8 September 2015, 09.30–10.30, Restaurant
PS-13 Poster Session Haematopathology

PS-13-004

Bilateral aleukemic leukemia cutis of the eyelids

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Objective: Leukemia cutis can exceptionally occupy eyelids. An unusual case of a 58-year-old male presenting erythematous eyelid lesions, proven

to be aleukemic leukemia cutis, is reported. Interestingly, the patient stated that he had had the lesions for 2 years.
Method: Biopsy was conducted and hematoxylin/eosin (H&E) stained sections were histologically evaluated. Immunohistochemistry was also performed.
Results: H&E stained sections revealed cutaneous infiltration by a neoplastic population, consisting of medium-sized cells. These cells infiltrated the overlying epidermis leading to focal micro-ulcerations. The neoplastic cells demonstrated the following immunophenotype: CD68+, CD43+, CD38+, CD45+, CD123+, MPO++/-, CD4++/-, lysozyme++/-, granzymeB++/-, CD15–/+, elastase-, CD56-, CD33-, CD34-, CD117-, CD10-, TdT-, CD1a-. B and T cell markers were negative. The morphological and immunohistochemical characteristics were compatible with leukemia cutis. Bone marrow biopsy was normocellular for age with no increase in myeloblasts. Routine laboratory tests were within normal ranges. Karyotypic analysis showed loss of Y chromosome in 3/30 metaphases. Although chemotherapy was strongly advised, the patient refused any treatment. He remains free of leukemia or evolution of eyelid lesions almost 1 year after diagnosis.
Conclusion: Leukemia cutis of the eyelids is a very rare manifestation of acute leukemia and may be aleukemic for a long time.

PS-13-005
Eosinophils, B-cells and macrophages in the microenvironment of Mycosis Fungoides
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Objective: The microenvironment has been proven to play a crucial role in solid tumours and seems to be important in hematological malignancies. The presence of eosinophils, B-cells and macrophages is evaluated in mycosis fungoides (MF) cases.
Method: Twelve cases with complete clinical data and known follow-up were included. In one case the patient was under corticosteroid therapy. A specimen of transformed large cell lymphoma (t-LCL), observed in one case, was also investigated. Hematoxylin and eosin stained sections as well as immunostained sections for CD20, CD45RA and CD68 were studied.
Results: Eosinophils were absent or scattered, independently of the clinical presentation of MF or corticosteroid use. Only in the t-LCL case eosinophils were found in large numbers. B-cells were few in the papillary dermis. The percentage of macrophages in relation to the infiltrating population was usually >10 and <30 %. There is no association between the estimated cells and the response to treatment.
Conclusion: Eosinophils and B-cells are generally absent or few in MF. There is a striking difference between the numbers of eosinophils, B-cells and macrophages observed in MF microenvironment and those of t-LCL. There was no association between the numbers of the estimated cells and the response to treatment.

PS-13-006
Pure white cell aplasia associated with thymoma
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Objective: Pure white cell aplasia (PWCA) is a rare immunological entity of unknown etiology and in several cases is associated with thymoma.
Method: A 46-year-old female patient was admitted with fever and severe neutropenia. Regarding her medical history recurrent myasthenia gravis and thymoma, removed 8 years ago, was referred. The patient was under continuous medication with pyridostigmine and methylprednisolone.
Results: Bone marrow aspiration showed reduced cellularity because of decreased myeloid cells, accounted approximately 3 % of mature cells. Bone marrow biopsy showed a slight hypocellular marrow. Granulopoiesis was absent, a finding confirmed by histochemical and immunohistochemical stains. Erythropoiesis and megakaryopoiesis were normal. Increased number of T-cells positive to CD3 antibody was observed, a significant number of which expressed CD8 and TIA1 antigens. The patient was treated with antibiotics, antifungals, albumin, growth factors and intravenous immunoglobulin. The patient was deteriorating steadily and finally she died due to acute respiratory failure and Gram negative septicaemia.
Conclusion: PWCA is a rare but recognized complication of thymoma and thymic carcinoma. Severe neutropenia may be found even a long period after thymectomy.

PS-13-008
Bone marrow morphology and immunohistochemistry as a prognostic factor of renal insuffiency in case of multiple myeloma
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Objective: Malignant plasma cells (PC) morphology and aberrant antigen expression play a role in the prognosis of MM (Ngo, et al., 2009). One of the most common complications of MM is renal insufficiency.
Method: Bone marrow (BM) biopsies from 70 patients with primary diagnosed MM were examied with CD138, CD56, p53 antibodies. Data was analyzed using Graph Pad Prism 5.
Results: Our study has proved a coherence between percentage of PC with plasmablastic differentiation and decreased GFR ($r = -0.267$, $p = 0.0255$). Statistically significant positive correlation by Spearman test was found between p53 protein expression in PC and creatinin ($r = +0.2628$; $p = 0.028$) level and with decreased GFR, BM cellularity ($r = -0.2625$, $p = 0.0282$) and p53 expression ($r = -0.2543$; $p = 0.0336$). A significant positive correlation was between CD56 expression and increased GFR ($r = +0.4674$, $p < 0.0001$) and decreased creatinin level ($r = -0.4387$, $p = 0.0001$).
Conclusion: Increased BM cellularity, high amount of PC, increased percentage of PC with plasmablastic differentiation, p53 immunoexpression and lack of CD56 antigen in PC statistically significantly correlated with increased creatinin level and decreased GFR These correlations are criteria for chronic renal failure progression and poorer prognosis of MM.

PS-13-009
The main key in diagnosis of myelodysplastic syndromes: Cell morphology
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Objective: Myelodysplastic syndromes (MDS) are clonal hematopoietic stem cell diseases characterized by cytopenias and dysplasia in one or more of cell lineages. The common pathological manifestations of dysplasia are nuclear fragments and multinuclearity of erythroid cells, hypogranulation/hyposegmentation of the granulocytes, and micromegakaryocytes. We aimed to group the dysplastic features in MDS to organize a useful, schematic approach for pathologists to achieve the accurate diagnosis.
Method: The demographical and histomorphological features of BM aspirates and biopsies of 40 MDS cases were revised and regrouped. The cellularity of BM biopsy and the percentage of blasts in aspirates and biopsies, confirmed by CD34 and CD117 immunostaining, were compared and noted.
Results: Twenty two female (55 %) and 18 male (45 %) patients with a mean age of 69. 17 were included. The mean cellularity of biopsies was

49.2 %. The highest dysplastic lineage was erythroid lineage (75 %) in aspirates and the most common dysplastic features were nuclear abnormalities and binuclear erythroid cells. However, megacaryocytic lineage was the highest dysplastic lineage in biopsies (84 %) and the most common dysplastic feature was found as hypolobulation/ monolobulation. The mean percentage of blastic cells was 2.55 % in aspirates and 3.62 % in biopsies.
Conclusion: The most common dysplastic lineages and features should be remembered and investigated on every BM aspirate and biopsy by every pathologist in order to reach an accurate diagnosis of MDS.

PS-13-010
Multiple myeloma and bone marrow microenvironment: Immunohistochemical study
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Objective: Neoplastic milieu is an integral part of all malignant diseases including multiple myeloma and plays variable role in their development, retention/adhesivity, resistency or sensitivity to a therapeutic approach. Relatively genetical stabile milieu may play more important role in a new specific molecular therapeutic approaches and therefore should be contextually studied with neoplastic cells. The expressions of 11 proteins were analyzed in consecutives multiple myeloma specimens.
Method: Bone marrow trephine biopsy specimens with multiple myeloma were included in our prospective study. FFPE tissues were processed in app. Five microm sections and placed on charged slides. The indirect immunohistochemical staining was applicated. The expressions of MIP1alfa, Annexin A2, TRAP, DKK-1, RANK, RANKL, OPG, Sclerotisin, Activin A, NFkappaB proteins (p50, p52, p65), p62 and MMP9 were analyzed.
Results: Bone marrow multiple myeloma specimens showed variable positivity of MIP1alfa in 61 %, Annexin A2 in 28 % (myeloma cells) and in 40 % (stromal cells), TRAP in 64 %, DKK-1 in 20 %, RANK in 44 %, RANKL in 66 %, OPG in 3,6 %, Sclerotisin in 100 %, Activin A in 36 %, cytoplasmic positivity of p50 in 24 %, p52 in 84 %, p62 in 100 %, p65 in 76 % and positivity of MMP9 in 56 %.
Conclusion: Preliminary study showed variable expression of observed proteins in multiple myeloma and its bone marrow microenvironment that implicate different biological "stage", development and/or stromal plasticity in this complex hemato-oncological disease including myeloma cells itself and myeloma bone disease. The knowledge of engaged signaling pathways may suggest more specific or tailored therapeutic approches in a particular patient and also in his stabile or progressive multiple myeloma disease. Supported by NT 14393.

PS-13-011
C-MYC and bCL2 translocation frequency in diffuse large B cell lymphomas
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Objective: The aim of this study was to investigate the frequency and prognostic impact of BCL2 and MYC rearrangements.
Method: MYC, BCL2 rearrangements were investigated by FISH on tissue microarrays in 97 DLBCLs.
Results: MYC rearrangements were observed in 11 of 97. There was no association with other clinical features, including age, sex, nodal/ extranodal disease. MYC rearrangement was associated with significantly worse overall survival (p = .00) BCL2 rearrangements were observed in 14 of 97. There was no association with other clinical features, including age, sex. BCL2 rearrangement had prognostic impact on outcome (p = .00). MYC and BCL2 rearrangements were observed in 3 of 97 cases. Three cases were 53 (female), 53, 63 years years old, respectively. The patients were died in 24,18 and 35 months after diagnosis. Double-hit lymphoma patients included one female and two males with a median age of 56 years. Two cases had primary nodal and one case primary extranodal presentations. The majority of patients had stage IV disease.
Conclusion: We concluded that C-MYC and BCL2 may contribute to aggressive transformation, and more mechanism-based therapy should be explored. Analysis of MYC gene rearrangement along with BCL2 is critical in identifying high-risk patients with poor prognosis.

PS-13-012
A case of follicular lymphoma with Hodgkin and Reed-Sternberg-like cells
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Objective: We present an unusual case of Follicular Lymphoma (FL) with Hodgkin and Reed-Sternberg-like cells (HRS-like).
Method: A 79 year-old male patient presented with an inguinal mass, which was clinically evaluated as a soft-tissue tumour and was resected. Macroscopically the specimen measured 6.2 cm in greatest diameter. Sections from the mass were studied by means of morphology and immunohistochemistry.
Results: The mass consisted of multiple fused lymph nodes with complete disturbance of their architecture due to the presence of lymphoid nodules consisting of small/medium-sized cells. Among them there were blastic cells that numbered, in average, 12 cells per HPF. Immunohistochemically the neoplastic cells were positive for B-cell markers, CD10, Bcl2, Bcl6, CD23 and MUM1, while they were negative for T-cell markers, cyclin D1, κ and λ. Based upon the above finding the diagnosis of FL, grade II, was reached. There were also scattered HRS-like cells, which were arranged in a site in loose group. Those cells presented the following immunophenotype: CD30+, CD15+, LMP1+, PAX5+, OCT2+, BOB1+, CD45-, ALK1- and EMA-.
Conclusion: There were only few cases similar to this presented. HRS-like may be the precursors of Hodgkin lymphoma or a FL variant or centroblasts transformed by Epstein-Bar virus.

PS-13-013
Primary mantle cell lymphoma of the tonsil: Report of a rare case
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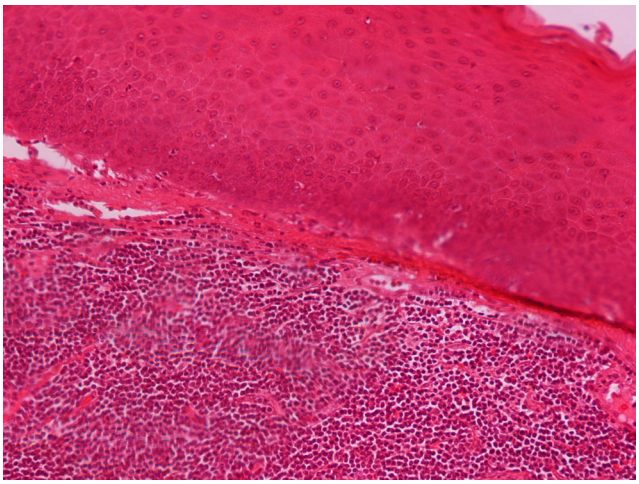
Objective: Non-Hodgkin's lymphoma of the Waldeyer's ring is a relatively rare entity and the palatine tonsil is the most frequently involved site. Although, the exact etiology remains unclear, a number of predisposing factors have been identified, including human immunodeficiency virus and Epstein-Barr infection.
Method: A 82 year old man presented with a sensation of fullness of the throat.On physical examination an approximately 3,5 × 3 cm. Smooth non-tender mass was observed in the right palatine tonsil. Computer tomography scan revealed a non-enhancing right tonsillar mass but no signs of neck lymphadenopathy. The patient underwent bilateral tonsillectomy.
Results: Histological examination confirmed a diagnosis of mantle cell lymphoma of B phenotype. Immunohistochemically the neoplastic cells were positive for CD19, CD20, CD79a, CD22, Bcl 2, CD5, Cyclin D1 and negative for CD10, CD57, EBV, CD3. Bone marrow biopsy did not reveal lymphomatous involvement. The patient received chemotherapy based on CHOP protocol combined to Rituximab. During follow-up he remains disease-free 18 months after diagnosis.

Conclusion: Non-Hodgkin's lymphomas rarely involve tonsils and the vast majority of them are of B-cell origin. A combined treatment consisting of chemotherapy and radiotherapy leads to a satisfactory outcome in patients with this uncommon neoplasm. The current results supported it's good prognosis at early stage.

Mantle cell lymphoma of the tonsil (H-Ex200):



PS-13-014

Reliability and accuracy of frozen section diagnosis in a series of 185 lymph node lesions

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Objective: Frozen section lymph node analysis is of paramount importance in diagnosis and therapy for mainly tumoural pathologies. This study was performed to evaluate frozen section analysis of lymph nodes and propose ways to improve its performance.
Method: We undertook a retrospective study including 185 frozen section examinations performed in pathology department of the Military Hospital of Tunis, during a 5-year period (January 2008–December 2012) that we compared to definitive histologic results.
Results: We received single lymph nodes in 153 cases and lymph node curettages in 32 cases. Lymph node curettages were for urologic cancers in 23 cases (71, 87 %) and head and neck cancers in nine cases (28, 12 %). The sensitivity was 89, 2 %. The specificity and the positive predictive value were 100 %. The negative predictive value was 97, 4 %. The concordance was 93 %. The disconcordance, which was 7 %, was due to 4 false negative cases including 3 patients with a Hodgkin lymphoma and 1 patient with a B cell lymphoma whose frozen section examinations concluded to reactive lymph nodes.
Conclusion: Our results put emphasis on the diagnostic relevance of the frozen section analysis. To improve its efficacy, a closer collaboration between surgeons and pathologists is necessary.

PS-13-015

Prognostic significance of Hans's algorithm in diffuse large B-cell lymphoma nowadays

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Objective: Diffuse large B-cell lymphoma is one of the most common lymphomas in the world. It is usually a primary disease but also it can develop secondary as a result of progression of low grade lymphomas. In most cases the disease begins in lymph nodes. Hans's algorithm divides cases using immunohistochemical antibodies CD10, BCL6 and MUM1 to subtypes: germinal center-like (GCB-like) and non-germinal center-like (non-GCB-like). Former used to be linked to better prognosis and later to worse prognosis.
Method: Our research has included 92 patients whom were diagnosed at the Institute for Oncology of Vojvodina since 2003 to 2011. They were treated according to modern standard protocols including Rituximab. We have used immunohistochemical antibodies CD10, BCL6 and MUM1 to follow Hans's algorithm. Sex and survival were found in medical files.
Results: CD20 was positive in all available samples, CD10 in 20,23 %, BCL6 in 51,72 % and MUM1 in 62,07 %. GCB-like subtype and non-GCB-like subtype did not show significant correlation with survival, nor did expressions of CD10, BCL6 and MUM1 individually.
Conclusion: The results are suggesting that prognostic significance of Hans's algorithm has lost importance today in Rituximab era.

PS-13-016

Case report of a lymph node diffused by a B-CLL combined with a T-anaplastic lymphoma

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Objective: Our aim is to describe a unique case of a male patient with invasion of a lymph node by a non-Hodgkin's lymphoma composed from B chronic lymphocytic leukemia and simultaneous T- anaplastic lymphoma.
Method: A 61-year old male patient admitted to our hospital with a cervical expansion measuring 3 cm. He underwent clinical, radiographic and hematologic evaluation. Excision of the cervical mass and later a bone marrow biopsy was performed.
Results: The mass was whitish in hue and compact in consistency and measuring 3 × 2 × 1 cm. The bone marrow biopsy was composed of a bony in consistency specimen which was decalcified. Microscopically the mass involved a lymph node which had obliteration of his normal architectural structure and it was completely invaded by a monotonous, small cleaved neoplastic cells with diffuse growth pattern. A complete immunohistochemical evaluation was done with CD3, CD20, CD134, CD34, CD5, CD10, bcl2, bcl6, CD30, ALK. The main mass of the tumour reacted against CD20, while in intrasinusoidal locations, at the periphery of the lymph node, neoplastic cells where reactive against CD3, CD34, CD30 and ALK.
Conclusion: The findings were consistent with infiltration of the cervical lymph node by a B-CLL combined with an ALK + T anaplastic lymphoma with intrasinusoidal invasion.

PS-13-017

Case report of Hamartoma of the Spleen

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Objective: Spleen Hamartoma (SH), is a rare, benign, vascular tumour, usually congenital. SH is composed of aberrant mixture of normal splenic tissue and is nodular in shape and variable in size. It is derived from the splenic sinus-lining cells.
Method: A 56 year old female patient admitted to our hospital with a sudden, painful, palpable mass in the splenic area. On imaging techniques a single, splenic tumour appr. 9 cm was revealed. The patient has a known history of thalassaimia. Grossly, the spleen, measured 12 × 10 × 9 cm and weighted 450 gr, on dissecting the spleen a relatively well described, brownish, soft, mass, measuring 9 cm, was found occupying most of the splenic parenchyma.

Results: Histologically, the splenic tumour composed of an extremely fibrous in consistency stroma with abundant, disorganized blood vessels of varying size, infarct foci, Gandi-Gumna bodies and a great degree of extramedullary hematopoiesis. Signs of any malignancy were not noted. The adrenal tumour was a well circumscribed, adenoma of the adrenal gland, composed mainly of clear cells in diffuse pattern of growth and low mitotic rate.
Conclusion: SH, usually is an incidental finding, which may rupture spontaneously and could be a medical emergency. It is also associated with conditions like thalassaimia, Wiskott-Aldrich syndrome, hypersplenism.

PS-13-018
Light chain deposition disease: A rare pulmonary involvement of the disease
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Objective: Light Chain Deposition Disease (LCDD- Randall disease), is the result of a plasma cell, or rarely a lymphoplasmacytic, neoplasm, which causes the deposition of an abnormal light chain in tissues. The outcome of these depositions is organ dysfunction, not related to amyloid β-plated sheets formation (Congo Red negative).
Method: A 61-year old patient admitted to our hospital with a known history of multiple myeloma, for re-evaluation. On imaging screening multiple nodules where revealed in both lungs.
Results: On histological examination deposition of refractile eosinophilic material in the fatty tissue and thickening of the vessels' wall was noted (Congo Red stain was inconclusive). The main B.M. finding was the increase (8–10 %) in the interstitial, scattered and occasionally in small clusters, plasma cells (cIgk), with mild morphological changes. The lung biopsies revealed, relatively well circumscribed, nodules of eosinophilic material in the lung parenchyma and the blood vessels and scattered neoplastic plasma cells (CD138+, cIgk+) in it.
Conclusion: Our findings, in combination with the clinical information, were more compatible with LCDD. LCDD is a rare entity with median onset age 56 years. There is no male/female predilection. The main sites affected are the kidneys, liver, heart.

PS-13-019
The Haematopathology of HIV/AIDS: A case of a plasmablastic lymphoma
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Objective: HIV infected patients are at increased risk of developing cancer. Despite the advent of highly active anti-retroviral therapy (HAART), malignancy in this population is a leading cause of morbidity and mortality. Plasmablastic lymphoma is an aggressive variant of diffuse large B-cell lymphoma initially described in the oral cavity of these patients. The incidence of plasmablastic lymphoma has increased since the introduction of HAART in 1996. We will report a case and highlight some clinical-pathologic considerations.
Method: We present the case of a 35 years old male with HIV, HCV and HBV who has presented a painful vestibular mass for the last 3 months. An oral mucosa biopsy was performed.
Results: The microscopic examination revealed a diffuse infiltrate of large lymphoma cells. The cells appear cohesive and have a squared-off appearance, with eccentric nuclei. Mitotic activity is brisk. The immunophenotype is CD45-, CD20-, CD3-, CD138+, EMA-, Kappa light chains+, Lambda light chains-, CK AE1/AE3- and Melan A-. They are associated with a high proliferation (Ki67) index (>90 %).
Conclusion: Plasmablastic lymphoma represents a diagnostic challenge given its characteristic morphology and lack of CD20 expression, and also a therapeutic challenge, with early responses to therapy, but with high relapse rates and poor prognosis.

PS-13-020
Amyloid typing using immunohistochemical and proteomic analysis
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Objective: Determination of amyloid subtype by using two different methods, immunohistochemistry (IHC) and proteomic analysis.
Method: Formalin-fixed paraffin embedded tissue samples (22) from 11 patients with previously known diagnosis of AL amyloidosis were examined using indirect immunohistochemistry with anti-kappa, anti-lambda, anti-amyloid A and anti-transthyretin commercially available antibodies. Three different amyloid-rich areas from each tissue sample were obtained by laser capture microdissection (LMD) and processed through liquid chromatography coupled with mass spectrometry (LC-MS).
Results: LC/MS clearly designated the type of amyloidosis in all 22 tissue samples (five cases were Ig kappa, six cases Ig lambda). Immunohistochemistry established amyloid protein with certainty only in five specimens. The positive staining for more than one antibody was detected in 13 samples (most of false-positive results with anti-TTR and anti-SAA antibodies). In these cases, the properly diagnosis could not be determined.
Conclusion: A multidisciplinary diagnostic approach is required to determine the precise type of amyloid. According to our results, a combination of the widely accessible immunohistochemistry and the highly specialized laser capture microdissection-LC/MS approach as an additional analysis in some complicated cases seems to be the most reliable tool in the amyloid typing. Supported by CK TAČR TE02000058, IGA MZ CR NT14400 and LF_2015_008.

PS-13-021
Secondary Epstein-Barr virus-associated diffuse large B-cell lymphoma of the skin in a patient with angioimmunoblastic T-cell lymphoma: A case report
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Objective: Angioimmunoblastic T-cell lymphoma (AITL) is one of the most common types of non-Hodgkin T-cell lymphoma. This lymphoma typically presents with generalized lymphadenopathy, hepatosplenomegaly, fever, skin lesions, hypergammaglobulinaemia, etc.. In rare cases, secondary Epstein-Barr virus associated diffuse large B-cell lymphoma (DLBCL) can develop together with AITL due to immunodeficiency to the neoplasia and consecutive clonal expansion of EBV positive immunoblasts.
Method: We present a case of a 47 year old male with generalized lymphadenopathy and splenomegaly, who was diagnosed with AITL based on a biopsy of the right inguinal lymph node. The patient initially received four cycles of chemotherapy with CHOP, but the disease progressed. Twenty five months after the initial diagnosis, generalized lymphadenopathy persisted and the patient developed a skin lesion.
Results: A skin biopsy and axilar lymph node biopsy was performed. In the lymph node, AITL was confirmed, and in the skin, a secondary EBV-associated B-cell lymphoma was diagnosed.
Conclusion: The prognosis of these patients remains unclear, but it is generally accepted that secondary DLBCL is a sign of poor prognosis and

shorter overall survival. To our best knowledge, only 23 cases of this tumour have been described in English literature.

PS-13-022

Primary central nervous system lymphoma in immunocompetent patients our experience with review of literature

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Abstract: Primary CNS lymphoma is a rare form of non-Hodgkin's lymphoma that occurs within the craniospinal axis and accounts for less than 5 % of all primary brain tumours. It is defined as lymphoma occurring in the brain, leptomeninges, spinal cord or eyes without evidence of lymphoma outside the CNS. Eighteen patients with primary CNS lymphoma were analyzed for their clinico-histopathological characteristics and followed-up for the treatment and subsequent management in Neurosurgery, and Medical and Radiation Oncology. The temporoparietal and parietal region was the commonest location of CNS lymphoma; a mean age of 54,68 years and an age range of 33–83 years. Females outnumbered males with a ratio of 1.25:1. The commonest presentation was headache. This was followed by neurological deficits. All the patients histologically had diffuse B-cell lymphoma. Two patients had multiple lesions. Four of the patients died within 2 years. Four of the patients could not be followed. In conclusion the incidence of primary CNS lymphomas is increasing not only in patients with AIDS, but also in the non-AIDS population and should be considered in the differential diagnosis of all tumours of the CNS.

PS-13-023

p53 protein as useful immunohistochemical marker for predicting leukemic transformation of the myelodysplastic syndrome

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Objective: The assessment of risk factors predisposing to acute myeloid leukemia (AML) in myelodysplastic syndrome (MDS) patients.
Method: In our study we reevaluated 30 bone marrow biopsies (BMB) from patients diagnosed with MDS, in according to the p53 protein expression of the myeloid cells, detected by the immunohistochemistry (IHC). We applied digital morphometry method to quantify the p53 positive myeloid cells and the CD34 positive blasts. The count of positive p53 cells was compared with extent of blast infiltration, microvessel density and survival periode used correlation analysis.
Results: The 30 cases were included in the following categories: RCMD 20 %, RAEB-1 26,67 %, RAEB-2 33,33 %, MDS-U 20 %. In the bone marrow of patient with MDS, p53-positive cells constituted about 10 to 35 % of the total bone marrow cells. Increased bone marrow blast count was accompanied by intensified angiogenesis, but without significant correlation ($p < 0.05$) between the two prognostic factors. IHC-p53 positive cases (included blasts and mature myeloid cells) have a significantly higher incidence of leukemic transformation compared to the p53 negative cases.
Conclusion: Based on the results, we consider that the simultaneous examination of p53 protein and CD34 in myeloid cells are useful markers for predicting leukemic transformation of the MDS.

PS-13-024

Interdigitating dendritic cell sarcoma: A rare diagnosis of an axillary mass

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Objective: Interdigitating dendritic cell sarcoma (IDCS) is an extremely rare neoplasm. Only approximately 100 cases have been reported in the literature to date. We received in consultation the case of a 75-year-old man. The specimen consisted of a surgically excised axillary mass showing a spindle and ovoid cell proliferation with vesicular nuclei and eosinophilic cytoplasm having indistinct borders. Our aim was to make the differential diagnosis and reach the final diagnosis by histological and immunohistochemical analysis.
Method: We used the hematoxilin and eosin stain and applied a panel of immunohistochemical markers to differentiate between a sarcoma, carcinoma and melanoma.
Results: The tumour cells were negative for pancytokeratins, HMB45 and melan A, thus excluding a carcinoma and melanoma. Positivity for vimentin and S100, indicated a sarcoma. CD56 was negative, making MPNST less likely. Histology was suggestive of a dendritic cell sarcoma (IDCS or follicular cell sarcoma). Fascin and CD68 were positive but do not differentiate between the two. Negative stain for CD23, CD21, CD35, and clusterin excluded follicular cell sarcoma. p53 showed focal, weak nuclear staining. The patient is currently under chemotherapy, 4 months from diagnosis.
Conclusion: Our diagnosis was that of interdigitating dendritic cell sarcoma and was substantiated by the immunohistochemical stains.

PS-13-025

BCL2-negative Low-grade Follicular Lymphoma (LGFL/BCL2-): A study of 11 cases

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Objective: Although BCL2 immunoreactivity is an important diagnostic criterion in LGFL, about 15 % of cases are negative for BCL2 (LGFL/BCL2-). These cases may show confusing histiologic, immunohistochemical and genetic profiles. We describe the immunohistochemical findings and BCL2 gene status of our LGFL/BCL2- cases.
Method: Eleven LGFL/BCL2- cases from our institution (2007–2014) were immunohistochemically studied for CD20, CD3, CD10, BCL6, CD23, CD21, BCL2 and Ki67-MIB1. BCL2 and BCL6 FISH and clonality (IGH, IGK) studies were performed in all cases.
Results: B receptor clonality (IGH, IGK) was present in all instances. FISH showed BCL2 translocation in 2 of the 11 cases. Of the remaining 9, BCL2 gains were present in 2 and BCL6 translocation in 1. CD10 was negative in the 3 cases without BCL2 or BCL6 gene alterations. BCL6 was variably immunopositive in all cases. Ki67 cell proliferation index was 5–80 % (average, 29 %). It was over 50 % in 3 cases, 2 of which were negative for BCL2 and CD10.
Conclusion: Negative BCL2 immunostaining in LGFL is sometimes due to protein changes that may be clarified by FISH. BCL2 negativity may be associated with rare phenotypes (CD10 negativity, high proliferation index) that make diagnosis difficult. The molecular underpinnings of LGFL/BCL2- continue to be poorly defined.

PS-13-026

Case report: Richter's transformation of chronic lymphatic leucemia into diffuse large B-cell lymphoma

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Objective: A 50-year-old man with prior history of Chronic Lymphatic Leucemia (CLL CSIV Rai), was presented with a pulmonary infiltration and suspected pulmonary embolism. CBC showed elevated WBC count 60 × 109, Hgb 70 g/l and platelet count od 30 × 109. CT scan revealed hepatosplenomegaly.

Method: First diagnosis was established before a year, presenting with a symptoms of weakness, fever, night sweats and lymphadenopathy. Back than, refused bone marrow biopsy. Diagnosis was based on the following results of the flow citometry: in the periferal blood count was found 85 % lymphocytes CD45+, with the CLL SCORE 5/5 (FMC7-, CD79b-, CD23+, CD5+, sIg-). Diagnose of the CLL was established.
Results: After 1 year patient was adimitted to the hospital having abovementioned pulmonary symptoms. Now, biopsy of the bone marrow was performed and pathohistology revealed supressed hematopoesis regarding diffuse infiltraton of the bone marrow with immunoblastic appearance medium large and large lymphocytes, imunohistochemicaly positive for CD20+, MUM1 +, bcl6+, negative for CD23, CD5, SOX11, CD3, CD10, CD11c, Cyclin D1, TdT. Cytogenetic analysis was performed, using FISH method with the probe LAMP1, revealed disomy of 13q34 region.
Conclusion: Diagnose of the Richter's transformation of the CLL into Diffuse Large B Cell Lymphoma was established.

PS-13-027
Chronic lymphocytic leukemia involved palatinal tonsils: A case report
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Objective: A case report of 57-old women with a 2 years of chronic lymphocitic leukemia (CLL) history, with involving palatinal tonsils.
Method: Disease began with sponatneous haemathoma of skin. Laboratory tests showed lymphocytosis, with maximum level of lymohocytes of 45–50. "Watch and wait" terapy were performed. After 2 years of disease troat pain started and enlargment of left tonsil diagnosed. Bilateral tonsillectomy preformed. Patients have long term history of hypertension and hearth problem. Family anamnesis with malignant disease were negative.
Results: Patohistological exam found infiltration of tonsills with small lymphocyt with round nuclei, condens chromatin and scanty cytoplasm. Mild irregularity of nuceli observed. About 15 % of cell were larger, with opet chromatin and distinct nucleoli, coresponding to prolymphocyts. Rare immunoblasts with vesicular nuclei and obvious nucleoli were present. Remnant tonsils folliculs were visible, mostly at periphery of tissue. Immunohistochemistry showed positivity for CD45, CD23, CD20 and CD5. Ki67 stains about 10–15 % of cells nuclei. CD68 stained histiocyt at follicular center of normal tonsilar tissue. Level of erythrocyt, platelets and other biochemical analisis were in referent values. No lymphadenopathy, splenomegaly and hepatomegaly where found. There was no B symptoms.
Conclusion: It is uncommon and rare for CLL/SLL to involve tonsils.

PS-13-028
Detection of minimal residual disease in chronic myeloid leukemia using a real time quantitative RT-PCR assay
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Objective: Chronic myeloid leukemia (CML) is a clonal proliferative disorder of hematopoietic stem cell and is characterized by the presence of "bcr-abl" fusion gene. The objective of the current study was to evaluate the minimal residual disease by RQ-PCR assay in patients with CML treated with Imatinib mesylate or allogeneic stem cell transplantation.
Method: Sixty CML patients, 34 males and 26 females, median age 40 years (12–71) hava 128 RQ-PCR analyses at different times during their therapy: 49 CML patients treated with Gleevec for a median of 6 months after they achieved complete cytogenetic remission (CCyR) and 12 CML patients after allograft for a median of 24 months.
Results: By analyzing the value of bcr-abl/abl levels measured by real-time quantitative PCR, we show the patients could be divided into 3 groups (1) in 49 patients transcripts level continues to decline; in 13 of these patients bcr-abl transcript became undetectable on repeated testing. (2) in 2 patients the transcript levels reached a plateau and (3) in 9 patients the transcript level increased and the initial CCyR was lost.
Conclusion: RQ-PCR is a sensitive tool to monitor minimal residual disease for the early detection of relapse and the assessment of treatment response in patients with CML.

PS-13-029
Cutaneous involvement as a unique presentation of a histiocytic sarcoma: Case report and review of the literature
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Objective: The histiocytic sarcoma (HS) is an uncommon neoplasm that occurs in lymph nodes and more often in the gastrointestinal tract, skin and soft tissues. The current World Health Organization defines HS as a proliferation of neoplastic cells showing immunophenotypic and morphologic features similar to histiocytes. In the literature is described as an aggressive disease without a standard treatment.
Method: Female 64 years with appearance of four erythematous lesions on the dorsum of the hands 6 months before the diagnosis. After no improvement of the lesions and the appearance of another lesion with similar clinical characteristics a punch was performed.
Results: The biopsy presents a malignant proliferation occupying the dermis. This is composed of large polygonal cells with eosinophilic cytoplasm and vesicular nuclei with pleomorphism and prominent nucleoli. Mitosis and abundant foci of necrosis were diffusely observed. Immunohistochemistry study results: - Tumour cells express CD68, CD163, Lysozyme and leukocyte common antigen CD45. - CKAE1-AE3, EMA, S100, HMB45, CD20, CD3 and CD4, CD30, CD15, CD1a, CD21, CD35, myeloperoxidase and CD33 are negative. The patient was treated with cyclophosphamide, hydroxydaunorubicin, vincristine and prednisone and after 4 months the clinical evaluation of the lesions show improved with no complete regression.
Conclusion: We report a patient with primary histiocytic sarcoma with unique skin involvement. The differential diagnosis includes the interdigitating dendritic cells sarcoma, Langerhans cell histiocytosis, anaplastic large cell lymphoma, melanoma and other sarcomas. This requires immunohistochemical markers for the diagnosis. In the literature review, the majority of the cases of histiocytic sarcoma are diagnosed in advanced clinical course but there are a few reports with better improvement in patients treated in the initial presentation of the disease. In the cases reported in the literature, the skin manifestation as a unique presentation is also rare because a great number of the cases has another involvement before the cutaneous lesions.

PS-13-030
Follicular dendritic cell sarcoma of the tonsil: A case report
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Objective: Follicular dendritic cell sarcoma (FDCS), is a rare hematolymphoid neoplasm with a close resemblance to the normal FDC and a biological behavior more like that of sarcoma. Most of them arise in lymph nodes, although extranodal presentations, including oral cavity and tonsils as most common ones, have been reported.
Method: A 52-year-old man, presented with a globus sensation of the right pharynx because of slowly enlarged mass. CT and preoperative first FNB estimation indicated that the tumour could be a lymphoma. A right tonsillectomy with ipsilateral cervical lymph nodes excision, was performed. Postoperatively, local adjuvant rathiotherapy was planned.
Results: Histologically, a well-circumscribed tumour of 2 cm, covered by a normal squamous epithelium, was revealed. Tumour was composed of

ovoid to spindle -shaped cells in a storiform - whorled pattern with a low mitotic activity. Lymph nodes had features of reactive hyperplasia. Tumour cells were immunoreactive for CD35, CD20, CD21, fascin, D2-40 with negative in situ EBERS (EBV), an immunophenotype compatible with FDCS.
Conclusion: FDCS arising in the tonsil is uncommon neoplasm with only a total of 43 cases reported. It is a challenging problem both for pathologists diagnostically and for clinicians therapeutically as its optimal treatment remains unclear.

PS-13-031
IgG4-related disease of the adrenal gland: A case report
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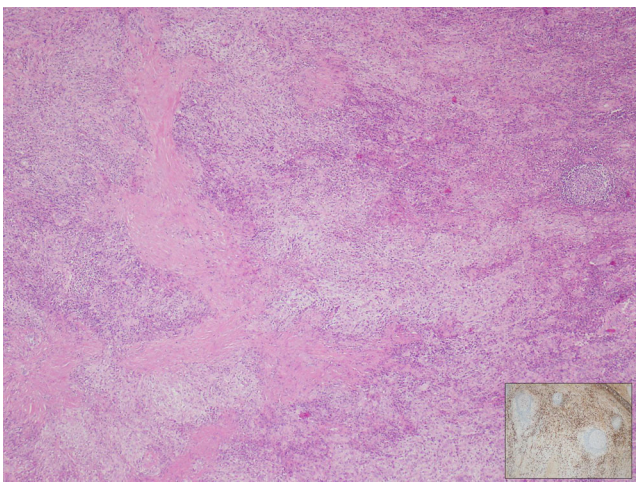
Objective: IgG4-related disease is an emerging clinical entity which was first described in 2001 as an autoimmune pancreatitis associated with high serum levels of IgG4. As a systemic condition, it was recognized in 2003. It is characterized by an inflammatory reaction rich in IgG4-positive plasma cells that can be diffuse or mass forming and is associated with fibrosis, sclerosis and obliterative phlebitis. In order to better characterize and understand this disease, case reports are essential.
Method: We report the case of a 20 year-old male patient forwarded to our institution for an abdominal mass.
Results: MRI showed a solid nodule in the right adrenal gland with 55 mm of greater axis and "aspects suggesting atypical lesion - not adenoma". Histological examination allowed for a diagnosis of IgG4-related disease according to current guidelines, supported by serological data and response to therapy.
Conclusion: More prevalent in men, particularly after the middle age, since the first report, it has been described in several organ systems, most commonly in the pancreas as well as the hepatobiliary tract, salivary glands, orbit, and lymph nodes. However, besides our case, just one has been described in the adrenal gland, consolidating the place of this organ in the expanding list of possible targets of the disease.

H&E with thumbnail IgG4 immunostain:



PS-13-032
Cutaneous Squamous Cell Carcinoma metastasis in lymph node with Chronic Lymphocytic Leukemia (CLL) / Small Lymphocytic Lymphoma (SLL): A case report
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Objective: Cancer to cancer metastasis of cutaneous squamous cell carcinoma and chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) is rarely described in literature. We hereby report a case where lymph node metastasis of squamous cell carcinoma was seen together with an CLL/SLL.
Method: The case concerns a 57-years old male, with cutaneous squamous cell carcinoma of ear and external acoustic meatus with suspect metastatic neck disease, and with previously diagnosed CLL/SLL. Radical surgical neck dissection was performed. Fifty-four lymph nodes were collected, which size were from 2 to 18 mm (mediana 8 mm). Those lymph nodes were hystopathologically and immunohistochemically analyzed.
Results: CLL/SLL was found in all 54 lymph nodes. Immunohistochemically, lymphoid cells were positive for CD20, CD79a, CD5, CD23, bcl-2. In only one lymph node with CLL/SLL, which size was 15 mm, squamous carcinoma cells filled subcapsular sinuses. Immunohistochemically they were CK positive.
Conclusion: In patients with both CLL/SLL and SCC, lymph node enlargement does not always indicate metastasis of SCC. Metastasis of SCC does not need to bee localized in the largest lymph node. This might represent a problem in lymph node selection for fine needle biopsy.

PS-13-033
Concurrent presentation of low and high grade B-NHL in a normal sized spleen
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Objective: Although secondary involvement of the spleen by NHL is frequent, concurrent splenic involvement by marginal zone lymphoma with plasmacytic differentiation and DLBCL has never been reported.
Method: We present a case of a 106 gr spleen, focally involved by post GC-DLBCL with some hybrid features, in a 76-year old man with dry cough and low grade fever, in association with subtle infiltration of the surrounding parenchyma by a low grade B-NHL with marginal and/or plasmacytic differentiation and identical kappa light chain expression. CT scanning showed a solitary, 3.2 cm splenic mass lesion, abdominal, retroperitoneal and mediastinal lymphadenopathy and thickening of pulmonary interlobular septa.
Results: Microscopy revealed a DLBCL with fibrosis and some morphologic and immunophenotypic features of Hodgkin's lymphoma, surrounded by a lymphoplasmacytic infiltrate composed of centrocytoid, monocytoid and plasma cells with Dutcher and Russel bodies in a diffuse and micronodular pattern, occasionally involving large vessels. Splenic white pulp was slightly hyperplastic with some follicles featuring monotypic intrafollicular plasma cells with Dutcher bodies.
Conclusion: This case suggests possible MZL transformation to DLBCL with hybrid features, taking place in the spleen. Dissemination of a primary MALT lymphoma is a strong consideration but further investigation is needed in order to substantiate it.

PS-13-034
Follicular dendritic cell sarcoma vs inflammatory pseudotumour: Histological continuum and peculiarities of differential diagnosis
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Objective: To analyze the morphological, immunohistochemical and molecular features of the spectrum of lesions comprising dendritic cell sarcoma (DCS), the variant type of inflammatory pseudotumor DCS (DCS-IPT) and IPT.
Method: We reviewed 13 cases of DCS and abdominal located IPT collected during the period 2000–2015. Expression of dendritic cell

markers (CD35, CD21, CD23 and CNA42), EBV RNA (EBER) expression, V600E BRAF and MAP2K gene mutations were investigated.
Results: The series included 6 DCS, 1 splenic DCS-IPT and 6 IPT. A liver IPT was reclassified as DCS-IPT based on morphology and EBER positivity. All DCS and DCS-IPT were positive for at least one dendritic cell marker. One DCS and one DCS-IPT were positive for all dendritic cell markers. EBER was only positive in the two DCS-IPT. The only case with V600E BRAF mutation corresponded to a DCS-IPT.
Conclusion: The presence of EBV in a spindle cell proliferation in hepatosplenic locations should lead to suspicion of DCS-IPT, especially when positivity for dendritic cells markers may be limited, focal and weak. The presence of the V600E mutation of the BRAF gene may help in the differential diagnosis with ITP and locates this neoplasm closer to DCS.

PS-13-035
Lymphocyte-rich Classical Hodgkin's Lymphoma (LRCHL) mimicking Peripheral T-cell Lymphoma, Not Otherwise Specified (PTCL, NOS)

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Objective: LRCHL is characterized by RS cells and variants in a background dominated by small lymphocytes in a nodular or rarely diffuse growth pattern.
Method: A 60 year-old, asymptomatic, male patient, presented with cervical, mediastinal and abdominal lymphadenopathy. Cervical lymph node biopsy was performed.
Results: Lymph node architecture was effaced by a diffuse and vaguely nodular infiltrate. Nodular areas corresponded to B-cell rich follicular structures where RS cells and variants were located and surrounded by (CD3+/CD57-) T-cell rosettes, with occasional regressed germinal centers. Diffuse areas consisted of large numbers of small/medium sized T-cells with irregular nuclear contours and moderate amount of pale cytoplasm expressing (CD2, CD3, CD5, CD7, Bcl-6, CD8>CD4, Ki67 high) with RS cells and variants admixed among them. Clonality assessment for TCR rearrangements was negative.
Conclusion: Follicular variant of PTCL, NOS can have overlapping morphologic features with LRCHL. Clonality studies in association with immunohistochemistry are indispensable in order to differentiate atypical appearing background T-cells in a LRCHL case, from PTCL, NOS with RS-like cells or rarely, a composite lymphoproliferative process.

PS-13-036
CD56 and EMA immunoexpressions in multiple myeloma: Any prognostic relevance?

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Objective: Multiple Myeloma (MM) has highly heterogeneous outcome, so prognostic factors become very important. Although several immunophenotypic molecules have been studied so far, prognostic importance of CD56 and Epithelial Membrane Antigen (EMA) have not been well described. Our aim is to define if any correlation between those markers and prognostic parameters in MM.
Method: We retrospectively analyzed MM patients diagnosed between January 2009 and October 2014 in our institution. Fourty patients were divided into 4 groups and each group had 10 patients. Group 1: EMA(+), CD56(+); Group 2: EMA(-), C56(-); Group 3: EMA (+), CD56(-); Group 4: EMA (-), CD56(+). International Staging System data, immunoglobulin subtype, hemoglobin, calcium, creatinin levels were documented. Statistical analysis was performed between groups and prognostic parameters.
Results: There were 18 males, 22 females. Median age was 56, 63, 60, 58.5 in group 1, 2, 3 and 4 respectively. We could not find any statistical difference between groups and the prognostic parameters, except hemoglobin level was lowest in group 4.
Conclusion: To the best of our knowledge, this is the first pilot study introducing the results of using CD56 and EMA immunoexpression correlation with prognosis of MM. Although we could not find any significant difference between groups, new prospective large cohort studies should be designed with survival analysis.

PS-13-037
An infant of osteopetrosis and hypopituitarism diagnosed with bone marrow biopsy

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Objective: Malignant infantile osteopetrosis is a rare severe disorder which presents early in life with general sclerosis of the skeleton. It is caused by functional defective osteoclasts which fail to resorb bone.
Method: Affected infants can exhibit a wide spectrum of clinical manifestations including impaired hematopoiesis, hepatosplenomegaly, visual impairment, and hypocalcemia. With the exception of secondary hyperparathyroidism, involvement of the endocrine system seem to be quite rare.
Results: Hypopituitarism is defined as underproduction of the growth hormone alone or in combination with deficiencies of other pituitary hormones. Any lesion that damages the hypothalamus, pituitary stalk or anterior pituitary can cause secondary pituitary hormone deficiency. In this report, we presented a rare combination of malignant infantile osteopetrosis and secondary hypopituitarism in a newborn infant who presented predominantly endocrinologycal symptoms.
Conclusion: This is the first report of malignant infantile osteopetrosis in the literature accompanied by hypopituitarism secondary to sclerosis of the sella turcica in the neonatal period. On the other hand, this is very interesting case who was diagnosed with bone marrow biopsy without the clinical suspicion.

PS-13-038
Expressions of microRNA of mix cellularity Hodgkin lymphomas are different in pediatric and adult patients

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Objective: MicroRNAs represent an emerging class of small noncoding RNAs that play important roles in the posttranscriptional regulation of gene expression. The aim of this study is evaluation the relevance for microRNA in classical mixed cellularity Hodgkin lymphoma (MCHL) pathogenesis.
Method: The expressions of 157 microRNAs in lymph nodes from 20 pediatric and 20 adult patients with MCHLs. We examined microRNA expression in MCHL and the influence of age on the miRNA expression profiles, clinical features and prognosis.
Results: The mean age was 7.4 years (2–13 years) in pediatric cases and 47.4 years (18–75 years) in adult cases. Most patients were male (70 %, $n = 14$) in both groups. Stage III disease ($N = 9{,}45$ %) was common in pediatric group, while stage II disease ($N = 18{,}90$ %) in others. Thirty-six cases (90 %) were alive, while four (10 %) were deceased. Rate of relapses was slightly higher in adults (15 %,$N = 3$) than children cases (10 %,$N = 2$). With microRNA sequencing it was determined that miR-1273e, miR-4322, miR-5008-5p, and miR-6511b-5p were upregulated, while miR-508-5p was downregulated in pediatric tumours.
Conclusion: These results suggest that microRNAs may play an important role in the biology of pediatric Mixed Cellularity Hodgkin lymphomas and may be useful in developing therapies targeting microRNAs.

PS-13-039

Is the follicular lymphoma grade 3B variant of the diffuse large B cell lymphoma?

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Objective: Follicular lymphoma (FL) is the second most common lymphoma following diffuse large B cell lymphoma (DLBCL). FL was graded as grade 1–2 and 3 (3A and 3B). On immunohistochemical staining, cells of FL are positive for CD10, BCL-6 and BCL-2. Some of the cases negative for CD10 and BCL-2 are positive for MUM-1/IRF-4. MUM-1 positive cases usually express diffuse pattern and this phenotype resembles non-germinal center type DLBCL.
Method: Eighty eight cases of FL and 39 cases of DLBCL are included in the study.
Results: A decrease of follicular pattern was identified parallel to an increase in grade (P = 0,011). CD10 was negative in 40 % of grade 3B cases and 50 % of those cases of grade 3A coexpressing DLBCL. Correlation of CD10 and diagnoses revealed negativity of CD10 with an increase in the grade and diffuse pattern (P < 0, 001). As the grade got higher, the MUM-1 and Ki67 staining was more intense (P = 0,003 and P = 0,001, respectively). There was no prognostic difference between the groups of patients diagnosed as FL and DBBHL. On evaluation by FLIPI2 grade 3 cases presented worse prognoses.
Conclusion: As a result, some cases of FL grade 3B express a different immunophenotype compared to other grades and this phenotype presents some similarities to DLBCL. But this difference of grade 3B was not significant due to the low number of cases in our series. Our study reveals that if larger series of grade 3B were evaluated, FL grade 3B may no longer be classified under FL, but may be accepted as a variant of DLBCL.

PS-13-040

Pathogical findings and immunophenotype evaluation in diffuse large B-cell lymphoma: Report on 13 cases

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Objective: We will study the immunohistochemical and pathological characteristics of DLBCL.
Method: Hospital records and pathological slides were reviewed for 13 patients with diffuse large B cell Lymphoma treated at Salah Azaiez institute of carcinology between 2012 and 2015. The clinical data included age and gender. Microscopic examination was performed on all cases.
Results: The median age of the patients was 55,83 years (range 26–90 years). The disease is often symptomatic (10/13). They were presenting with localized (3/10) or generalized adenopathy (7/10). They occur more frequently in men than in women (9/13) and have a peak incidence in the seventh decade. Macroscopically, lymph nodes usually (10/13) present with homogenous fish-flesh replacement of most if not all of the structure. Occasionally (2/13), the involvement is only partial. Morphologically, DLBC typically replaces the normal architecture of the underlying lymph nodal in a diffuse pattern (12/13). Lymph node involvement may be complete (8/13), partial (3/13) or interfollicular (1/13). The malignant proliferation was composed of medium sized to large lymphoid cells with vesicular nuclei and fine chromatin. DLBC express various pan B markers. They were immunoreactive for CD20 in 11 cases.
Conclusion: Knowledge of Clinical, pathological, immunological and molecular features will enable to define the best therapeutic options likely to modify the natural course of the disease and allow complete recovery.

PS-13-041

Sytemic anaplastic large-cell lymphoma ALK negative: A case report

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Objective: To define the clinicopathologic spectrum of anaplastic large cell lymphomas (ALCLs) involving the nervous system.
Method: We the case of a woman of 42 years old, who had chronic with acute episodes of menigitis, encephalitis and polyradiculoneuritis, recently diagnosed Guillain - Barre syndrome, tetraparesis, thrombocytopenia, chronic bronchitis and disseminated intravascular coagulation. After 4 months, patient died. The course was generally rapid and fatal due to progressive neurological deterioration.
Results: Pulmonary, splenic and intracerebral anaplastic large cell lymphoma ALK negative is highlighted at necropsy. Immunohistochemical stains reveal CD 30, CD 43, Granzyme B positive and CD20, ALK negative, Ki 67 index 85–90 %. Another poor significant predictor of outcome is a high serum LDH level. Anaplastic large cell lymphoma ALK - negative (ALCL-ALK−) is included as a provisional entity. It is defined as a CD30+ peripheral T-cell neoplasm that is not reproducibly distinguishable on morphological grounds from ALCL-ALK positive, but lacks the ALK protein. Most cases express T-cell-associated markers and cytotoxic markers.
Conclusion: ALCL involvement of the central nervous system (CNS) is uncommon.

PS-13-042

Two cases of an enigmatic entity: Kikuchi's Disease

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Objective: Kikuchi's disease (KD) is a self-limited rare disorder characterized by necrotizing lymphadenopathy in especially women (mean age: 30 years). It mostly arises in the posterior cervical triangle (85 %). Lympadenopathy is usually (70–80 %) accompanied by fever, chills, myalgias, arthralgias, splenomegaly, and/or skin rashes. KD's etiology is unknown, and it is commonly misdiagnosed as lymphoma. Herein, we present two cases of KD consulted to our institute in 2 weeks period.
Results: The first case was a 41 year-old male with a posterior cervical lymphadenopathy (2 × 1.7 × 1 cm). The second case was a 33 year-old female with a left axillary lymphadenopathy (1.5 × 1 × 1 cm). The parraffin blocks of lymph node biopsies were evaluated. Similar findings were detected in both cases, microscopically. There were multiple foci of patchy necrosis. Necrotic foci were composed of nuclear dusts phagocytosed by numerous histiocytes with crescentic nuclei that were positive for myeloperoxidase immunohistochemically. Numerous immunoblasts with atypical nuclei were detected.
Conclusion: It should be noted that discriminating KD from systemic lupus erytematosus, cat-scratch disease, and particularly some lymphomas showing necrosis in the lymph nodes is usually difficult. A brief summary about the clinicopathological characteristics and clues about the differential diagnosis of KD are given in this report with two demonstrative cases.

PS-13-043

Angiomyomatous hamartoma of the inguinal lymph node: A rare case report

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Objective: Angiomyomatous hamartoma (AMH) of the lymph node is rare primary vascular tumour of unknown etiology, first identified as a distinct entity by Chan et al. in 1992. AMH is a benign condition primarly

affecting the hilum, characterized by haphazardly arranged bundles of fibrous tissue, blood vessels, smooth muscle cells and fat lobules. To date, 29 cases heve been reported, mostly involving inguinal and femoral lymph nodes.Isolated cases have also been reported in the cervical and popliteal lymph nodes.

Method: We report a 34-year-old male patient without other health problems presented with palpable left groin mass. The tumour was surgically removed. Microscopically, in the affected node, the parenchyma was mostly replaced with bundles of smooth muscle cells, variably sized vascular spaces and lobules of mature adipocytes.The lymphoid tissue is only preserved in the thin subcapsular area.

Results: Differential diagnoses include lymphangiomyomatosis, leimyomatosis (lacking the fascicle formation typical of the these conditions) and angiomyolipoma (usualy affects retroperitoneal lymph nodes, and positivity for HMB-45).

Conclusion: The pathogenesis of this lesion is unclear. A possible explanation is that chronic impairment of lymphatic flow or to previous nodal inflammation. There have been no recurrences reported, meaning that extensive resection may not be needed.

PS-13-044

Prognostic relevance of the lymphocyte/monocyte ratio in advanced stage Hodgkin lymphoma: Correlation with IPS and TAM

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Objective: We analyzed prognostic significance of the absolute lymphocyte/monocyte ratio (ALC/AMC), its additional prognostic value to the International Prognostic Score (IPS), and correlation with the CD68+ tumour-associated macrophages (TAM) in diagnostic lymph nodes in 101 advanced stage Hodgkin lymphoma patients.

Method: The receiver operating characteristic curve analysis identified the best cut-off values as 2.0 for ALC/AMC (AUC = 0.728, sensitivity 70.6 %, specificity 67 %) and 25 % for CD68+TAM (AUC = 0.680, sensitivity 67.7 %, specificity 67.2 %).

Results: Patients with ALC/AMC<2, IPS>2 and >25 %CD68+TAM had inferior overall survival (OS) ($p < 0.01$; $p < 0.01$; $p < 0.01$ respectively) and event-free survival (EFS) ($p < 0.01$; $p < 0.01$; $p < 0.01$ respectively). Spearman's test uncovered a significant correlation between ALC/AMC and TAM ($p < 0.05$). Multivariate analysis identified ALC/AMC<2, IPS>2 and CD68+TAM as prognostic factors for OS ($p < 0.05$; $p < 0.01$; $p < 0.05$ respectively). Apart from CD68+TAM, ALC/AMC<2, and IPS>2 remained significant for EFS ($p < 0.01$; $p < 0.05$, respectively). After evaluating ALC/AMC and IPS, we stratified patients into 3 risk groups (low: 0; intermediate: 1 risk factor; high: 2 risk factors) with progressively worse outcome ($p < 0.01$).

Conclusion: Our findings supports the combination of ALC/AMC with IPS, thus providing better risk stratification in advanced HL patients.

PS-13-045

Disseminated mucormycosis with predominant liver involvement: An autopsy case

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Objective: The case of fatal disseminated mucormycosis with huge liver involvement, in patient after autologous steam cell transplantation.

Method: A 36-year-old female with diffuse large B-cell lymphoma received CHOP-R, than DHAP-R, high-dose chemotherapy and autologous steam cell transplantation. Insufficiency of transplant was diagnosed and second transplantation performed. Acute pain at right upper quadrant of abdomen occurred after transplantation. Multifocal liver alteration was revealed by CT and ultrasonography. She deteriorated rapidly, liver function deficiency progressed, and she died at second day after repeat transplantation of steam cells.

Results: In the autopsy, liver enlargement with multiple hemorrhagic foci in the liver parenchyma and the same foci on the pancreas head, on the wall of different parts of the colon were the most significant findings. Microscopic examination showed occlusion of lumens of arteries and veins of several organs (liver, spleen, pancreas, peritoneum, lymph nodes, lungs, adrenal glands, meninges, colon and gall bladder) and invasion of walls by fungal hyphae, morphologically compatible with mucormycosis, ischemic infarction.

Conclusion: Mucormycosis is a rare human infection primarily occurs in immunodeficiency patients. Disseminated form is extremely rare and generally fatal.

PS-13-046

Kaleidoscopic views in the bone marrow: Oxalate crystals in a patient presenting with bicytopenia

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Objective: The most common causes of pancytopenia depending on depositions in the bone marrow (BM) are amiloidosis and accumulation of iron. Primary hyperoxaluria (PH), a genetic disorder associated with nephrolithiasis, kidney and liver failure, also causes depositions rarely. Herein, we report a case of crystal deposits in the BM causing bicytopenia concordant with oxalate crystals seen in PH.

Method: A 24 year old female applied to hospital with fatigue, weakness and swelling on feet. In medical history, she has had two operations for nephrolithiasis at the age of 9 and 12, and she underwent renal transplantation on 2013, but she is still going on hemodialysis. Laboratory tests showed bicytopenia (anemia and leukopenia) and she underwent a BM biopsy. No genetic tests were performed up to now.

Results: Microscopically, an almost complete suppression of haematopoetic cells with the replacement of BM cells by foreign body reactive fibrous tissue and numerous birefrigent crystallines were detected. The crystals formed rosettes with needle-like radial extensions surrounded by foreign body type giant cells. Under polarized light, the crystals formed multicolored rosettes. In BM aspirates envelope-like crystals were found in a background of few myeloid cells with normal morphology. Depending on histopathological examination integrated with clinical results, a diagnosis of hypocellular BM associated with crystal deposition concordant with oxalate crystals was given.

Conclusion: Pancytopenias associated with BM infiltration of different deposits are rare conditions. The medical history of nephrolithiasis at early ages, crystals forming rosettes in the BM and the envelope-like forms in the BM aspirates supported the diagnosis of PH, which is best confirmed by genetic studies.

PS-13-047

The degree of bone marrow fibrosis correlates with aggressive clinical and laboratory features in primary myelodysplastic syndromes

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Objective: Bone marrow (BM) fibrosis is considered an adverse prognostic factor for patients with primary myelodysplastic syndromes (MDS). We assessed the prognostic impact of BM fibrosis and its correlation with clinical and laboratory parameters in MDS patients.

Method: We performed reticulin staining on baseline BM biopsies of 181 patients with primary MDS. BM fibrosis was graded according to the European bone marrow Fibrosis Network criteria.

Results: 101 (55.8 %) patients had fibrosis grade 0–1 (group-I), 38 (21 %) an intermediate grade 1–2 (group-II) and 42 (23.2 %) grade ≥2 (group-III). Male/female ratio was 1.73/group-I and 3.00/groups-II+III ($p < 0.01$). An Int-2/High IPSS was found in 11 of group-1 patients and in 25 of groups-II+III (10.9 vs 31.2 %, $p < 0.01$). Group-II+III patients had hypercellular marrow ($p = 0.0052$), higher marrow blast percentage (7.4 ± 6.3 vs 2.8 ± 3.7 %, $p < 0.001$), higher serum ferritin ($p = 0.023$), CRP ($p = 0.003$) and LDH ($p = 0.0034$), and lower WBC count ($p = 0.038$) and albumin levels ($p = 0.0094$). Sixteen patients from group-I and 33 from groups-II+III evolved to a more aggressive MDS or AML ($p < 0.001$). Median overall survival was 28.7 and 20.1 months for group-I and -II+III, respectively ($p < 0.01$).
Conclusion: Careful evaluation of the degree of marrow fibrosis adds prognostic value and should be performed, as part of the baseline screening of all patients with MDS.

PS-13-048
Diffuse large B-cell lymphoma preceded by progressive transformation of germinal centers with paracortical T-cell proliferation: An atypical debut
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Objective: Diffuse large B-cell lymphoma (DLBCL) is an aggressive malignancy of mature B-lymphocytes that can arise de novo or as a result of transformation from a lower grade lymphoma. No significant association between DLBCL and reactive lymph node changes was previously observed.
Method: We report the case of a 61-year-old male patient recently diagnosed in our department with DLBCL associated with many cytotoxic T-cells dispersed throughout the B-cell proliferation.
Results: Three years before, the patient presented with generalized peripheral lymphadenopathy and B-type symptoms, for which a lymph node biopsy was performed. The diagnosis of progressive transformation of germinal centers (PTGC) associated with paracortical expansion by a CD3+,CD8+ T-cell population was made. The case is notable because of the unusual association between PTGC and DLBCL. Was PTGC only an incidental finding or could it play a role in the pathogenesis of DLBCL? Did the cytotoxic T-cells participate in this progression? DLBCL is a heterogeneous entity including various morphological and molecular subtypes, one of them characterized by bcl-6 gene rearrangements, which were also described in some PTGC cases.
Conclusion: Our case might offer an insight into a possible pathway of tumorigenesis from PTGC to DLBCL, but further studies are required to conclude a causal association. Cioplea and Sticlaru have equal contribution.

PS-13-049
Chronic lymphocytic leukemia /small lymphocytic lymphoma with Reed-Sternberg-Like cells: A case report
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Abstract: Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is an indolent lymphoproliferative disease derived from mature B cells. Approximately 3 to 10 % of cases of CLL/SLL develop high-grade lymphoma, a process known as Richter's syndrome. Rareyl, this transformation manifests in the form of Reed-Sternberg (RS)- like cells. Case presentation: A 70 years old male patient was admitted to our Ear, Nose and Throat out-patient clinic with a palpable neck mass. Ultrasound detected multiple abnormal enlarged lymph nodes in bilateral neck region. A fine needle aspiration (FNA) of the largest cervical lymph node was performed and interpreted as atypical lymphoid proliferations. The lymph node excision were applied and microscopic findings were a monotonous population of small lymphocytes with scattered larger lymphocytes with paler chromatin and prominet nucleoli. Immunohistochemically, the small atypical lymphocytes were positive for CD45, CD20, PAX-5, CD5, CD23 negative for CD3, CD10, cyclin D-1, Bcl-2, EMA and RS- like cells were positive for CD15, CD30 negative for CD45, CD20, EMA. Conclusion: Transformation to Hodgkin lymphoma may occur during the course of CLL/SLL. This phenomenon must be distinguished histologically from cases of CLL/SLL that show admixed background RS- like cells.

PS-13-050
MUM-1 expression in follicular lymphoma
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Objective: Recently MUM-1 expression has been shown in follicular lymphomas (FL) and seems to correlate with grade. We aimed to study MUM-1 expression in our FL cases including Bcl-2 negative ones.
Method: 111 FL cases were chosen for the study. MUM-1 positivity was examined using immunohistochemistry by tissue microarray construction (TMA) and could be assessed in 75 of the cases due to loss of tissue samples in TMA blocks. MUM-1 positivity was defined as >20 % nuclear staining in the neoplastic follicles. Bcl-2 status was assessed with immunohistochemistry.
Results: There were 18 grade 1, 47 grade 2 and 10 grade 3A cases. 66 of these cases (88 %) were MUM-1 negative, 9 (22 %) were positive. There were 5 cases (6.7 %) of Bcl-2 negative FL. MUM-1 positivity was more common in high grade cases (30 %) compared to low grade cases (10 %); and in Bcl-2 negative cases (2/5) compared to Bcl-2 positive (7/64) cases.
Conclusion: MUM-1 positivity was seen to be more common not only in high grade cases but also in Bcl-2 negative cases. This seems plausible since Bcl-2 negative FLs are presumed to be derived from late germinal center B cells. Further studies with higher number of Bcl-2 negative cases are needed to confirm this observation.

PS-13-051
Bone marrow biopsy as initial and the only specimen for diagnosis of large B-cell lymphoma
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Objective: Bone marrow (BM) involvement by large B-cell lymphoma (LBCL) usually represents the systemic dissemination of lymphoma. However, BM biopsy as the only specimen for diagnosis of lymphoma may be very challenging, especially in cases when infiltration is minimal.
Results: A-44-year-old women was admitted on July 2014. Due to pancytopenia, hepatosplenomegaly and liver failure for 10 months duration. There was no lymphadenopathy. Autoimmune and viral diseases were excluded. Splenectomy was not possible due to bleeding diathesis. Liver and bone marrow biopsy was performed. The liver tissue revealed fibrosis, necrosis and congestion (no signs of lymphoma). Bone marrow showed marked hypoplasia and scanty perivascular lymphoid infiltration by small and scattered large lymphoid cells. Immunohistochemically, the large lymphoid cells were LCA+, TdT-, EMA+, PAX5+, CD20+, CD3-, CD5-, CD10-, bcl2+, CD30-, CD15+, MUM1+, ALK-1-, CD56-, CD138-. These cells were admixed with reactive T-lymphocytes. Fibrosis was prominent in lymphoid infiltrates. The diagnosis of LBCL was obtained. Six cycles of chemotherapy led to a significant improvement of the state of the patient, with repair of liver function and reduction of hepatosplenomegaly.
Conclusion: In cases of unknown primary localization, BM examination for initial assessment of cytopenias and diagnosis of lymphoma is diagnostic challenge.

PS-13-052

Sickle cell disease: 2 autopsy cases

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Objective: Sickle cell disease (SCD) is an inherited hemoglobinopathy that affects millions worldwide. It was traditionally a disease from tropical and sub-tropical regions, but migration of these populations to low prevalent areas has dramatically increased the number of cases in developed countries.
Method: We searched in our autopsy files from 2006 to 2015 for patients with history of SCD; we found two cases.
Results: Case 1: 28-year-old male, admitted in the emergency room (ER) with lower back pain. He died unexpectedly shortly after. Case 2: 28-year-old male with a history of a recent cold was admitted in the ER for severe pain referred to the back and limbs. He died unexpectedly after 3 days. At the autopsy, both presented as the main finding extensive generalized vaso-occlusive phenomena. We also observed chronic multi-organ damage related to SCD mainly in the spleen, liver, gallbladder, bone marrow and heart.
Conclusion: SCD remains a cause of significant morbidity and mortality. The autopsy examination provided us the opportunity to observe and fully document this not so frequent and sometimes forgotten disease.

PS-13-053

MDS/EVI1 gene fusion in myelodysplastic syndrome-five year retrospective analysis of bone marrow biopsy samples in children

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Objective: Myelodysplastic syndrome (MDS) is a complex disorder comprised of seven entities. The aim was to determine the frequency of MDS/EVI1 gene fusion in cases of histologically diagnosed primary MDS in children on bone marrow biopsy samples.
Method: In a 5 year period (2010–2014) 12 bone marrow biopsy samples of children were examined at the Institute of pathology in Skopje using standard hematoxylin/eosin and Giemsa stained sections. Six of them were diagnosed as having myelodysplastic syndrome. We isolated DNA from all 6 bone marrow biopsy in order to test for MDS/EVI1 presence. MDS/EVI1 fusion was detected with touch-down-direct PCR.
Results: We found the presence of MDS/EVI1 gene fusion in 5 cases (overall 83 %).
Conclusion: As was previously mentioned, the myelodysplastic syndrome is a complex disorder. It may arise as a primary disorder, in a setting of an underlying disease, or is therapy related (secondary myelodysplastic syndrome). Some cases show MDS/EVI1 gene fusion. In our 5 year retrospective study of 6 histologically diagnosed myelodysplastic syndromes in children at the Institute of pathology in Skopje, we found the MDS/EVI1 gene fusion in 5 of them.

PS-13-059

Mantle cell lymphoma involving the colon (Multiple Lymphomatous Polyposis): A case report and review of treatment modalities

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Objective: Mantle cell lymphoma (MCL) is a rare B-cell lymphoma with a median survival of 3–5 years. We present a case of MCL of the colon in an attempt to highlight potential prognostic features and therapeutic approaches.
Method: An 83-year-old male presented with multiple polyps and polypoid masses throughout the colon. Formalin-fixed paraffin embedded tissue obtained from biopsy of the polyps was examined with histology and immunohistochemistry.
Results: Microscopically, a diffuse lymphoid neoplasm with small to medium-sized monomorphic cells with indented nuclear contours and high mitotic rate was observed. Immunohistochemically, neoplastic cells were CD20(+), IgA>>IgG, κ>>λ, CD5(-), CD10(-), bcl2(+), bcl6(+ focally), CyclinD1(+), p53(80 %), Ki-67(40 %). An immunophenotype of MCL, blastoid variant, was suggested due to the overexpression of p53, high mitotic rate and high Ki-67.
Conclusion: Expression of the cyclin D1 in MCL is due to the chromosomal translocation t(11;14)(q13;q32) between IGH and cyclin D1 genes. Blastoid morphology, overexpression of p53 and a high mitotic rate could be adverse prognosticators. Treatment approaches, such as CHOP or R-CHOP with or without radiotherapy, followed sometimes by Ara-C along high-dose chemotherapy, as our case might benefit of, could prolong patient's survival.

Tuesday, 8 September 2015, 09.30 – 10.30, Restaurant
PS-14 Poster Session Neuropathology

PS-14-001

Granular cell astrocytoma with loss of ATRX protein

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Objective: Granular cell astrocytoma represents a rare variant with a peculiar morphological resemblance of neoplastic astrocytes to granular histiocytes.
Method: A 60 year old woman presented with an irregularly enhancing lesion of the frontal lobe in T1 weighted image. Surgical resection followed.
Results: Histopathological examination revealed sheets of cells with distinct cellular borders, uniform, mildly atypical nuclei and abundant, coarsely granular, lysosomal-rich, eosinophilic or even targetoid cytoplasm. Immunophenotypically all of the neoplastic cells expressed the histiocytic marker CD68(KP1) while a significant proportion co-expressed GFAP, EMA and S-100. On the contrary the specific macrophage markers CD163 and CD14 were negative but revealed the accompanying histiocytes in the background of the neoplasm. Proliferation index was less than 5 %. The mutated form of isocitrate dehydrogenase (IDH1 R132H) was not detected and interestingly the cells showed complete loss of the nuclear expression of the ATRX protein while the FUBP1 protein was retained. Fluorescent in situ hybridization did not reveal amplification of the EGFR gene.
Conclusion: Granular cell astrocytoma behaves aggressively although the WHO classification has not assigned specific grade. Its immunophenotypical profile, especially the loss of ATRX protein, confirms its astrocytic origin and highlights its differential diagnosis from histiocyte-rich mimics like multiple sclerosis or progressive multifocal leukoencephalopathy.

PS-14-002

The recurrence-free survival of human meningiomas may be predicted by the density of microvessels positive for Wilms' Tumour protein-1 (WT-1)

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Objective: To investigate the immunohistochemical expression of Wilms Tumour-1 (WT-1) protein and its correlation with the clinico-pathological variables in human meningiomas.
Method: The immuno-expression of WT-1, CD34 and VEGF was assessed in 60 meningiomas of different histotype and histological grade. WT-1 staining was recorded in the neoplastic cells and in the tumour

vessels of each cases. Then the statistical correlation between the density of microvessels positive for WT-1 (WT-1 MVD) and the various clinico-pathological variables of meningiomas was investigated.
Results: None of the cases expressed WT-1 in the neoplastic cells, while endothelial expression was evidenced in a variable number of tumour vessels in all the meningiomas. The number of microvessels stained by WT-1 was always lower than the one revealed by CD34 staining. WT-1 MVD was significantly higher in meningiomas with higher histological grade (P = 0,0191), growth fraction (P = 0,0201), expression of VEGF (P = 0,0288) and recurrence risk (P = 0,022). In addition, high WT-1 MVD was a significant independent predictor of shorter recurrence free survival in patients with completely resected meningiomas (P = 0,0028).
Conclusion: WT-1 expression in the tumour vessels of meningiomas is correlated with their biological aggressiveness and might represent a target for immuno-therapy aimed at reducing their blood supply and growth.

PS-14-003
Paraganglioma of the filum terminale: A case report
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Objective: Paragangliomas affecting the filum terminale are extremely rare, benign tumours. The literature yielded 32 cases of paraganglioma in this site.
Method: A 23 year-old-man, whose presenting symptoms were low back pain and left leg weakness, was diagnosed as having a paraganglioma of the filum terminale. The clinical, histological and radiological characteristics of this case, that brings the total number of cases described to 33, are discussed in the light of published data.
Results: Histological evaluation of the tumour showed it to be made up of uniform cells arranged in large lobules, or smaller nests, known as "Zellballen". The aggregated chief cells were surrounded by capillaries, present throughout the lesion. There was a flattened layer of sustentacular cells, positive for S100 which encompassed both the lobules and the "Zellballen". Immunohistochemical testing gave a positive reaction for chromogranin in the chief cells.
Conclusion: Paraganglioma in the cauda equina/ filum terminale is very rare and can be misdiagnosed as ependymoma especially when it exhibits ependymoma-like histology. This rare form of paraganglioma behaves like a WHO grade I tumour of CNS like classic paraganglioma. No recurrence or metastasis is expected when it is totally resected. Morphology can be misleading hence immunohistochemistry and/or ultrastructural study is necessary for correct diagnosis.

PS-14-004
Supratentorial and cerebellar metastases in patient with pulmonary giant cell carcinoma: Case report
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Objective: Giant cell carcinoma of the lung has been regarded as an aggressive cancer with a poor prognosis; as a rule, in most cases, the diagnosis is established at autopsy. This report describes a case of giant cell carcinoma of the lung correlated with clinical parameters and prognosis.
Method: We present a case of a 49-year-old male, smoker, diagnosed with stage IV lung cancer with occipital and cerebellar metastases. After external radiotherapy combined with chemotherapy, an enhanced CT-scan revealed the disappearance of supratentorial metastasis with no residual traces and the increasing in size of both, cerebellar metastasis and primary tumour. The patient's condition continued to deteriorate with death after 11 months from the initial presentation.
Results: An autopsy was performed and the findings confirmed the lung tumour. There was no gross evidence of the metastatic occipital lesion. Only the cerebellar lesion was identified occupying the entire right hemisphere. The cerebellar biopsy showed a carcinomatous infiltration with dyscohesive bizarre malignant giant cells, uni- or multinucleated with dense eosinophilic cytoplasm and pleomorphic nuclei, positive for TTF-1, EMA and CK7.
Conclusion: We report a case of an aggressive giant cell carcinoma of the lung with multiple brain metastases.

PS-14-005
Primary spinal glioblastoma multiforme (GM) in a young man: A case report
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Objective: To show the difficulty in initial diagnosis (indistinctive image findings) in spinal GM, a rare and devastating condition.
Method: A primary spinal GM with its clinical, image and pathological studies (a necropsy).
Results: A 29 year old man presented with lower limbs paraparesis and hemiplegia besides sphincters incontinence after 5 months. Initial spine magnetic resonance (MRI) showed a T8 spinal cord expansion suggestive of an inflammatory condition (acute transverse myelitis); serial MRI revealed an increase in size plus a cystic cavit. He started with prednisone, azathioprine, cyclophosphamide and immunoglobuline IV with no response, requiring a diagnostic biopsy, not performed because for sudden death. The necropsy showed a medullary mass (10′5 × 2′5 × 2 cm) with a necrotic-cystic area proximally. The histopathology revealed a hypercellular tumour with highly pleomorphic glial cells, mitosis, necrosis with pseudopalisading and microvascular proliferation. Immunohistochemichal studies showed diffuse expression of glial fibrillary acidic protein(GFAP), S100 protein and Neurofilament. A high proliferation rate(ki67). p53 was negative, besides IDH-1, these results support the diagnosis of primary GBM. A massive bronchoaspiration was the last event.
Conclusion: This case highlights the difficulty of initial diagnosis in these rare conditions, with its prognostic implications.

PS-14-006
Discovered post mortem of a choroid plexus papilloma: About two cases
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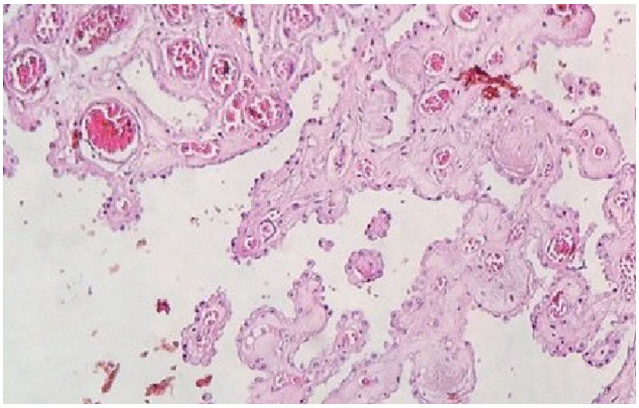
Objective: Choroid plexus tumours are very rare in adults, representing 0.4 to 0.6 % of intracranial tumours. Nearly half of these tumours occur before 10 years with a mean age of 35.5 years. The most common telltale sign remains intracranial hypertension.
Method: We report two cases: Case 1: There is a 60 years old patient who presented a sudden death, the autopsy revealed the presence of cystic formations suggestive intra cerebral ventricular aneurysm formation. Case 2: This is a patient aged 45 died following a sudden violent dead, the autopsy revealed the presence of a small brain mass in the corpus callosum measuring 0,5 × 0,5 cm crumbly consistency and brownish color.
Results: Microscopic examination showed a proliferation of papillary tumour is of cylindrical cells supported by connective axes vascular calcifications in many homes. Immunohistochemistry showed low Ki67 proliferation index and the positivity of tumour cells to CK7 and CK20.
Conclusion: Choroid plexus papillomas are benign tumours that evolve slowly. They are usually treated with surgery alone.Can rarely observe leptomeningeal disseminations and have recurrences.

Choroid plexus papilloma: HEGX20:



PS-14-007

Lafora disease: A case report

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Objective: We propose to study the epidemiological, clinical and pathological features of Lafora disease.
Method: We report a case of Lafora disease.
Results: We report the case of a 16 year old girl, which shows from the age of 14 myoclonus epilepsy. Neurological examination showed cerebellar syndrome and intellectual deterioration. The electroencephalogram showed an epileptic encephalopathy. Histological study of skin biopsy performed at the axillary region shows the presence of eosinophils Lafora bodies in cytoplasms of epithelial cells of apocrine sweat glands. These Lafora bodies were PAS positive. The diagnosis of Lafora disease was made.
Conclusion: Lafora disease has significant clinical and evolutionary characteristics. Resistance to antiepileptic and progressive cognitive deterioration should guide the clinician to achieve axillary skin biopsy to find Lafora bodies.

PS-14-009

Malignant Melanoma (MM) metastatic to the pituitary gland

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Objective: Tumours metastatic to the pituitary gland may account for 1 % of surgical specimens. We report a case of a 69-year-old woman who presented a sudden headache persisting for a few days before she consulting the hospital. MRI images demonstrated a circumscribed mass lesion measuring 2.9 × 2.2 × 2 cm in pituitary gland and suprasellar compressing the optic chiasm. Neurological examination disclosed bitemporalhemianopsia. Laboratory investigation revealed pituitary deficiency, with moderate high levels of prolactin. Radiological and laboratory data suggested pituitary hemorrhagic macroadenoma and 1 month later surgical excision was performed through a transsphenoidal approach.
Method: We received five brown and grayish tissue fragments measuring 1.5 × 0.8 × 0.4 cm.
Results: The histological examination of the specimen revealed a malignant tumour with focal melanotic pigmentation. The cells had nuclear pleomorphism, high mitotic activity and stained immunopositive for S-100 protein, Melan A and focally for HMB-45. Ki-67 (MIB-1) was estimated 10–15 %. The diagnosis was pituitary metastatic melanoma.
Conclusion: Neoplastic disease from extrasellar sources can present as pituitary masses. Patients with metastatic disease are more likely to present with diabetes insipidus or pituitary stalk and visual deficits. Lung, breast and GI tract are the most common sources. Hematopoietic lesions and melanomas usually involve pituitary gland in advanced stage disease.

PS-14-010

Two in one: Metastasis of melanoma and adenoma of the hypophysis. What are the odds?

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Objective: To report the case of a male with an adenoma of the hypophysis and metastasis of melanoma. The involvement of hypophysis by metastasis is rare and like in others intracranial locations, breast and lung metastasis are more common.
Method: A 67-year-old male presented with left visual impairment. In 1995 he was diagnosed with an adenoma of the hypophysis which was partially resected and in 2010 with a Clark IV nodular melanoma. Cerebral MRI demonstrated a 26 × 42 mm mass consistent with enlargement of the previous adenoma. There were no other brain lesions. He was submitted to transsphenoidal surgery.
Results: A 2 gr specimen of multiple brown fragments was received. The specimen had two different populations, one consisting of large cells with eosinophilic and ill defined cytoplasm and irregular nuclei, granular chromatin and conspicuous nucleolus, immunopositive for melanocytic markers. And the other composed of homogeneous nested cells with eosinophilic and well defined cytoplasm, regular nuclei with inconspicuous nucleolus with disrupted acinar structure and immunopositive for neuroendocrine markers and FSH.
Conclusion: Max et al showed that in patients with metastatic cancer a sellar lesion is actually twice as likely to be a benign pituitary adenoma as a metastasis. The patient presented the both.

PS-14-011

Expression of the serine-arginine protein kinase 1 in human gliomas and glioma cell lines

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Objective: Splicing aberrations occur frequently in malignancies. Important regulators of splicing process are serine-arginine protein kinases (SRPKs). SRPK1 is involved in cell cycle progression, apoptosis and tumorigenesis. Herein, we investigated the expression of SRPK1 in human gliomas and glioma cell lines and its potential biological significance.
Method: SRPK1 protein expression was studied by immunohistochemistry in paraffin tissue sections from 38 gliomas ($n = 38$) and by RT-PCR and Western blot analysis in U87, U251, D54 and T98 glioma cell lines.
Results: Cytoplasmic SRPK1 expression was observed in tumour cells. No staining was detected in glial cells of the adjacent normal glia, except of neurons. Higher SRPK1 expression was observed in glioblastomas than in low-grade gliomas and was correlated with high Ki67 index ($p = 0.0078$) and worse survival ($p = 0.03$). Expression of the protein was detected in all glioma cell lines. Small interfering RNA-mediated down-regulation of SRPK1 in cell lines inhibited tumour cell growth. The disruption of SRPK1 expression partially enhanced sensitivity of glioma cells to killing by cis-platin, whereas no such synergistic effect was observed with 5-FU.
Conclusion: SRPK1 expression is implicated in tumour growth and associated with patient outcome. The potential of SRPK1 inhibitors as anticancer agents may be a promising therapeutic issue.

PS-14-012

Unexpected recurrence of a pineal region mature teratoma as germinoma, 10 years after

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Objective: The pineal region lodges a variety of pathologic entities, among which germinal cell tumours represent a challenging issue especially when children are involved. A joining effort performed by radiologist, surgeon, pathologist and oncologist provide a good chance for cure of these young patients.
Method: Fragments of a 37/31/28 mm heterogeneous midline pineal region mass producing an active triventricular hydrocephalus to a 12 years old boy, were routinely processed and supplementary sections submitted for histochemistry (PAS) and immune reactions with PLAP, c-kit, D2-40 and Ki-67. Retrospectively, 10 years ago, the same patient underwent a radical excision of a pineal region tumour, which proved to be a mature teratoma. No adjuvant therapy was done afterwards.
Results: H&E and PAS aspects in junction with positive reaction for PLAP, c-kit and D2-40 assure the germinoma diagnosis. A high proliferation rate (Ki-67 = 40 %) and subtotal excision added to the diagnosed subtype of the germinal cells tumour indicate radiotherapy.
Conclusion: As the presented case proved, even after a long period (10 years) a pure mature teratoma in pineal region can recur as a nonteratomatous germinal cells tumour. Even so, with adjuvant therapy, the prognosis is still good.

PS-14-013

Metaplastic meningioma with significant ossification

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Objective: Metaplastic meningioma is a rare subtype of benign meningiomas, classified as WHO grade I and these with significant ossification are uncommon. The mesenchymal components are osseous, cartilaginous, lipomatous, myxoid or in combinatios.
Method: We present a 57-years-old woman with hard and painfull palpable swelling of the frontal region. She complain dizziness and headache during 4 years.
Results: A tumour measured 5,8 × 5 × 1 cm with focally hard consistency was received, having histological picture of metaplastic meningioma with ossification.
Conclusion: The current literature indicates that metaplastic meningioma grows like other grade I meningiomas with similar recurrence rates. The biological behavior of intracranial metaplastic meningioma is poorly understood, partly to a limited number of reported cases, but is believed to carry a good prognosis with little given its low chance for recurrence. Metaplastic bone must be distinguished from the reactive bone overrun by meningiomas invading the skull. Correlation with intra-operative findings is occasionally needed to distinguish ossified meningiomas from ones exhibiting bone invasion. The tumour sites were mainly convexity, spinal cord, sphenoid wing and sellar region, intraventricular, CPA, sinus region, petroclivar and cranial fossa. The clinical symptoms of metaplastic meningioma are usually various, which depend on the location and volume of the tumours.

PS-14-014

Esthesioneuroblastoma: A borderline lesion in neuropathology and head and neck pathology

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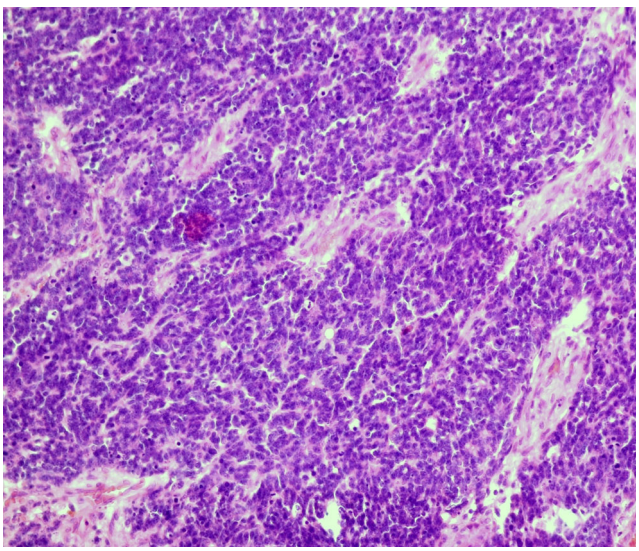
Objective: Esthesioneuroblastoma is a complex, uncommon neuroectodermal tumour. Its origin has been widely debated but it's now accepted that it arises from immature olfactory receptor cells. Unlike most neurons, those undergo continuous replacement from basal stem cells. It was first acknowledged in 1924 by Berger and referred to as "esthesioneuroepithelioma".
Method: A 24 years old man accusing sleepiness, attention and memory deficiency and headaches was admitted to the Bagdasar-Arseni Emergency Hospital for neurological examination. Neuroimaging revealed a large hourglass shaped mass involving both frontal lobes and extending through the ethmoid plate to the right nasal cavity and orbit. The intracranial component, about 7 cm in diameter, was neurosurgically resected and the patient underwent skull base reconstruction. Two months later, the same surgical team removed the sinonasal component.
Results: Microscopically, the tumour presented sheets of relatively uniform small blue cells with scant cytoplasm and ovoid nuclei. Mitotic rate was high and both Homer Wright pseudorosettes as well as true Flexner Wintersteiner rosettes were present. It was diagnosed as an esthesioneuroblastoma.
Conclusion: Although assigned to head and neck pathology, esthesioneuroblastomas are tumours of neural origin with a tendency for cerebral involvement. Neurological symptoms may replace nasal obstruction or anosmia and neurosurgical treatment is usually required, making acknowledgement necessary for neuropathologists everywhere.

Esthesioneuroblastoma HE 20x:



PS-14-015

Medulloepithelioma - A rare primitive neoplasm of the central nervous system: Case report

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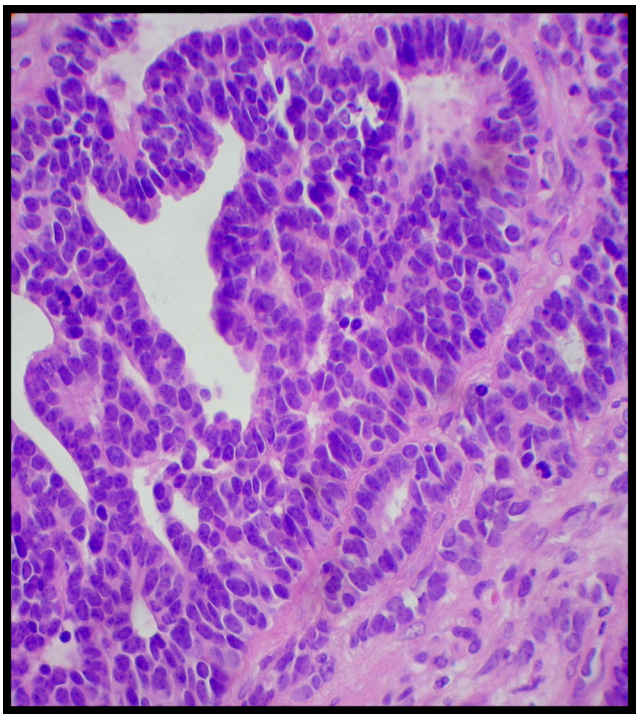
Objective: Medulloepithelioma is a rare, malignant embryonal tumour affecting young children. Due to its origin from the primitive medullary plate and neural tube, it has been described as the most primitive neoplasm of the CNS. Theories about its etymology include neoplastic transformation during fetal or early postnatal development or the result of abnormal gene re-expression.
Method: A 1 year and 7 months girl was admitted to the Bagdasar-Arseni Emergency Hospital after generalized tonic-clonic seizures followed by temporary right side hemiparesis. Neuroimaging revealed a left temporal cortico-subcortical solid mass with a cystic component which was excised neurosurgically.

Results: Macroscopic appearance was of a grayish-white irregular growth measuring 4,5/3/2 cm. HE sections revealed a cellular lesion with pseudostratified columnar cells arranged in ribbons and tubules on a thick, continuous eosinophilic basement membrane. These structures greatly resemble the primitive neural tube. Additionally, the tumour was densely cellular with numerous mitotic figures and a characteristic small blue round cell appearance. It was diagnosed as a medulloepithelioma. One year later, the patient presented a 2 cm nodule in the left temporal lobe. Oncologic treatment was continued.
Conclusion: Medulloepitheliomas are rare pediatric tumours that display characteristic features of the primitive neural tube. Their behavior, while not entirely known, is highly malignant with early progression and recurrence.

Medulloepithelioma HE:



PS-14-016
Myxopapillary ependymoma of the sacrum - A complex lesion with uncertain prognosis: Case report
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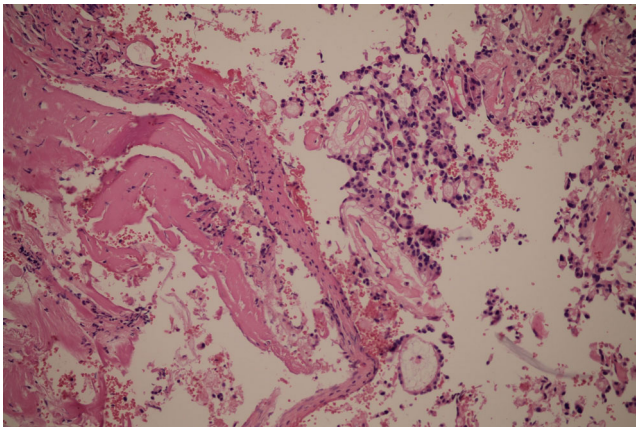
Objective: Ependymomas are common spinal cord tumours with the myxopapillary type being most frequent in the lumbosacral region. It usually involves the nerve roots of the cauda equina but few cases of primary intrasacral lesions have been described. This is a complex tumour causing important bone destruction and requiring a different surgical approach.
Method: A 22 year old man was admitted to the Bagdasar-Arseni Emergency Hospital accusing lumbosacral pains, bladder dysfunction and walking abnormalities. CT scans revealed an expansive, osteolytic lesion from S1 to S4, invading the sacral canal, vertebra, sacral wings and anterior pelvic tissues. It measured about 8,5/10/10 cm. Surgical procedures involved subtotal resection sacrificing the S3 - S5 nerve roots due to the highly infiltrative nature of the tumour.
Results: Grossly it presented as a soft, grayish, slightly hemorrhaging mass. Light microscopy revealed the characteristic features of a myxopapillory ependymoma with cuboid cells around pools of basophilic mucinous material. Despite important bone destruction the nuclear pleomorphism and mitotic index were very low.
Conclusion: Myxopapillary ependimomas of the sacrum are extremely rare, probably arising from extradural remnants of the filum terminale or the coccygeal medullary vestige. Despite benign appearance they have a high risk of recurrence and distant metastasis.

Myxopapillary Ependymoma of Sacrum HE 20x:



PS-14-017
Clinicopathologic analysis of pituitary lesions: Preliminary evaluation of consecutive cases
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Objective: The pituitary and parasellar region is an anatomically complex area where a number of neoplastic, inflammatory, developmental and vascular pathologies can occur. Pituitary adenomas (PA) are typically benign, slow-growing tumours and represent majority of pituitary neoplasms.
Method: Authors analyzed 109 surgically resected and pathologically proven pituitary and parasellar lesions of the Tepecik Education and Research Hospital from 2008 to 2015.
Results: The lesions were categorized as: PAs (n = 94), craniopharyngioma (n = 7), epidermoid cyst (n = 2), Rathke's cleft cyst (n = 1), inflammatory lesions (n = 1), metastatic carcinoma (n = 1), gangliocytoma (n = 1) and unsatisfactory specimens (n = 2). PAs were slightly more prevalent in men (F: M = 1:1.21) with a mean age of 52.1 years (18–85 years). Of the 94 PA cases 37 had immunohistochemical hormonal analysis and prolactin-producing PAs (n = 6) and growth hormone-producing adenomas (n = 6) were the most common functional PAs. Plurihormonal PAs and nonfunctioning (null cell) adenomas were found in n = 9 and n = 15 of patients with PAs, respectively. The recurrence rate of PAs was 5.4 %.
Conclusion: The pituitary lesions and the proportions of hormone-producing PAs in our patients are similar to those of previous reports except nonfunctioning (null cell) PAs, which are unusually frequent.

PS-14-018
Expression of protein biomarkers in cerebrospinal fluid in frontotemporal lobar degeneration and other neurodegenerations
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Objective: Neurodegenerations are proteinopathies characterized by accumulation of pathologically conformed proteins. Definite diagnosis of

these disorders is possible neuropathologically after the autopsy. Disease-associated proteins in the cerebrospinal fluid (CSF) of patients could serve as a biomarkers for clinical diagnosis. The aim of our study is to examine levels of selected CSF biomarkers in neuropathologically confirmed cases.
Method: We analyzed CSF (n = 17) collected postmortem and antemortem according to standardized protocols during the autopsy and clinical neurological examination. Study include neuropathologically confirmed cases of frontotemporal lobar degenerations (FTLD-TDP, progressive supranuclear palsy (PSP), Alzheimer disease (AD) and mixed neurodegeneration (FTLD+AD). CSF levels of total-tau (T-tau), phospho-tau (P-tau), beta-amyloid (Abeta), TDP-43 and progranulin were measured and quantified using ELISA and statistically evaluated.
Results: In examined diseases, we did not find any statistically significant difference in the CSF levels of T-tau, P-tau, Abeta, TDP-43 and progranulin.
Conclusion: In limited number of autopsy-confirmed neurodegenerative diseases, we did not find any statistically significant differences in evaluated CSF biomarkers. However, only autopsy-based biomarker studies can give feedback for further development of diagnostic and prognostic biomarkers, which are important part for clinical diagnosis, treatment and prognosis of the patients suffered by different neurodegenerations.

PS-14-019
Giant cell tumour of the sellar clinically appearing as prolactinoma
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Objective: We present a case of giant cell tumour of bone, not only at an unusual site but with an extremely unusual clinical appearance.
Method: A 21 year-old female presented with persistent galactorrhea. On serum examination she had increased levels of prolactin. On clinical examination a left side paresis of the oculomotor nerve was revealed. Radiologically a mass at the sellar region was observed that expanded to the sphenoid sinus and bone. A differential diagnosis of pituitary lesion was elaborated and a decision for surgical excision had been taken. It is remarkable that there was galactorrhea during the operation, which stopped immediately after the excision of the mass along with the dramatic drop of prolactin levels.
Results: We received for histological examination multiple specimens of elastic composition. Microscopy revealed that the mass was a giant cell tumour of the bone. The proliferation marker Ki67/MIB1 was positive for 30 % of the spindle cells. Despite the multiple sections, no pituitary gland tissue was found. The post-operative follow-up showed improvement of the oculomotor paresis.
Conclusion: The clinicopathological correlation indicated that the elevation of prolactin levels and consequently the galactorrhea were due to pressure phenomena of the mass against the pituitary gland.

PS-14-020
Rosette forming glioneuronal tumour of fourth ventricle: A case report
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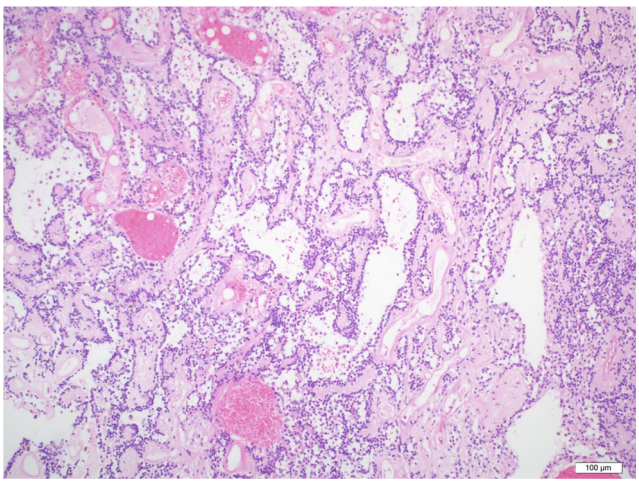
Objective: The rosette forming glioneuronal tumour (RGNT) of the fourth ventricle is an extremely rare tumour. Seventytwo cases have been reported since its first description by Komori et al in 2002.
Method: Twenty nine -year-old woman admitted to the hospital with the complaints of weakness and numbness in right side of her body. Imaging studies revealed a solid mass with a cystic component nearby the fourth ventricle. Histopathological examination of the resected mass showed a biphasic tumour with a neurocytic and an astrocytic component. Neurocytic rosettes with an eosinophilic core, positive for NSE and synaptophysin has been observed in the neurocytic component. Astrocytic component composed of bipolar and spindle cells displaying strong positivity with GFAP. Ki-67 labeling index was very low.
Conclusion: The tumour has been reported in a wide age range of the patients (12–59 years of ages, mean age is 31). A slight female dominance (1.75 / 1) is seen. Its typical localization is in the midline ventricular system, however, pineal, pontine and thalamic regions may also be involved. Although the tumour has a benign clinical course, one reported case presented as multifocal lesions with leptomeningeal spread. Therefore, the presentation and its exact response to treatment is mostly unclear.

H&E X200:



PS-14-021
Calcifying pseudoneoplasms of the neural axis: Two case-reports
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Objective: Calcifying pseudoneoplasms of the neuroaxis are non-neoplasic, calcified lesions occurring anywhere in the central nervous system. There are 45 cases reported in the literature, 33 intracranial and 12 spinal. Two spinal cases are described.
Method: A 58-year-old man presented with cervical pain, reduced muscle strength of the left lower limb and tremors of the left upper limb. Computed tomography (CT) scanning and Magnetic resonance imaging (MRI) showed a lesion on the left anterolateral region of the foramen magnum with compression of the spinal cord. A 49-year-old man presented with spastic tetraparesis. MRI showed a calcified lesion in the cruciform ligament and posterior ligaments in C0-C1, T1 and T2 hypointense with T2-weighted hyperintensity in the adjacent medulla. Both patients underwent surgery.
Results: Histopathological examination allowed the diagnosis of calcifying pseudoneoplasm. In both cases follow-up imaging studies showed residual lesion and both patients developed a clinical picture consistent with hydrocephalus, consequently requiring a ventriculoperitoneal shunting.
Conclusion: Increasing number of reports, imaging features that can suggest the diagnosis and distinctive histopathologic appearance should raise de importance of this benign entity in the differential diagnosis of intracranial and intraspinal calcified lesions.

PS-14-022

Peculiar small blue cell tumour of the brain with prevailing sarcomatous component

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Objective: The presence of sarcomatous component in brain tumours (gliosarcoma, PNET) is quite rare. To our knowledge, the cases with evident dominance of sarcomatous component (Sa) over neuroepithelial (Ne) in brain neoplasms have not been reported yet.
Method: MRI detected a heterogeneous tumour mass (65 × 40 × 38 mm) in the basal region of right temporal lobe in a 79-year-old male. During surgery, a cherry red fibrillary tumour with the zones of solid-elastic texture, moderately vascularised, without clear margins, was excised.
Results: Histopathological examination of the resected specimen revealed rare aggregations of small blue cells forming unclear rosettes and extensively presented sarcomatous component of predominantly fibrous structure with small number of elongated cells and zones of mild myxomatosis. The regions of angiomatosis and vast necrosis were also present. Immunohistochemical study detected the following: Vim was positive in both Sa and Ne components; GFAP, Syn, S-100, CD117, CD56, NSE were positive only in Ne component; Des, SMA, MSA stained positively in Sa component; EMA, AE1/AE3, CK 7, NF, NB, TTF-1, CD34, CD99, bcl-2 were negative in both tumour components; Ki-67 – 76 % in Ne and 14 % in Sa. Molecular-genetic testing (quantitative PCR) was successful only for Ne component and revealed high levels of TP, β-tubulin III, Ercc1, VEGF, TOP2α, C-Kit and PDGFRα, and medium level of MGMT mRNA expression.
Conclusion: Immunochistochemical profile of the tumour is more characteristic of PNET than of gliosarcoma. This observation is unusual in the terms of the patient's age and the predominance of sarcomatous component.

PS-14-023

Desmoplastic infantile ganglioglioma: Report of a case and review of the literature

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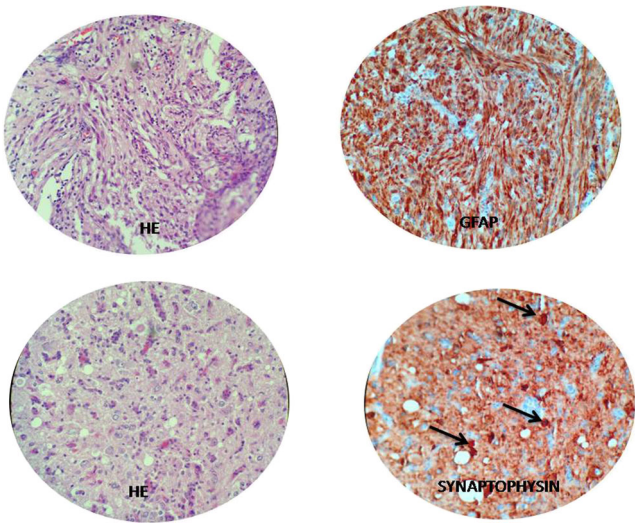
Objective: To facilitate the awareness of this distinctive lesion, we describe the histology, immunohistochemistry, and differential diagnoses of a desmoplastic infantile ganglioglioma (DIG).
Results: A 6-year-old girl was admitted with the chief complaint of seizure without family history. Neurological examination was normal. Magnetic resonance imaging scan showed a hypodense area in the right temporal region, with contrast enhancing solid as well as large cystic components. A right temporal craniotomy was performed and the tumour was excised. The pathologic examination revealed a markedly desmoplastic tumour, showing deposition of dense collagen fibers. The neoplastic cell population was heterogenous, composed of spindle-shaped astrocytes with a fascicular arrangement. Scattered ganglion cells were also observed, indicating neuronal differentiation. No mitosis or necrosis was present. The first component was GFAP positive, and the latter component was reactive with synaptophysin. Diagnosis of DIG was made.
Conclusion: DIG is a rare supratentorial brain tumour occurring before 2 years. Until now, <60 cases of DIG have been described. The main histologic differential diagnoses are reticulin-rich desmoplastic tumours such as pleomorphic xanthoastrocytoma which occur in adults, have prominent cells' lipidization and no neural component, gliofibroma which is infratentorial and lacks also the neural component, ganglioglioma which occurs in adults, and lacks of desmoplasia.

Histological specimen: The astrocytic component was reactive with GFAP, and the neuronal component was reactive with synaptophysin:



PS-14-024

Neurocytoma: Clinical and histopathopathological features

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Objective: To describe clinical, histological, and immunohistochemical features of neurocytoma.
Method: This is a retrospective study of 12 cases of neurocytoma diagnosed in the department of Pathology at the Rabta's hospital. We analyzed the following parameter: age, sex, histological features, and expression of GFAP, synaptophysin, and MIB1.
Results: The median age was 24 years with five men and seven women. All tumours were intra-ventriclar. Signs of obstructive hydrocephalus were detectable in all patients. A feature common to all of these tumours was the isomorphous neoplastic cell population. Honeycomb architecture reminiscent of oligodendroglioma was a prominent feature in three of the neoplasms. Other distinct patterns included perivascular pseudorosettes in four cases, and cell-free neuropil islands in seven. Calcifications were observed in four cases. The mitotic activity was low. There were no cases exhibiting areas of necrosis and vascular endothelial proliferation. Immunohistochemical examinations was made in nine cases and revealed a consistent and uniform expression of synaptophysin in all neurocytomas. GFAP was negative. MIB1 was inferior to 20 % and correlated to mitotic index.
Conclusion: Our findings demonstrate that central neurocytomas represent a tumour entity with characteristic clinical and histopathological properties. The central neurocytoma is included in the differential diagnosis of intraventricular neoplasms in young adults.

PS-14-025

Primary diffuse large B-Cell lymphona of the central nervous system: A clinicopathologic study of 29 cases

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Objective: Primary diffuse large B-cell lymphoma of central nervous system (CNS DLBCL) is a rare tumour. The aim of this study was the presentation of clinicopathologic characteristics of this type of non-Hodgkin lymphoma.

Method: Retrospective analysis of patients with CNS DLBCL registered in our data base of neurosurgical biopsies from 2009 to 2013.
Results: During 5-years period CNS DLBCL was diagnosed in 29 patients (17 females and 12 males). The mean age of the patients was 52.63 ± 18.80 years, ranging from 22 to 85 years. Supratentorial localization was observed in 72.41 % patients. In the majority of cases (86, 2 %) tumour was a solitary mass lesion. Presenting symptoms of short duration were hemiplegia (31 %), followed by psychiatric symptoms (13.80 %), vomiting (10.30 %), headache (6.90 %) and low back pain (3.50 %). The past medical history included hypertension (17.24 %), schizophrenia (3.44 %) and malignant melanoma (3.44 %). Morphologically, 89.65 % DLBCL were of centroblastic and 10.35 % of immunoblastic type. Based on immunohistochemistry, 63,2 % DLBCL were non-GCB type according to Hans algorithm. Eleven patients (38 %) died, living from 1 to 143 weeks from the moment of diagnosis, with average survival of 23.2 ± 42.1 weeks.
Conclusion: Clinicopathologic characteristics of CNS DLBCL of our study, except gender distribution, are in compliance with literature data.

PS-14-026
Histochemical and electrophysiological study of deep paraspinal muscles in idiopathic scoliosis

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Objective: The pathogenesis of idiopathic scoliosis (IS) has been poorly understood. The potentially involved local changes in deep paraspinal muscles have remained unknown.
Method: 18 patients with IS (14 females, 4 males) and five controls were enrolled into the study. Ninety-two biopsy samples from different deep paraspinal muscles were obtained during corrective spinal surgery. The muscle tissue samples were frozen in isopentane and the cross-sections were stained to establish the distribution of muscle fiber types (myofibrillar ATPase, fast myosin immunohistochemistry). Needle EMG of the paraspinal muscles at convexity and concavity of the curve was performed before biopsy.
Results: In all cases of IS, histological analysis revealed numerical predominance of type I fibers and occasional fiber type grouping on the convex side of the scoliotic curve. All patients examined by needle EMG showed increased amplitude of motor unit action potentials (MUP) on the convex side of the curve.
Conclusion: Our data demonstrate a significant asymmetry in fiber type distribution corresponding with an altered function in paraspinal muscles with predominance on the convexity of the curve. Thus, local neurogenic changes in the paraspinal muscles might play an important role in the development of IS. Supported by IGA NT/13693-4.

PS-14-027
Platelet-derived Growth Factor (PDGF) A and PDGF B/PDGFR beta axis in pituitary adenomas

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Objective: To evaluate the expression of PDGF A, PDGF B and PDGF receptor β (PDGFR β) with emphasis to their possible role in pituitary adenoma progression.
Method: Our study included 60 specimens of pituitary adenomas with a well defined hormone profile immunohistochemically assessed, followed by the use of immunohistochemical staining methods with specific antibodies against PDGFs and PDGFR β.
Results: Sixty six percent of total cases expressed PDGF A, with cytoplasmic and membranous pattern, and an isolated positive nuclear reaction was observed. PDGF A expression was statistically significant correlated with prolactin-secreting pituitary adenomas ($p = 0{,}011$). PDGF B had a nuclear staining pattern in tumour cells for most of the cases, few cases having a combined nuclear and cytoplasmic pattern. PDGF B expression was noted with the highest score (+3) in case of GH-secreting adenomas ($p = 0, 010$).Pituitary adenomas with acidophilic cells, the majority being GH-secreting adenomas, presented an important expression of PDGFR β in the tumour cells.
Conclusion: Our results suggest the influence of the PDGF family members on the hormone profile and partially confirm these data, namely the fact that the two versions, PDGF A and PDGF B seems to have differential effects reported to the hormone profile.

PS-14-028
Magnetic resonance microscopy of paraffin embedded histology specimens

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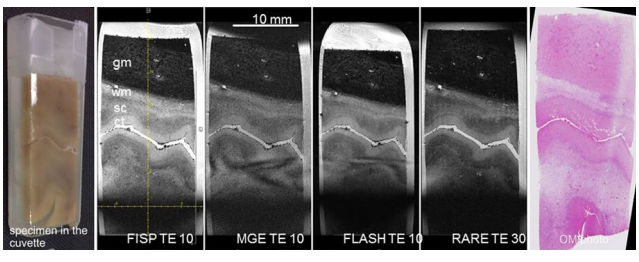
Objective: Magnetic resonance microscopy (MRM) could provide non-destructively three-dimensional (3D) images of centimeter-sized tissue blocks with resolution better than 50 um/pixel. We seek conditions to image formalin fixed paraffin embedded (FFPE) human brain tissue blocks using 16.4 tesla (MRM).
Method: Contrary to solid paraffin at ambient temperature, paraffin melt at 70 C seems quite suitable for MRM. MRM images were obtained from melted paraffin (by warming the sample to temperatures of 60–70 C). Good 3D images with isotropic resolution down to 32 μm/pixel were obtained with both, gradient echo and spin echo methods.
Results: To test achievable image quality of the embedded tissue in the paraffin melt we used post-mortem human brain specimens, ~30 × 15 × 5 mm, routinely prepared for the histological studies. Few standard methods (FLASH (Fast Low Angle Shot), FISP (Fast Imaging with Steady State Precession), MGE (Multi Gradient Echo) and RARE (Rapid Acquisition with Refocused Echo) were optimized to produce high contrast 3D images with isotropic resolution down to 32 μm/pixel.
Conclusion: High resolution 3D MRM images from FFPE tissue can be obtained at temperatures above paraffin's melting point (> 56 C). Although the resolution is far below the one in OM main advantage of 3D MRM of FFPE tissue is its nondestructive character. Even with such modest resolution (compared to OM) it could open new avenues to guide pathologists to tissue segments with actual pathology, eliminating the "random sampling" nature of standard histology slide generation.

MRM vs OM image of the human brain specimen:



PS-14-029
Subependymal giant cell astrocytoma: Clinical and histopathological features

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Objective: The authors report their experience in the clinical and histological findings of the subependymal giant cell astrocytoma (SEGA).

Method: Retrospective study of the histologically proven cases of SEGA, diagnosed between 1995 and 2015 in the Pathology Department of La Rabta's Hospital. Clinical data were reviewed for each patient and the following parameters were evaluated: gender, age at diagnosis, initial clinical symptoms and site of onset, main imaging findings and histological features of the lesion.
Results: A total of 11 patients with histologically SEGA were investigated. The gender ratio was 1.2 for a male predominance (6 males and 5 females). The average age was 21.7 years (range 5 to 53). Clinical manifestations were presented in an acute manner, such as symptomatic hydrocephalus, or an acute intratumoral hemorrhage. Magnetic resonance imaging showed intraventricular tumours associated to hydrocephalus, mass effect or intratumoral hemorrhage. Histologically, tumours were composed of three types of cells: spindle, gemistocytic and ganglion-like.
Conclusion: SEGA is benign, WHO grade 1, slowly growing tumour linked to the tuberous sclerosis complex (TSC), but it can occurs also in patients without TSC. Parenchymal extension and worrisome histological features, such as necrosis, mitoses, microvascular proliferation or pleomorphism, are unusual in these tumours, but can occur.

PS-14-030
Pilocytic astrocytoma with anaplastic features: An unexpected diagnostic dilemma
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Objective: We report a case of spinal pilocytic astrocytoma, with anaplastic features at 15 years old girl because PA with anaplastic features is associated with decreased survival when compared with typical PA.
Method: A 15 years old girl presented with weakness of the extremities. The MRI exam of the thoracic and lumbal spine revealed a multifocal subdural extramedullar tumour mass involving the Th1 to Th7 and the Th10 to L2 segment, with compressive effect on the medulla and the conus medullaris. The patient underwent surgery and the specimen was referred to histopathological analysis.
Results: Histological sections demonstrate a glial tumour with biphasic appearance including astrocytic (GFPA, Vimentin positive; Synaptophysin, p53 and Neu N negative) and oligodendroglial-like (OLIG 2 positive) areas. Tumour cellularity and proliferative activity are low. Focally, the presence of palisading necrosis, glomeruloid capillary proliferation, and increased mitotic count was noted (up to 4 mitosis/10 high power fields). The diagnosis of pilocytic astrocytoma with atypical histological characteristics was made.
Conclusion: In this case, a tumour has atypical histological characteristics and we highlight the importance of recognition this atypical focuses in the tumours because they are associated with decreased survival when compared with typical PA.

PS-14-031
Clear cell meningioma: Report of a case
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Objective: Clear cell meningioma (CCM) represents a rare variant of meningioma localized mainly in spine or cerebellopontine angle and affecting primarily younger patients. We report a case of CCM in a middle-aged woman.
Method: A 50-year-old woman underwent craniotomy and excision of a meningeal tumour measuring 6 × 4 × 3,5 cm, localized in the left frontal lobe. Morphological and immunohistochemical study of the specimen was performed.
Results: A cellular neoplasm with a focal syncytial-whorling growth pattern was identified. The cytoplasm of the polygonal neoplastic cells was predominantly clear or vacuolated (PAS: +, PAS-Diastase:-, mucicarmine:-) while the nuclei were round-ovoid to slightly elongated with visible nucleoli, without obvious mitotic activity. Many congested vascular channels or others with hyalinized walls were distributed within the tumour. The tumour cells immunohistochemically expressed EMA, Vimentin, CD56, Progesterone Rec. (approximately 40 % of the cells), whereas were negative for Pankeratin, GFAP, Chromogranin, RCC. Ki67 index was 5 %. The histopathological features were consistent with a diagnosis of a CCM.
Conclusion: CCM is a grade II meningioma variant which is important to be distinguished from other, metastatic (mainly clear cell renal cell carcinoma) or not, neoplasms. The tumour demonstrates a higher recurrence rate compared to other meningioma variants and the extent of initial surgical resection seems to be the most important prognostic parameter.

PS-14-032
Atypical teratoid / Rhabdoid tumour on CNS in pediatric patient: Case report
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Objective: Atypical teratoid/ rhabdoid tumour (AT/RT) is a highly malignant CNS tumour predominantly manifested in children. It has divergent differentiation along epithelial, mesenhymal, neuronal or glial lines and typically containing rhabdoid cells with primitive neuroectodermal cells. Our aim is to present pathological hallmarks of atypical teratoid/rhabdoid tumour on CNS, as a rare entity which is frequently misdiagnosed.
Method: We present a male 10-month old patient with AT/RT. To the institute of pathology from the University Clinic in Skopje have been delivered 7 soft tissue fragments of irregular shape and size, with dimensions 3 × 2,5 × 1,5 cm for the bigger fragment and 1–1,5 cm for the others.
Results: The tissue was gray-pink to gray-whitish with medium coarse consistency with neovascularization and necrosis. Microscopically the tumour is composed of round cells with polygonal nuclei with vesicular chromatin and prominent eosinophilic nucleolus. From the applied immunohistochemical methods, the cells were positive for: Vimentin, EMA, CD99, CD34, S100, GFAP. The proliferative index Ki67 was nearly 50 %.
Conclusion: From the described morphology of the tumour and the immunohistochemical analysis, the diagnose of AT/ RT (WHO gr. IV) was made. This can be confirmed with the diagnostic methods that were used earlier like CT and MR.

PS-14-033
Rhabdoid Meningioma, malignant or not?: Report of a case
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Objective: According to WHO Classification of Tumours of the Central Nervous System (2007); Rhabdoid Meningiomas are the rare subtype of meningiomas and are accepted as grade 3. Although many has malignant morphology, early recurrence rate and poor outcome, there are case reports stating to only rhabdoid features but no any other malignant properties. We submit a case of rhabdoid meningioma which has no malignant histopathological features except rhabdoid morphology.
Method: A 55-year-old male who presented with headache of whose MRI of the brain demonstrated a left fronto-parietal iso-dense, contrast-enhancing dural based mass of 27 × 22 mm diameter which has neighboring sylvian fissure. The tumour was resected.
Results: Histopathological examination of the tumour showed sheets of entirely rhabdoid cells with prominent eosinophilic cytoplasm, eccentric nuclei and prominent nucleolus resemble described in rhabdoid tumours

in other sites. This case did not consist histological features of malignancy, such as mitosis, high Ki-67 proliferative indices, necrosis and brain invasion. Immunohistochemically tumour cells expressed vimentin, EMA, progesteron and INI-1. The proliferation index Ki-67 was < 2 %. Histopathological diagnosis was rhabdoid meningioma without malignant morphological features.
Conclusion: There are a few cases of patients with rhabdoid meningioma were reported in the literature. Most of the reports state that rhabdoid meningiomas are highly aggressive tumours. But a minority of meningiomas with rhabdoid features lack malignant properties as the presented case. The question is the malignant properties belong to rhabdoid features or the other histological features such as mitosis, necrosis and brain invasion. The proper answer most probably lies in the long term follow up of long series of tumour cases.

PS-14-034
Intradural solitary fibrous tumour of the servical spine
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Objective: Solitary fibrous tumours (SFT) are ubiqitous mesenchymal neoplasms putative fibroblastic origin. SFT may also occur in the meninges and central nervous system parenchyma; in addition, spinal cord and spinal nevre involment has been reported. A 60 years-old-female paitent was admitted to neurochirurgia department with painfull and numbness of neck, arms, legs for the last 2 months. Her cervical T1-weighted magnetic resonance imaging (MRI) showed a well circumflunced and hypointensive lesion with 27 mm lenght at right C2 vertebra level and inferior foramen magnum that was located intradural extramedullary. Lesion was presented encapsulated at gross of pathology 3 × 2 × 2 cm diameter and cut surface of color off white. Histopathologically, uniform spindle cells arranged in interlacing fascicles with deposition of scanty collogen between cells. Tumour cells were with elongated nuclei with slighytly granular chromatin. İmmunhistochemically, strong and diffuse immunopositivity with Vimentin, CD34, CD99 and weak immunpositivity with Bcl-2 were seen. Tumour cells were negative for SMA, Desmin, S-100, EMA, GFAP, CD68, CD31 and CD38.
Conclusion: Our case differs from other spinal SFT cases by being located in cervical area and inferior foramen magnum. Only %37 of those cases are found intradural and extramedullary. We presented that our case settled in cervical, intradural rare location.

PS-14-035
Tumour in the aging brain: A case report
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Objective: We present a case of a 60 years old man with histological finding of isolated cerebral amyloid angiopathy together with small cell glioblastoma, emphasizing the fact that these two conditions could be found in the elder.
Method: The patient presented with a history of epilepsy and weakness of the extremities after a seizure. He underwent an urgent surgery because of an expansive CT confirmed lesion of the cerebral cortex, but he died 2 days after the procedure.
Results: The tissue submitted to histopathological analysis revealed an infiltrating small cell glioblastoma with co-existing amyloid angiopathy confirmed with Congo red staining and αAmyloid immunostain, as well as βAmyilod positive plaque. The tumour cells were positive to GPAP, MAP2 and Synaptophisin, and negative to NF. The tumour proliferative activity was low. There were no foci of necrosis. The autopsy specimen did not confirm the presence of amyloid in other organs (salivary glands, nerve and rectum).
Conclusion: The presence of glial tumour together with cerebral amyloid angiopathy, as a sign of aging, should be expected in the elder. In this case, the αAmyloid positivity in blood vessels might be caused by involvment of the plexus chorioideus, which is a well known source of TTR positive amyloid deposits.

PS-14-036
A rare variant of meningioma: Clear cell meningioma
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Objective: Clear cell meningioma (CCM) is a rare variant of meningioma (WHO grade II). It is usually seen in young patients in cerebellopontine angle and cauda equina. Herein, we report a 23 year-old male with CCM in 5th lumbar vertebra.
Results: Peroperatively, the mass was submitted for frozen section. It was a well-circumscribed mass of 1.4 × 1.1 × 0.8 cm, macroscopically. During frozen section, a lesion composed of mostly spindle cells showing no sign of malignancy in a collageneous background containing rich vascular network was detected, microscopically. It was diagnosed as "suggestive of schwannoma or fibrous meningioma" at frozen section. Suprisingly, extensive solid sheets of polygonal cells with clear cytoplasms accompanying spindle cell component were detected, in parraffin sections. Immunohistochemically, positivity for vimentin, EMA, and PR; negativity for RCC, CD10, GFAP, pancytokeratin, chromogranin, synaptophysin, and CEA were detected in the tumour cells. Ki-67 proliferation index was 1–2 %.
Conclusion: It should be considered that CCM may be misdiagnosed as fibrous meningioma or schwannoma in frozen section due to the collagen-rich stroma and/or freezing artifact. The periphery of the lesion should be evaluated to find out the reminiscent of the grade I conventional meningioma pattern, microscopically. Metastatic carcinomas (particularly renal cell carcinoma) should be ruled out by immunohistochemistry.

PS-14-039
Correlations between morphological and electromyographic data in inflammatory myopathies
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Objective: Inflammatory myopathies (IM) are rare heterogeneous conditions, comprising polymyositis, dermatomyositis, inclusion body myositis and necrotizing myopathy alongside myopathies associated with connective tissue diseases or paraneoplasia. We aim to assess and quantify the morphological parameters of the muscle biopsies in cases with myopathic pattern in conventional myography and establish correlations between specific histopathological and electromyographic (EMG) features.
Method: 42 patients with IM were prospectively enrolled; we performed conventional EMG, as well as quantitative assay (QEMG) of multi-motor unit potential (MUP) and interferential pattern. In 21 patients with myopathic pattern, muscle biopsy was performed and histopathological parameters were quantified: necroinflammatory activity, fiber size variability, endomysial/perimysial fibrosis and structural abnormalities.
Results: We found positive correlations between fibrillations-necroinflammatory activity score (Pearson coefficient 0.582, $p = 0.006$), fibrillations-score of fiber size variability (Pearson coefficient 0.603, $p = 0.004$) and negative correlations between positive sharp waves-type II fiber atrophy (Pearson coefficient 0.512, $p = 0.018$), EMG pattern-type II fiber atrophy (Pearson coefficient 0.521, $p = 0.015$).
Conclusion: This study demonstrates the value of EMG and histopathological examination in the accurate diagnosis of IM and the usefullness of quantifying morphological parameters.

PS-14-041

Intradural extramedullary teratoma of the spinal cord having intramedullary extension

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Objective: The most common intramedullary tumours are ependymomas and astrocytomas. Excluding the sacro-coccygeal form often seen in neonates, teratomas in the spinal canal are rare. It consists of tissues from all three embryonic layers.
Method: A 30-year-old female complained of backache for 2–3 months. She had no neurological deficits. Imaging studies showed, intradural tumour formation extending to intramedullary with different densities in the spinal canal at T12 and L1 levels. Findings indicated that the tumour included heterogeneous tissues. The tumour was subtotally removed.
Results: Grossly, the lesional tissue (1,7 × 1,1 × 1,1 cm) was a dirty white mass which was containing solid and cystic (1 × 1 cm) components. Histologically, various findings were observed. There were cysts lined with columnar and stratified squamous epithelium, sebaceous glands, mucous glands, peripheral nerve bundles, adipose tissue, vessels surrounded by dense hyalinized tissue with calcification. Histological analysis demonstrated a mature teratoma with three ingredients: ectodermal, mesodermal and endodermal elements.
Conclusion: Though sacrococcygeal teratoma in newborn babies has frequently been reported, spinal teratoma in adults is uncommon. While only a very small proportion of CNS teratomas occur in the spinal cord, they need to be considered in differential diagnosis. Total resection is the treatment of choice, it is important to resect as much of the tumour as possible while preserving all neural tissue.

PS-14-042

Solitary Fibrous Tumour / Hemangiopericytoma of the central nervous system versus soft tissue: Differences and similarities in a retrospective cohort study

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Objective: Solitary fibrous tumour (SFT) is thought to represent a morphologic continuum, ranging from fibrous "classic" STF to cellular SFT, the latter corresponding to most "so-called" hemangiopericytomas (HPCs). Although now widely accepted for soft tissue (ST), the consensus is not so clear in the central nervous system (CNS). We aim to compare and understand if it is safe to consider HPC/SFT of the CNS and of ST as the same entity.
Method: Retrospective review of all cases (n = 22) identified as SFT/HPC from a single institution in a 10-year period (2004–2014), assessing patient demographics, tumour location, prognostic indicators (size, margins, cellularity, mitotic index, pleomorphism, necrosis and hemorrhage) and follow-up. The cases were grouped in CNS and extra-CNS location, and data were analyzed for statistical differences between groups.
Results: We had 11 patients in both groups, with equal gender distribution (4 males; 7 females). Of all variables studied, tumour size was significantly higher in ST-SFT (mean = 9,27 cm vs 3,87 cm, p = 0,013) and the 1-year and 5-year event-free is significantly lower in CNS-SFT (64 % vs 100 %, p = 0,034; 14 % vs 75 %, p = 0,019).
Conclusion: To extend the concept of SFT to the CNS, there are relevant statistical differences with ST-SFT that we have to be aware of, mainly site-related.

Tuesday, 8 September 2015, 09.30 – 10.30, Restaurant
PS-15 Poster Session Soft Tissue and Bone Pathology

PS-15-001

Cutaneous superficial malign peripheral nerve sheath tumour

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Objective: Malignant peripheral nerve sheath tumours (MPNST) include a group of tumours that originate from the peripheral nerves or show differentiation along various elements of the nerve sheath, namely, Schwann cells, perineural fibroblasts, or fibroblasts. MPNSTs occur in deep soft tissues of trunk and extremities, but superficial primary MPSNT with a cutaneous or subcutaneous origin have rarely been reported.
Method: A 22-year-old male patient presented with a swelling in the right forearm that had been existing since childhood. Microscopically, multinodular tumour organization was observed which cover the whole dermis and extending subcutaneus adipose tissue.
Results: The tumour consisted of atypical epitheloid cells which some had spindled-shape, had ovaloid-round, hyperchromatic-vesicular nucleus and widely eosinophilic cytoplasm. Regresive changes like necrosis, hyalinization were seen. The mitotic activity was high. Our case showed S-100, Vimentin, GFAP, CD68 positivity with over-expression of Ki-67 (mean 30 %). CK, CK7, CK19, EMA, HMB45, Desmin, CA125, CD31, CD34, Factor VIII did not expressed in 'MPNST of the dermis' and were used exclude other tumours. By this findings, it was diagnosed as MPNST of cutaneous tissue.
Conclusion: MPNST can arise in any unusual site. It may not be exist in or around a major nerve tissue. The diagnosis of MPNST of the cutis is based on combining clinical, histopathological and immunohistochemical results. Complete surgical removal should be the goal of treatment with definitive histological diagnosis.

PS-15-002

Dermal nerve sheat myxoma

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Objective: Dermal nerve sheat myxoma (DNSM) is a rare benign peripheral nerve sheat tumour, arises in patients ranging in age from 8 to 84 years, and are equally frequent in males and females. Histologically it has a characteristic appearance. Treatment of DNSM is a complete excision as recurrence may occur. However, the tumour is considered benign and has no evidence of malignant potential.
Method: A 45-year-old woman, who presented with a small nodule with a diameter of 1,5 cm. asymptomatic, and growing slowly and superficially located in her third finger. The tumour was radically removed.
Results: The lesion was circumscribed, typically forms a multinodular mass, and had a abundant myxoid matrix. The tumour nodules were separated by delicate fibrous septa and composed of small epithelioid, ring-like, stellate and spindled neoplastic schwann cells. The nucleus of most tumour cells were small, rounded, or ovoid, with a moderate amount of chromatin. Mitotic figures were uncommon. The neoplastic schwann cells were immunoreactive for S100 protein, GFAP, EMA, vimentina.
Conclusion: DNSM show true nerve-sheat differentiation by ultrastructural analysis. Incomplete removal is associated with a high rate of local recurrence. The main differential diagnoses arise with: neurothekeoma, superficial angiomyxoma, neurofibroma myxoid, dermatofibrosarcoma protuberans mixoide.

PS-15-003

Peripheral primitive neuroectodermal tumour of the parotid gland

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Objective: Peripheral primitive neuroectodermal tumours (pPNET) are highly malignant small round cell tumours with a poor prognosis. Few pPNET cases of the head and neck have been reported. We present a pPNET arising in the parotid gland.
Method: A 18-year-old female presented in our hospital with a solitary hard mass in the right cheek. Following surgical resection, pathologic examination was performed.
Results: Gross examination revealed a gray-whitish firm mass, measuring 4/3/1 cm, poorly circumscribed with a heterogeneous aspect on cut section. Microscopic examination showed an infiltrating undifferentiated malignant tumour composed of hyperchromatic small cells with atypical nuclei and large areas of necrosis. The cells were PAS-positive. Also, they showed positive immunostaining for: vimentin, MNF116, EMA, S100, CD99, NSE and synaptophysin. Mib 1 was 40 % positive. Immunostaining of the tumoural cells was negative for chromogranin, CD20, CD3, CD30, CK20, CD34, desmin, myogenin and PAX-5.
Conclusion: pPNET of the parotid gland is a rare and challenging diagnosis and immunohistochemistry should exclude other possible and similarly diagnoses such as lymphoma, rhabdomyosarcoma, undifferentiated carcinoma and other small round cell tumours.

PS-15-004
The critical role of CD34 and D2-40 in differantiation of Dermatofibroma and Dermatofibrosarcoma Protuberans
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Objective: Dermatofibroma (DF) is a benign fibrohistiocytic tumour usually seen in women as located in the limbs. Dermatofibrosarcomaprotuberans (DFSP) is a fibrohistiocytic tumour with intermediate malign potential. In this study we aimed to determine the expression of CD34 and D2-40 in DF and DFSP and if D2-40 can be used as a second step marker after CD34 in differentiating these lesions.
Method: This study includes 30 DF and 15 DFSP cases on which manuel immunohistochemistry procedure was performed with D2-40 (DAKO) and CD 34 (DAKO) antibodies. Cytoplasmic staining for CD34 and membranous and cytoplasmic staining for D2-40 were accepted as positive.
Results: No significant relationship was found between the DF and DFSPs according to age distribution. However, there was significant correlation for sex, localization and diameter of the lesion between the two entities. A significant difference was found between the positivity of CD34 and D2-40 in DF and DFSPs.
Conclusion: Additional immunohistochemical markers may be needed in DFs with CD34 positivity or DFSPs with myxoid degeneration and sarcomatous differentiation where the positivity of CD34 decreases. Our results showed that the higher positivity of D2-40 in DFs then in DFSPs, raises the additional helpful role of this marker in differential diagnosis of problematic cases.

PS-15-005
Desmoplastic Small Round Cell Tumour: Case presentation of a rare malignancy
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Objective: We present a case of desmoplastic small round cell tumour (DSRCT) in a 35-year old male patient, who was admitted to our hospital due to the presence of ascites and multiple abdominal masses.
Method: Examination of tissue samples from implantations in various abdominal organs.
Results: Macroscopically there were multiple coalescent tumour nodules and implantations of various size, with firm, gray-white cut surface, elastic consistency and foci of hemorrhage and necrosis. Histologically, the tumour was characterized by sharply outlined nests of small neoplastic cells surrounded by prominent desmoplastic stroma. The tumour cells had undifferentiated appearance, with scant cytoplasm, hyperchromatic nuclei and increased apoptotic and mitotic activity. Focally, some cells exhibited epithelial differentiation. The immunoprofile showed a multi-phenotypic differentiation (immunoreactivity for cytokeratins (AE1/AE3), epithelial membrane antigen, calretinin, WT-1, vimentin, desmin, CD56, CD99 and neuron-specific enolase˙ Negative for smooth muscle actin, chromogranin A, Synaptophysin, CD57 and CD117). The Ki67 index was high. Genetic studies were not performed due to the patient's demise.
Conclusion: DSRCT is a rare and aggressive tumour, composed of small round cells of uncertain histogenesis. The presence of the t(11;22)(p13;q12) translocation is a consistent cytogenetic feature, unique to the tumour. Despite multimodal therapy the prognosis is poor.

PS-15-006
Primary leiomyosarcoma of the small intestine: A study of four cases
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Objective: Most intestinal mesenchymal neoplasms are gastrointestinal stromal tumours (GISTs), primary leiomyosarcoma of the small intestine (PLSI) being extremely uncommon. We describe four cases of this poorly known entity.
Method: A search for our small intestinal smooth muscle tumours (2005–2015) was performed. PLSIs were identified and their clinicopathological features recorded.
Results: Four PLSI instances were found (see table). All cases were positive for desmin and negative for CD34, S100-protein and C-KIT.
Conclusion: Telling PLSI and GIST apart by accurate pathology diagnosis is crucial owing to their very different prognosis and therapy. Nevertheless, as shown by our cases, quantification of PLSI histologic criteria does not allow prediction of biological behavior in individual PLSI cases.

Table:

Case	Age	Gender	Wall involvement	Size (cm)	Mitoses	Necrosis	Histologic pattern	N1	M1	Local recurrence	Death
1	69	F	Transmural	15	26/50HPF	NO	Fusiform	-	YES	YES	YES
2	62	M	Transmural	8	86/50HPF	NO	Fusiform	0/10	NO	NO	NO
3	46	M	Transmural	4	198/50HPF	YES <10%	Fusiform	0/26	NO	NO	YES
4	59	M	Transmural	9	45/50HPF	YES <10%	Fusiform	0/4	NO	NO	NO

PS-15-007
Elastofibroma dorsi: A case report of an uncommon benign pseudotumour
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Objective: Elastofibroma dorsi is a relatively rare soft-tissue tumour, more common in women after 50. The typical presentation of ED involves a subscapular mass associated with a long history of swelling, discomfort, snapping of the scapula and can sometimes be bilateral. It was described for the first time by Jarvi and Saxen in 1961, its incidence is variable and infrequent although its true rate of incidence may be greater than that described in the literature.
Method: A 54-year-old female patient, with no past medical history, presented with unilateral subscapular slow growing tumour for 1 year. The predominant symptoms were swelling, discomfort and pain.
Results: Macroscopic findings showed a poorly defined fibroelastotic mass with slightly rubbery, elastic consistence measuring 12

cm × 9 × 1 cm. The cut surface showed strands of gray-white and yellow tissue. Histologically, the tumour was poorly circumscribed, and was composed of hypocellular fibrous collagenous strands admixed with large numbers of coarse, densely eosinophilic elastic fibers and entrapped mature fat cells. The elastic structures sometimes formed disks or globules.
Conclusion: Elastofibroma dorsi is a rare pseudotumoral lesion of the soft tissues that most frequently affects older females. In general, once the diagnosis is suspected radiological investigation is performed. CT, MRI or sonographic images can demonstrate the characteristic streaky collagen or elastic fibers of elastofibroma dorsi in the fatty background. Nevertheless, pathologic confirmation is necessary to formally rule out a malignant tumour diagnosis.

PS-15-008
Heterotopic mesenteric ossification: A case report
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Objective: Heterotopic ossification (HO) refers to the formation of bone in non-ossifying tissue. Heterotopic mesenteric ossification is a rare form of HO that is characterized by the formation of an ossifying pseudotumor at the base of the mesentery, usually following abdominal surgery.
Method: We report a case of heterotopic bone formation in the mesentery. The patient was a 52-year-man, who had in hits history abdominal trauma. On laparotomy, two sharps complex mesenteric peritoneal calcifications were encountered which were excised. The largest mass measured 15 mm.
Results: Microscopically, trabecular bone tissue had increased irregularly in the fat tissue of the nodules with fibrosis, which were partially lined with osteoblasts.
Conclusion: Heterotopic mesenteric ossification is a benign ossifying pseudotumor with no malignant potential. The major morbidity associated with the pathology is bowel obstruction, which usually requires surgical intervention.

PS-15-009
Intramuscular high grade myxofibrosarcoma of left buttock of 54-year-old-male patient - approach to systematic, histopathological reporting
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Objective: Here we present a systematic approach to histopathological reporting of high grade myxofibrosarcoma of 54-year-old-male patient.
Method: The tumour was biopsied with FNA and CNB and then the whole myxoid tumour was excised with left musculus gluteus maximus. The lesion was stained with H&E, PAS, alcian blue, Masson trichrome, Ki67, SMA, S100, CD34 and vimentin.
Results: FNA material grounded the diagnosis of non epithelial neoplasia, while CNB was enough to produce diagnosis of myxoid sarcoma. The tumour lied under superficial fascia with no extension beyond deep fascia or any invasion of skin, vessels or nerves, either. The tumour was intramuscular, mainly myxoid with hypercellular areas of highly atypical cells and some bizarre giant multinucleated cells which belonged to category of high grade sarcoma. According to FNCLCC the case was assessed for 5 points. MIB Ki67 index reached more than 80 % malignant cells. Alcian blue was strongly positive in myxoid background. Masson trichrome emphasized fibrillary structure of tumour. Negativity for S100, SMA with strong co-expression of CD34 and vimentin supported the diagnosis of myxofibrosarcoma.
Conclusion: The lesion was diagnosed as high grade myxofibrosarcoma (formerly myxoid malignant fibrous histiocytoma) G2 pT2b (7th edition pTNM), (code ICD-O 8811/3 in WHO classification 2013).

PS-15-010
From epistaxis to bone pain: Report of two cases illustrating the clinicopathological spectrum of a rare neoplasm - Phosphaturic Mesenchymal Tumour
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Objective: Phosphaturic mesenchymal tumour, mixed connective tissue type (PMTMCT) is a rare, recently defined neoplastic entity. It is characterized by a distinct set of histological features, which often occur in conjunction with the clinical syndrome of oncogenic osteomalacia (OO).
Results: We herein present two contrasting cases of PMT, one occurring in the sinonasal region, and the other occurring in bone (proximal femur). In the former case, local effects of the tumour including epistaxis and anosmia dominated the clinical presentation, whilst the latter case presented with refractory bone pain, muscle weakness and occult osteomalacia, the cause of which was only identified after a protracted series of investigations over 2 years. Both tumours showed characteristic histological features of PMTMCT including a monomorphic proliferation of round to ovoid cells, osteoclast-like multinucleated giant cells and areas of "grungy" basophilic calcifications. There was no evidence of malignant behavior in either of the cases, despite their debilitating clinical manifestations.
Conclusion: Thus, these two cases illustrate the importance of recognizing the varied clinical manifestations of PMTMCT, particularly in the context of occult causes of oncogenic osteomalacia.

PS-15-011
PAX3-FOXO1 and PAX3-NCOA1 fusion genes in biphenotypic sinonasal sarcoma
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Objective: Recent work has shown PAX3-MAML3 to be a recurrent fusion gene in biphenotypic sinonasal sarcoma (SNS) (Nat Genet 2014;46:666-668). However, a subset of SNS harbors PAX3 rearrangement without involving MAML3.
Method: We identified 17 cases of SNS with PAX3 rearrangement without MAML3 involvement and screened for alternate fusion partners using RNAseq, RT-PCR and FISH on paraffin-embedded tissues.
Results: Three cases were found to harbor PAX3 exon 7-FOXO1 exon 2 fusion. Two of these cases occurred in female patients (31, 47 years) in the ethmoid sinus and nasal cavity. The third case occurred in a 35-year-old male as two independent masses involving bilateral nasal sinuses - both lesions harbored the PAX3-FOXO1 fusion. The fourth case involved the left oropharynx/skull base of a 47-year-old male and exhibited the PAX3 exon 7-NCOA1 exon 13 fusion. All detected PAX3-FOXO1 are structurally identical to that reported in alveolar rhabdomyosarcoma (ARMS).
Conclusion: We report four cases of SNS with PAX3-FOXO1 and PAX3-NCOA1 fusions. As these fusions transcripts have been previously described in ARMS, our findings support the hypothesis that additional mutations and the environment of the cell of origin further modulate the oncogenic effects of PAX3 fusion genes in determining the distinct biologic behaviors of SNS and ARMS.

PS-15-012
Cutaneous solitary fibrous tumour of the hand
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Objective: Most solitary fibrous tumours are arising in the pleura, but the cases of extrapleural sites are increasing. Extrapleural solitary fibrous

tumour is exclusively located in deep soft tissue, such as thigh, pelvic fossa, retroperitoneum and serosal surfaces. Skin and subcutaneous involvement is extremely rare.
Method: We present a cutaneous solitary fibrous tumour of 43-year-old woman, which was arising in the thenar area of hand.
Results: The tumour was well circumscribed and occupied a whole dermis. It measured 1.2 × 1.2 cm in size. Cut surface was homogenously yellow-white, solid and firm. Histologically it was composed of uniform spindle cells with perivascular proliferation and interlacing fascicle formation. Periphery showed hypocelluar area with hyalinized collagen. Mitotic activity was minimal, less than 1/20 HPF. Vascular proliferation of small vessels was prominent, but hemangiopericytoma-like branching pattern was limited. Immunohistochemically tumour cells strongly expressed CD34 and CD99, but not EMA, Bcl-2 and S-100 protein.
Conclusion: We present this case because of some diagnostic difficulties, its unusual location and unique perivascular tumour cell proliferation.

PS-15-013
Retroperitoneal Primitive Neuroectodermal Tumour (PNET) mimicking a renal pelvis tumour
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Objective: PNET is a rare malignant soft tissue tumour, with variable degrees of neuronal differentiation. The incidence in the abdomen and pelvis, including the retroperitoneum, is about 14 % of peripheral PNETs.
Method: A 47-year-old male patient presented to our hospital with non-specific abdominal pain. CT scan showed an encapsulated mass adjacent to the renal pelvis of the left kidney. The patient underwent left nephrectomy. Macroscopic examination revealed a tumour adjacent to the renal pelvis and a renal calyx of the lower kidney pole.
Results: Microscopically the tumour was composed of uniform, small, round neoplastic cells with scant eosinophilic cytoplasm containing (PAS+, PAS/D -) granules. A wide panel of immunohistochemical markers was performed, from which only S-100 protein, Vimentin, Bcl-2 and Cyclin-D1 were positive, while Ki-67 was estimated at 25 %. It should be noted that CD99 was negative. Based on these results, a differential diagnosis between MPNST, PNET and unclassified round cell sarcoma was discussed and molecular genetic testing was advised. The molecular testing showed the translocation t(11;22).
Conclusion: In such cases where morphology and immunohistochemistry is inconclusive and differential diagnosis has to be made between many different neoplasms, molecular methods should be carried out, as they could be the deciding diagnostic factor.

PS-15-014
Clinicopathological features and risk stratification of Gastrointestinal Stromal Tumours (GIST) in Sudanese patients
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Objective: To determine the clinicopathological features and risk grades of GISTs in Sudanese patients.
Method: A cross-sectional study conducted on all patients referred to GIST Clinic at Radioisotope Center, Khartoum (January 2014 to February 2015). Only cases with signed informed consent and accessible tissue blocks were included. Non-GIST cases following histological reassessment were excluded. Risk was assigned using integrated risk assessment criteria (based on site, size, mitoses, tumour rupture and clinical metastasis.
Results: 25/60 cases fulfilled inclusion criteria; 44 % were males (mean age, 57.6 ± 13.6; range, 15–75). Tumour site was stomach in 64 % and small intestine in 24 % of cases. Tumour rupture was present in 28 % (not reported in 44 %). Metastasis was present initially in 36 % and unknown in 20 %. Tumour size was >2–≤ 5 cm (4 %), >5-≤ 10 cm (40 %), >10 (36 %), and not reported in 20 %. Histologic type was spindle in 76 % and epithelioid in 20 %. Mitotic index was <5/5 mm2 in 92 %. Using risk criteria pointed above; 32 % are clinically malignant at presentation, 24 % high risk, 16 % intermediate and 20 % low risk (8 % were not classifiable).
Conclusion: Sudanese patients with GIST do present late and most (≥56 %) correspond to the malignant/high risk category.

PS-15-015
Sclerostin expression in primary bone tumours
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Objective: Sclerostin is a non-collagenous matrix protein found in woven and lamellar bone which is highly expressed by osteocytes. Other bone matrix proteins have proved useful markers of osteogenic differentiation in bone tumours.
Method: We assessed immunohistochemically sclerostin expression in primary benign and malignant bone tumours. Sclerostin mRNA expression was also determined in specimens of osteosarcoma and osteosarcoma cell lines by real time PCR.
Results: In lamellar and woven bone, sclerostin was expressed in the matrix around osteocyte lacunae and canaliculi. Osteoblasts and other cell types in bone were negative. Matrix staining of osteoid and bone was seen in bone-forming tumours including osteoma, osteoid osteoma, osteoblastoma and osteosarcoma. Sclerostin staining was also seen in fibrous dysplasia, chondroblastoma and in reactive bone formed in fracture callus, myositis ossificans and in the wall of solitary and aneurysmal bone cysts. Sclerostin was not expressed in the tumour component of other primary bone tumours including chondrosarcoma, fibrosarcoma, giant cell tumour of bone, metastatic carcinoma. Sclerostin mRNA was expressed in osteosarcoma cell lines and tumour samples.
Conclusion: Our findings indicate that sclerostin is an osteocyte marker expressed in mature and reactive bone and that it can be identified in osteosarcoma and other bone-forming tumours/tumour-like lesions.

PS-15-016
When we have to risk: An osseous Kaposi sarcoma Human Herpes Virus type 8 "negative"
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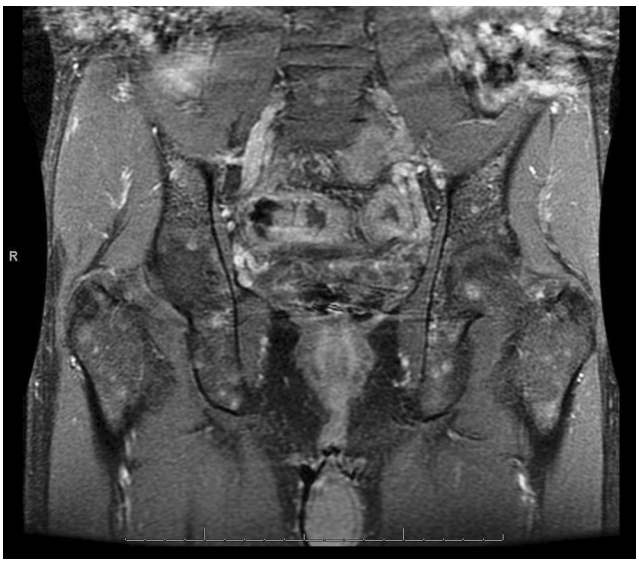
Objective: Kaposi sarcoma, an AIDS related tumour, is a malignancy associated with Human Herpes Virus type 8 (HHV-8). Kaposi sarcoma is generally multifocal and most commonly involves the skin and mucous membranes, although it can affect virtually any organ. Bone and bone marrow are rarely involved. We will report a case and highlight some clinical-pathologic considerations.
Method: We present the case of a 41 years old male with Von Recklinghausen disease, AIDS and visceral Kaposi sarcoma (HHV-8+). A CT scan revealed multiple osteolytic lesions. Bone and bone marrow biopsies were performed.
Results: Microscopic examination revealed a vascular proliferation of spindle cells (CD31+, CD34+). Immunohistochemical study was negative for HHV-8. We alerted the clinicians that morphology was suggestive of osseous Kaposi sarcoma despite HHV-8 was negative probably due to immunohistochemistry error. The clinical decision was to start chemotherapy. After six cycles some lesions regressed and others are stable.
Conclusion: Osseous Kaposi sarcoma is most often discovered accidently in the context of radiological investigations done for the screening of Kaposi sarcoma-visceral involvement. Little is known on clinical outcome and response to antiretroviral therapy and/or chemotherapy of these

lytic lesions. With this report we reinforce that morphology and clinical history are gold standarts.

MRI showing pelvic osteolytic lesions:



PS-15-017

Sclerosing epithelioid fibrosarcoma - a variant of low-grade fibromyxoid sarcoma or a distinct entity?: A case report

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Objective: Sclerosing epithelioid fibrosarcoma (SEF) is a rare variant of fibrosarcoma. These tumours have usually a bad prognosis, and therefore should be differentiated from low-grade fibromyxoid sarcoma (LGFMS).
Method: We analyzed an own case of SEF and reviewed the literature.
Results: A SEF of the forefoot of 71-year-old-woman was resected with positive resection margins. Despite refusing further treatment, the patient has shown no signs of tumour recurrence 20 months after surgery. The tumour showed the typical histology. Strong expression of Vimentin was detectable. Antibodies against Cytokeratins, EMA, INI-1 and S-100 were variable positive. There was no expression of MUC-4, CD34, SMA, Desmin, and HMB45. In genetic examinations the tumour showed no rearrangement of SYT-, FUS- or EWSR1-gene.
Conclusion: Up to March 2015 some more than 100 cases of SEF were published, but only a fraction of these were analyzed genetically. A great part of the published tumours shows pattern of LGFMS. But there is a small group of tumours like our tumour with the typical histologic patterns but without the genomic aberrations, gene fusions and immunohistochemical findings characteristic for LGFMS. We think only these tumours should be classified under SEF and should be further investigated.

PS-15-018

Phosphaturic mesenchymal tumour in the Halux: Case report and literature review

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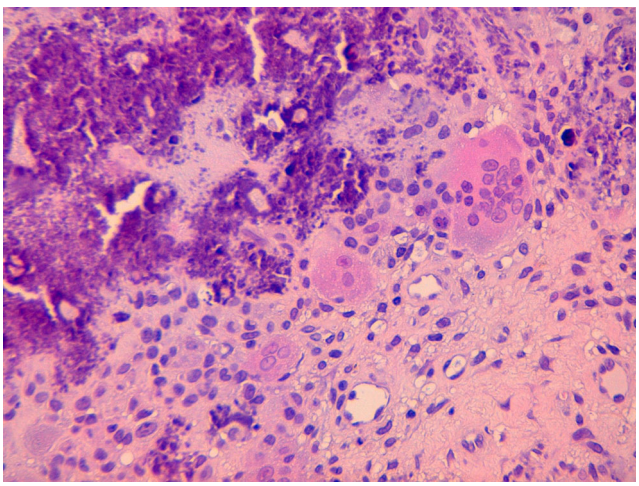
Objective: To present a case of phosphaturic mesenchymal tumour (PMT) of the foot and review the features of this entity in this location.
Method: A 38 year old man presented with a slow growing painful lesion in the halux soft tissues for the past 1.5 years. He had no record of trauma, or relevant past medical history.
Results: US, X-ray and MRI of the foot revealed a soft tissue nodule in the halux, measuring 1.8 × 1.7 × 1.2 cm, which was excised. Histopathologic analysis showed a spindle cell proliferation with a low cellular stroma interposed by myxochondroid areas. There were also variable degrees of hyalinization and multiple flocculent crystaloid deposits. Rare multinucleated giant cells were also observed. A diagnosis of PMT was made. Currently, the patient is asymptomatic. A brief review of the literature showed other 25 cases of PMT reported in the foot, all in adults, with no gender predilection, and with pathological aspects similar to PMTs found elsewhere in the body.
Conclusion: Clinicians and pathologists should be aware of this rare benign tumour, since there is a strong association with oncogenic osteomalacia that may probably be avoided by an early surgical excision.

Giant cells and flocculent microcalcifications in PMT:



PS-15-019

Chondromyxoid fibroma of the proximal phalanx of the toe: A case report

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Objective: Chondromyxoid fibroma is a rare benign tumour arising in the metaphysis of the long bones. The small bones of the foot are rarely involved. Histologically some cases of chondromyxoid fibroma overlap with those of chondroblastoma. We present a case of chondromyxoid fibroma involving the proximal phalanx of the toe because of extremely rare location and histologic resemblance to chondroblastoma.
Method: A 13-year-old female presented with a history of swelling in the right third toe. Radiograph revealed a 2 × 1 cm sized expansile and lytic lesion involving the proximal phalanx, which occupied the metadiaphysis extending to the distal epiphysis. There was an endosteal erosion, but no cortical destruction. Ring-shaped mineralization suggested enchondroma radiologically. Curettage was done.
Results: Microscopic examination revealed cellular areas of pseudolobules. Tumour cells were ovoid and spindle shaped with fine chromatin pattern and inconspicuous nucleoli. Some cells showed nuclear groove, resembling chondroblasts. Tumour cells were surrounded by pinkish chondroid matrix. Large numbers of osteoclast-like giant cells were noted at the edges of the lobules. Myxoid change was scant.
Conclusion: These radiologic and pathologic findings favored chondromyxoid fibroma, but poor lobulation and scant myxoid change reminded us to consider a possibility of chondroblastoma.

PS-15-020

A rare tumour of the breast. Dermatofibrosarcoma Protuberans: A case report

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Objective: Dermatofibrosarcoma protuberans is a slow-growing fibrous tumour of the subcutaneous tissue, frequently seen in proximal extremities and trunk. It rarely metastasizes but has local aggressive behavior. Its presentation in breast is uncommon.
Method: Here, a 44-year-old female with a breast mass was presented. Physical examination showed a 8 × 5,5 centimeter mass with multilobulated bulging from the skin. Radiological examination revealed a 7,5 × 6,5 centimeter mass with lobulated margins in the lower inner quadrant of the right breast. Due to the large size of the lesion simple mastectomy was performed.
Results: In macroscopic examination, skin over the lesion appeared ulcerated and necrotic. Grossly, cut surface showed pale white to tan, well defined, solid mass. Microscopic examination revealed monotonous proliferation of spindle cells with an arrangement of storiform pattern in the collagenous stroma. Mitosis was 2-3/ 10 HPF. Differential diagnosis composed of dermatofibroma, malignant fibrous histioctyoma, leiomyoma, leiomyosarcoma, myofibroblastoma and spindle cell sarcoma. Immunohistochemically tumour cells were positive for CD34 and negative for S100, EMA and SMA. Histopathologically and immunohistochemically the mass was diagnosed as dermatofibrosarcoma protuberans.
Conclusion: Treatment is the complete surgical excision of the lesion with wide margins. Radiotherapy and chemotherapy are only needed if margins are positive or in metastatic disease.

PS-15-021

A rare case of malignant neoplasm with perivascular epithelioid cell differentiation of the uterus

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Objective: Neoplasms with perivascular epithelioid cell differentiation (PEComas) are rare tumours composed of cells supposed to originate from blood vessel walls, having smooth muscle and melanocytic features. There are significant more cases in women, the uterus being frequently involved.
Method: We present the case of a 60 years old woman having a large nodular uterine tumour of 19/15/10 cm.
Results: The tumour had a fleshy cut surface with necrotic, hemorrhagic and cystic areas. Microscopic examination revealed sheets and trabeculae composed of large, polygonal cells having clear/foamy cytoplasm, nuclear atypia and mitotic activity (8 mitoses/50 high power fields). Some cells were radially arranged around hyalinised blood vessels. Sheets and trabeculae of smaller cells were noted towards the periphery. Tumour necrosis was present. Tumour cells were HMB45 positive, Melan A, SMA and desmin focally positive and S100 negative. Based on gross and microscopic features the final diagnosis of malignant PEComa was rendered.
Conclusion: Malignant PEComa represents a rare tumour with an aggressive clinical course. The criteria for malignancy are not widely accepted. Establishing this diagnosis implies exclusion of other more frequent malignancies such as carcinoma, mesothelioma, metastatic melanoma or leyomiosarcoma.

PS-15-022

Giant cell tumours of bone: A case series

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Objective: Giant cell tumour (GCT) of bone is a rare benign but aggressive neoplasm that accounts approximately 5 % of all primary bone tumours in adults. It most often occurs at the end of long bones of young adults, with a slight female predominance. We are presenting our experience with the diagnosis and management of 11 cases of GCT of bone in our Center.
Method: A retrospective study was conducted of all GCTs managed at Fundacion Jimenez Diaz, in Madrid, from 1997 to 2015. The histopathologic, clinical features, surgical management and follow-up were recorded.
Results: On histopathologic examination all cases displayed typical features of GCT. The most common location was the distal femur. The mean age of presentation was 42 years old. There was an even distribution among male and female. Pain was the most common symptom. Most of the cases had extension through the bone into surrounding soft tissue. Most of the cases were treated with curettage and complete en-bloc excision. Only 3 cases had local recurrences during the follow-up period.
Conclusion: Our patients developed GCTs at a slightly older age and there was no difference in gender distribution. There were few recurrences, probably related to en-bloc excision of the tumour.

PS-15-023

Patient characteristics, locations and histopathological features of pilomatrixomas in Erzurum / Turkey

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Objective: The aim of this study is to examine the patient characteristics, locations, presentations and histopathological features of pilomatrixomas in a group of patients.
Method: We analyzed 41 patients that histopathologically diagnosed as pilomatrixoma in Erzurum Region Research and Training Hospital between 2009 ad 2014, retrospectively.
Results: Patient's mean age was 30 years (age range: 3–78 years), with a female to male ratio of 26:15. There were 12 patients in the pediatric age group (<16 years). The average diameter of the lesion at presentation was 18.5 mm (range: 2–55 mm). A total of 36 out of 41 (87.8 %) patients presented with solitary lesion, while 5 patient (12.2 %) had two lesions. Most common location in our patient group was head and neck region and second most common location was limbs. The most common clinical presentation was a painless solitary skin lesion which was noticed incidentally. All cases more or less shared the same microscopic features of pilomatrixoma such as basophilic cells, eosinophilic shadow cells, calcification and foreign body type giant cells.
Conclusion: Pilomatrixoma is not an uncommon benign lesion. It is more common in female gender, adult age group and at the head and neck region.

PS-15-025

Idiopathic retroperitoneal fibrosis of the pelvis: A case report

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Objective: Retroperitoneal fibrosis (RF) is a rare disease, typically occuring in middle-aged men, characterized by a fibrotic reaction that replaces normal tissue and affects retroperitoneal organs, especially the urinary tract. The fibroblastic proliferation, usually accompanied by chronic inflammation, starts at the aortic bifurcation. Approximntl two-thirds of RF cases are idiopathic.
Method: A 61-year-old female presented with flank pain, dysuria and anemia. Echo and CT scan showed lithiasis of the right kidney and a retroperitoneal tumour mass, encasing aortic bifurcation and left ureter. A FNB, performed elsewhere, demonstrated a benign mesenchymal neoplasm, characterized as neurilemoma.

Results: The surgical specimen encompassed a rather circumbscribed, elastic tumour, measuring 4 cm. Microscopically, a fibroblastic proliferation of elongated, slender spindle-shaped cells of uniform appearance and of low mitotic activity, arranged in sweeping bundles and surrounded by abundant hyalinized collagen, was revealed. The cells were immunoreactive to KP1, MAC387, PGM1 and S100 protein. Lymphoplasmacytoid aggregates were also demonstrated. The diagnosis of IRF was confirmed.
Conclusion: IRF is a rare reactive process that may be confused with mesenchymal neoplasms especially in small biopsies. The elevated IgG4-plasma cells, that have been reported in many cases, may indicate an autoimmune origin, a finding with essential therapeutical implications.

PS-15-026
Intramuscular lipomatous tumour in a 14-year old patient with lobulated adipocytes using fluorescence in situ hybridization analysis
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Objective: To present a case of lipomatous tumour with a morphological appearance and histological overlap with other lipogenic tumours like lipoblastoma and even atypical lipomatous tumour.
Method: A 14 years old patient underwent excision of the 14 mm sized soft tissue mass from the medial frontal area. Lesion appeared a few months before excision and after initial growth period it had a static growth.
Results: Microscopically, the lesion was intramuscular, poorly defined, consisted of multivacuolated adipocytes in different sizes and shapes and in places spindle cells. There was no marked hyperchromasia and no mitotic figures. Our differential diagnoses were intramuscular lipoma, lipoblastoma and in the end atypical lipomatous tumour. The sample underwent additional FISH analyses which did not revealed amplification of MDM2 gene, a gene specifically rearranged in atypical lipomatous tumour, which is necessary to prevent misdiagnosis.
Conclusion: These findings indicate that this tumour was no atypical lipomatous tumour, which is of clinical relevance. We excluded lipoblastoma because lipoblastoma is a rare benign tumour, which occurs primarily in infancy and early childhood and usually arises from the limbs and the trunk, but head and neck involvement is rare. Making a correct diagnosis would be only possible on cytogenetic basis, through the identification of the characteristic PLAG1-HAS2 fusion gene by FISH analysis.

PS-15-027
Alveolar soft part sarcoma of the right lower extremity: A case report
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Objective: Alveolar soft part sarcoma (ASPS) represents a very rare entity of soft tissue tumour with special features such as young peak age and frequent metastases to the brain.
Method: Report of a 40 year old female patient with a painless, slow growing palpable mass of the right knee. A core needle biopsy, followed by radical resection and 1 year later, amputation of the right lower extremity due to bone metastasis were performed.
Results: Histologically, the tumour (maximal diameter 9 cm.) had an organoid pattern of growth, consisting of uniform nests separated by delicate partitions of connective tissue, in a well vascularized background. The tumour cells were polygonal, with distinct cytoplasmic borders, eosinophilic or finely granular cytoplasm and big, rounded nuclei with prominent nucleoli. PAS-diastase histochemical stain accentuated the presence of intracytoplasmic rhomboid crystalline inclusions. Less than 5 % of tumour cells showed nuclear positivity for Ki-67/MIB-1 and they also stained negative for Smooth Muscle Actin, Desmin, Epithelial Membrane Antigen, Cytokeratin 8/18, CD34, S-100 protein, Vimentin, Chromogranin, Synaptophysin and Thyroid Transcription Factor-1.
Conclusion: Differential diagnosis of ASPS is fairly broad, including metastatic renal cell carcinoma, adrenal cortical carcinoma, hepatocellular carcinoma, paraganglioma and alveolar rhabdomyosarcoma.

PS-15-028
Case report: Calcifying aponeurotic fibroma
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Objective: Histopathological examination of a surgically resected, subcutaneous, painless mass located on the plantar side of the foot of a 14 year old female patient.
Method: Standard histochemical and immunohistochemical staining methods.
Results: Microscopic examination showed infiltrative fibroblast growth surrounded with dense collagen stroma and multiple foci of chondroid differentiation with calcification. The lesion showed diffuse positivity for vimentin and was negative for S-100.
Conclusion: Calcyfying aponeurotic fibroma is a rare, benign, soft tissue tumour with predilection for forming in the hands and feet of adolescent children. Peak incidence is between the age of 8 to 14, with a 70 % male predominance. Two primary sites of growth are the hands and the feet, most commonly, the palm and the fingers of the hand. Plantar side of the foot is a less common site. Infiltrative nature of growth accounts for a high rate of local recurrence. Malignant alteration is uncommon, and only a few cases of malignant transformation have been reported.

PS-15-029
Primary liposarcoma of the mediastinum: A report of a case and literature review
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Objective: Liposarcoma as a group, are the most common soft tissue sarcoma of adults and usually arise in the deep soft tissues of the extremities or the retroperitoneum. Primary mediastinal liposarcomas are rare, and are thought to represent <1 % of all mediastinal tumours. Because of its low incidence it is unclear whether this sarcoma represents a high-grade variant of myxoid liposarcoma, a distinct variant of myxoid liposarcoma or an unique form of liposarcoma.
Method: Here we describe a 28-year-old man presenting with acute dyspnea and pleural pain. Radiological imaging revealed a large and circumscribed left mediastinal mass. Surgical excision was performed with the previous diagnosis of celomic cyst.
Results: Histologically, consists of pleomorphic tumour cells with severe cytological atypia and increased mitotic activity in a myxoid matrix with a delicate plexiform capillary network, and scattered lipoblasts. FISH techniques using LSI FUS (16p11) Break apart, LSI CEP 12/MDM2 and LSI EWSR1 (22q12) y DDIT3 (12q13) Break Apart probes were performed.
Conclusion: Pleomorphic myxoid liposarcoma usually occurs in young patient and is a very rare and still poorly understood entity. A consensus is yet to be made on the precise classification and terminology of this subtype of aggressive liposarcoma, especially in children and young adults.

PS-15-030
Solitary fibrous tumour: A pathological and clinical challenge
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Objective: Solitary fibrous tumours (SFT) are rare spindle cell neoplasms, most commonly arising from the pleura. The aim of the present paper is to present a difficult case to diagnose and to manage case as SFT.
Method: The patient, a 48 years-old woman, was admitted to the hospital for dyspnea, cough and fatigue. The imagistic investigation revealed metastatic lung and liver nodules and a retroperitoneal mass of 8.7/7 cm. Her medical history mentioned a retroperitoneal tumour back in 1998.
Results: One of the metastatic nodules from the lung was biopsied and the diagnosis established in various laboratory from Romania and abroad were: benign heterotopic lesion, spindle cell carcinoid, neuroendocrine intermediate grade tumour, sarcoma, hemangiopericytoma, SFT. The tumour cells were positive for NSE and the serum level of NSE was elevated (145 ng/ml). On the basis of the IHC profile the diagnosis of SFT was established. Following chemotherapy the serum level of NSE decreased to 6.63 ng/ml but brain metastases appeared. The patient refused another chemotherapeutic scheme and died 3 years later.
Conclusion: SFT is a rare and challenging tumour in the term of diagnosis, treatment and prognosis. It can behave aggressively even in the absence of histological signs of malignancy as illustrated by the present case.

PS-15-031
Hibernomas: Three new cases
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Objective: Hibernoma is a benign tumour arises from brown fat tissue.
Method: We present 3 cases of hibernomas which were localzed at back.
Results: Two was female and one was male. Median age was 27 (31, 30 and 22 years old). Lobulated lesion was composed an admixture of mature adipocytes and cells characterized by a small, central nuclei and a finely vacuolated cytoplasm. Lobules of adipocytes, capillaries, nerves and connective tissue. Adipocytes are smaller (25–40 microns) than usual in white fat, are polygonal with acidophilic multivacuolated and granular cytoplasm and central spherical nucleus with fine indentations. Each of these tumours overexpressed CD 68 and p53 protein by immunohistochemistry. CD 34 was negative. Hibernomas are rare, asymptomatic, benign tumours that arise mostly in adults from the remnants of fetal brown adipose tissue, and usually affect muscle and subcutaneous tissue. A review of the literature highlights recent advances that may help confirm the diagnosis and explain the biology of these rare tumours.
Conclusion: We suggest that hybernomas should be included among the differential diagnosis in every growing mass, especially if the detection of the tumour is a fortuitous coincidence in an asymptomatic patient.

PS-15-033
Infantile myofibromatosis in a newborn: A wide morphologic spectrum easily overlapped
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Objective: Infantile myofibromatosis (IM) is an entity with a wide clinical and morphologic spectrum. Recently some lesions with mixed features of congenital infantile fibrosarcoma (CIFS) and IM called composite infantile myofibromatosis (COIM) have been described.
Method: A 6-day-old girl with a 6 cm forearm mass in the deep soft tissue and bone nodules, with no visceral involvement.
Results: Microscopic findings showed a mesenchymal proliferation where two distinct morphologic features were observed. The mayor part revealed plump, spindle-shaped cells resembling myofibroblasts arranged in an irregular spiral pattern. Around these leiomyoma-like areas, there were, focally, less well differentiated rounded cells in a vascular hemangiopericytoma- like pattern, with no evidence of intravascular projections. The mitotic rate ranged from 5 to 15 per 10 high-power fields. Inmunohistochemically, the cells were inmunoreactive for vimentin, muscle-specific actin (HHF35) and alfa actin. CD34 and calponin was weakly positive and S100 negative. The tumour was diagnosed as IM.
Conclusion: IM may resemble CIFS and infantile hemangiopericytoma, so it must be considered in the differential diagnosis of tumours in early infancy, despite its low frequency. Molecular analysis for the characteristic translocation between chromosomes 12 and 15 in CIFS will contribute to distinguish among these entities.

PS-15-034
Chondrosarcoma developing on synovial chondromatosis: A case report
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Objective: The progression of synovial chondromatosis to chondrosarcoma is very rare. We describe a case who presented with synovial chondromatosis and progression to synovial chondrosarcoma.
Method: A 47-year-old man presented with a large, painful mass in left knee. Magnetic resonance imaging (MRI) scans showed synovial thickening with effusion and an destructively growing lesion involving the distal femur and tibia. The clinical and radiological impression was that of malignant transformation of a recurrent synovial chondromatosis. Bone biopsy specimens suggested a grade 1, focal grade II chondrosarcoma. The patient was treated with a limb-saving, wide resection of the knee region.
Results: The specimen showed a 12 cm, lobulated cartilaginous tumour located in the joint space, infiltrating the articular surface of distal femur, proximal tibia and surrounding soft tissue. Histological sections confirmed the diagnosis of a grade 1 chondrosarcoma. The resection margins were free.
Conclusion: Chondrosarcoma of the synovium is extremely rare. It may arise de novo of the synovium or preexisting synovial chondromatosis may undergo malignant transformation. Distinction between chondromatosis and its progression to low grade chondrosarcoma is difficult at histological level, and must involve clinical and radiographical data. We interpret this case synovial chondromatosis with transformation to chondrosarcoma.

PS-15-035
Clear cell sarcoma of tendon sheath: The two cases
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Objective: Clear cell sarcoma (CCS) of tendons and aponeuroses, is a rare melanin producing soft tissue sarcoma, that usually presents in the distal lower extremities of young adults, frequently attached to tendons or aponeuroses. The aim of this report is to present the histopathological aspects of two cases of clear cell sarcoma of tendon sheath.
Method: Case 1: A 20-year-old man presented with a mass on left thigh region. MRI results showed 10 cm contrast enhancing mass. Case 2: A 45-year-old man presented with a large, painful mass on the right knee of several weeks duration. MRI showed an expanding, 6 cm mass in lateral side of the right knee.
Results: In both cases, microscopically the tumours were composed of nests and fascicles of epithelioid cells, surrounded by a fibrocollagenous tissue continiuous with the adjacent tendons. The tumoural cells have indistinct cell borders, round to ovoid vesicular nuclei with prominent basophilic nucleoli and clear or pale cytoplasm. By immunohistochemistry, S100, MelanA, HMB45 was positive.

Conclusion: Multiple local recurrences and late metastases are usually seen during the clinical course of CCS. Poor prognostic indicators include tumour size, presence of metastasis and necrosis. The treatment is wide excision of the tumour. The distinction of CCS from other melanin producing lesions can be problematic.

PS-15-036
Fibromyxoid Low-grade Sarcoma (FMLGS) versus Desmoid-type Fibromatosis (DTF): Comparative clinicopathological and immunohistochemical features in two similar case

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Objective: DTF and LGFMS may have similar clinicopathological features but their outcome is completely different. The aim of our study is to differentiate these lesions based on immunohistochemical profile.
Method: We present two cases of a 33 years-old and, respectively, 28 years-old women, each of them with an abdominal wall mass. Both lesions were surgically removed with marginal type excision. They were poorly circumscribed, firm, white on cut surface, measuring 15 cm and, respectively, 8 cm. On routine staining, both lesions were diagnosed as fibromatosis. The immuhistochemical panel that we used in both cases was: EMA, SMA, Desmin, Beta-catenin, Ki-67.
Results: Histologically, both lesions showed a proliferation of bland spindle cells with no mitotic figures, embedded in a collagenous background, with arcades of small blood vessels in the first case, and ectatic blood vessels, in the second one. Based on immunohistochemical profiles, first lesion was diagnosed as FMLGS (β-catenin negative, SMA and Desmin focally positive, EMA positive, Ki-67 positive 3–5 %), and second lesion, as DTF (β-catenin positive; SMA focally positive, Desmin and EMA negative; Ki-67<1 %).
Conclusion: Although LGFMS and DTF have similar site of involvement and epidemiological, clinical, macroscopic, histological features, these tumours should be properly diagnosed, given the metastatic potential of LGFMS.

PS-15-037
Benign lipomatous tumours with atypical features

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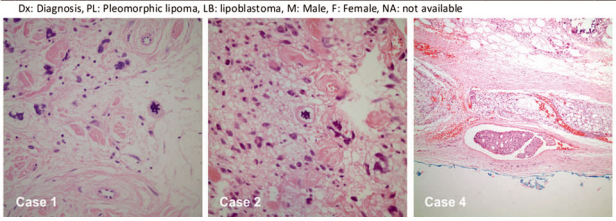
Objective: In this study, we examined 5 cases diagnosed as benign lipomatous tumours (3 pleomorphic lipomas and 2 lipoblastomas) showing atypical morphological features.
Method: 3 pleomorphic lipomas and 2 lipoblastomas were reviewed. Immunohistochemically, p16 (BD Pharmingen, 1:25), CD34 (Novocastra, 1:100), MDM2 (Neomarkers 1:150) and CDK4 (Neomarkers 1:150) were performed using Leica Bond automated system in all cases, MDM2 FISH (Zytovision) was performed in 2 pleomorphic lipomas and 2 lipoblastomas.
Results: Of the 3 pleomorphic lipomas, 2 were females and 1 was male, with a mean age of 46, and locations were cheek, back and gluteal region. One year old male and 2 years old female lipoblastomas were located at head and neck region. Atypical mitoses were detected in all cases of the pleomorphic lipoma. Additionally, hypercellularity and scattered lipoblasts were encountered in 15 cm sized pleomorphic lipoma located at back. One lipoblastoma revealed overt vascular invasion and the other showed ulceration and scattered MDM2 positive atypical cells with irregular nuclear membranes. Immunohistochemically, both MDM2 and CDK4 were negative in all pleomorphic lipomas. CD34 and P16 was diffusely positive in all pleomorphic lipomas and one lipoblastoma. No amplification was observed in studied cases by MDM2 FISH. Complete resection was applied to all cases and no recurrence or metastasis during follow-up periods ranging from 2 to 14 months.
Conclusion: Some benign lipomatous tumours demonstrate atypical morphological features suspicious for malignancy, such as vascular invasion and atypical mitosis that may lead to misdiagnosis of sarcoma in an otherwise benign lipomatous tumour. More cases and longer clinical follow-up are needed in order to reveal the nature of these cases.

Main characteristics of the cases and atypical morphological features:

	Dx	Age	Sex	Location	Size	Duration	Prognosis	CD34	P16	MDM2	CDK4	MDM2 FISH	Atypical Morphological Features
1	PL	45	F	Buccal fat pad	3 cm	NA	No recurrence (14 mos)	+	+	-	-	-	Atypical mitoses
2	PL	46	F	Gluteus	3 cm	120 mos	No recurrence (2 mos)	+	+	-	-	-	Atypical mitoses
3	PL	48	M	Back	15 cm	24 mos	No recurrence (3 mos)	+	+	-	-	NA	Hyperselluarity, atypical mitoses, large size
4	LB	1	M	Neck	7 cm	3 mos	No recurrence (5 mos)	+	+	+ few cells	-	-	Vascular invasion, few MDM2(+) cells
5	LB	2	F	Buccal fat pad	4 cm	24 mos	No recurrence (14 mos)	-	-	+ few cells	-	-	ulceration, atypical cells, few MDM2(+) cells

Dx: Diagnosis, PL: Pleomorphic lipoma, LB: lipoblastoma, M: Male, F: Female, NA: not available



PS-15-038
p16 expression in adipocytic tumours: Immunohistochemical study of 34 cases

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Objective: We aim to study p16 immunohistochemical expression in adipocytic tumours either benign or malignant.
Method: 34 specimens, including 17 liposarcomas (LPS) and 17 benign adipous tumours (BAT), were studied. LPS were well-differentiated in 17.6 %, myxoïd in 64.7 % and pleomorphic in 17.6 %. BAT included lipomas (58.8 %), angiolipoma (35.2 %) and lipomatosis (5.8 %). P16 expression was evaluated using immunohistochemistry. Positivity was scored as 1+ (1–10 % focal nuclear staining), 2+ (11–50 % multifocal nuclear staining), 3+ (>50 % diffuse nuclear staining). Absence of nuclear staining, cytoplasmic or membrane staining were considered as negative.
Results: 23.5 % of BAT were p16 negative, 70.5 % were scored 1+, 6 % were 2+ and none was 3+. 6 % of LPS were p16 negative, 17.5 % were scored 1+, 6 % were 2+ and 70.5 % were 3+. 3+ positivity was seen in only LPS. 20 % of negative staining was seen in LPS.
Conclusion: Our study showed that diffuse p16 immunostaining in adipocytic tumours is highly suggestive of LPS. Its negativity cannot exclude malignancy. P16 may be used in combination with other immunohistochemical stain such as CDK4 and MDM2 to increase the sensitivity and the specificity in resolving the differential diagnosis.

PS-15-039
Primary intracerebral alveolar soft part sarcoma in an 11-year-old girl

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Objective: Alveolar soft part sarcoma (ASPS) is a very rare soft tissue sarcoma typically occurring in young patients. It accounts for approximately 0.5–1 % of all soft tissue sarcomas. It usually occurs in the lower extremities. According to the literature, only three cases of primary intracranial ASPS without a demonstrable lesion elsewhere were described.

An 11-year old girl was operated because of fronto-parietal mass lesion by craniotomy. Because of possibility of metastasis the patient has to be followed up for long period.
Method: Neurological examination revealed 4/5 monoparesia in the right arm. MR imaging revealed a solitary well-defined lobulated mass lesion of left frontal lobe that was located in the subcortical white matter and extending to the deep white matter.
Results: On pathological examination, the tumour was showing alveolar nesting pattern with tumour cells containing abundant eosinophilic cytoplasm and discohesive nature. There were PAS-positive and diastase-resistant rod shaped multiple crystalline materials in the cytoplasm of some tumour cells and reticulin (silver) framework surrounding the tumour nests. Tumour cells were showing focal immunoreactivity with GFAP and no immunoreactivity with S100 protein. These findings revealed alveolar soft sarcoma.
Conclusion: To the best of our knowledge, this is the fourth case of primary intracranial ASPS without a demonstrable lesion elsewhere.

PS-15-040
Adenolipoma: Case report
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Objective: Adenolipoma, which is a rare form of lipoma, is first described by Hitchcock et al. and characterized by eccrine sweat glands between mature adipose cells. Adenolipoma usually occurs in the dermis or the subcutaneous tissue.
Method: 48-years old male patient was admitted to our hospital with complaint of a neck mass. Ultrasonography report was highly echogenic, regularly contoured solid lesion which was 2,5 × 1 × 2,5 cm in diameter and these signs were compatible with lipoma or fibrolipoma. Macroscopically material was 6 gr in weight, had irregular contours and the cut surface was yellow. Microscopically we identified mature adipose tissue arranged in a lobulated pattern and there were eccrine gland and ductal structures entrapped in this adipose tissue.
Conclusion: Adenolipoma is a very rare benign tumour. Usual site for adenolipoma is thigh and there is only one more report of adenolipoma on the neck region. Since it is a very rare localization for adenolipoma it must be kept in mind while investigating head and neck region lipomatous lesions.

Wednesday, 9 September 2015, 09.30–10.30, Restaurant
PS-16 Poster Session Digestive Diseases Pathology III: Liver / Biliary

PS-16-001
A rare indication for liver transplantation: Epithelioid hemangioendothelioma of the liver
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Objective: Epithelioid hemangioendothelioma (EH) is an uncommon tumour of vascular origin that may develop in the soft tissue, bone, lung, brain, liver and stomach. Primary hepatic EH is rare. It is frequently seen in middle-aged women. We report a case of a man who was found to have multipl hepatic masses in the all segments of the liver.
Method: A 45-year-old male patient presented with abdominal pain. Imaging studies showed multiple nodules in the liver and had features suggest a diagnosis of metastatic carcinoma. Ultrasonography guided needle core biopsy from the voluminous nodüle (segment VIII, diameter: 12 × 10 mm) was taken.
Results: Microscopically, the section showed polygonal epithelioid tumour cells with intracytoplasmic vacuoles, vesicular to hyperchromatic nuclei and prominent nucleoli. Immunohistochemistry revealed the tumour cells to be strongly and diffusely positive for CD34, factor VIII, vimentin. The tumour cells were negative for CEA, SMA and S-100. Therefore, a final histologic diagnosis of hepatic EH was made. Liver transplantation was performed 1.5 months later. At the last follow-up (33 months after diagnosis), the patient appeared well with no complaint or recurrence diagnosed on the liver.
Conclusion: In case of liver localization, EH presents as multiple hepatic nodules. Liver transplantation appears to be the only hope for patients with hepatic EH because of the multifocality of the tumour. Partial resection of the liver is possible for the localized tumour with good results.

PS-16-002
Relations of arterial and portal blood flow to hepatocellular cancer in varying degrees of differentiation: Radiologic-pathologiic correlations
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Objective: To study the characteristics of blood supply of hepatocellular carcinoma (HCC) with varying degrees of histological differentiation without liver cirrhosis.
Method: Were examined 19 patients (12 men and 7 women aged 18–72 years) with HCC: well differentiated (WD) (n = 6), moderately differentiated (MD) (n = 10) and poorly differentiated (PD) (n = 3) HCC. In preoperative stage was performed multislice computed tomography (MSCT). Calculated CT-exponent of tumour vascularization counting and the ratio of the portal and arterial blood.
Results: Maximum values of the degree of vascularization installed in WDHCC tissue, minimum - PDHCC. The largest index of blood flow to tumours by the hepatic artery-80,7 %, of the total flow of blood (portal-19, 3 %), is set to PDHCC. The level of inflow of arterial blood into the MDHCC less the values of the PD version, and was 67,6 % of the total (portal-32,4 %). Minimum parameters of inflow of arterial blood were observed in the WDHCC-41,9 % (portal-58.1 %) of the total tumour blood flow.
Conclusion: Conducting MSCT with bolus contrast allows to estimate the degree of vascularization liver tissue and HCC nodes. Increasing the share of inflow of arterial blood and reducing the share of the venous inflow occurred with decreasing degree of histological differentiation.

PS-16-003
Th17 and FoxP3 cells prevailed in the tumour microenvironment of hepatocellular carcinoma and liver metastases
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Objective: Nowadays, CD4 T-helper cells are divided into four major subsets based on their expression profile of transcription factors and secreted cytokines: Th1, Th2, Th17 and Tregs. IL-17 promotes tumour progression and Tregs inhibit activation and differentiation of CD4+ CD25- or CD8+ T cells and NK cells. Our aim was to evaluate the number of CD3+, CD4+ and CD8+, CD56+/CD57+, FoxP3 cells and IL-17 cells in primary liver tumours and liver metastases. The tissue expression of TGF-beta, IL-10 and IL-17 was measured.
Method: Immunohistochemical investigation was done: liver metastases from primary colorectal cancer (n = 19); hepatocelular carcinomas (n = 18); haemangiomas (n = 5).
Results: In tumour stroma the numbers of FoxP3+ and IL-17+ cells, were increased and CD3+, CD4+ and CD8+ cells were decreased as compared to peritumoral compartment. Concerning the expression of CD56/CD57 cells it was decreased in peritumoral tissue as compared to haemangioma patients. The expression of IL-17 was lower than that of TGF-beta and IL-10 in tumour and immune cells.

Conclusion: Therefore, the main cells in the tumour microenvironment are Tregs and tumour- promoting Th17 cells, which together with the increased expression of studied immunosuppressive cytokines induced tolerance and promoted tumour development, while the peritumoral compartment contained anti-tumour effector cells such as CD8.

PS-16-004

Oncocytic variant of biliary intraductal papillary neoplasm

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Objective: Intraductal papillary neoplasms of the bile duct (IPNBs) is a collective term for such neoplasms and bile-duct mucin-producing and cystic tumours. We have found in the relevant international literature only 10 case descriptions of the oncocytic variant of IPNB.
Method: Due to the rare incidence of IPNB oncocytic variant, we provide here our clinical observations.
Results: A woman, Sh., 56, skin and mucosal ochrodermia, darkened urine, pale stool. Abdominal USI: Biliary hypertension; block at mid-third segment of hepaticocholedochus. Abdominal CT, a 40 × 20 × 20 mm local wall thickening zone is found in mid third segment of hepatic duct at cystic duct opening. Gross choledoch fragment. A pinky-reddish 'cauliflower' polypoid proliferation with ulcerated surface, soft elastic consistency, 1.5 × 1.7. Histology: bile duct lumen with oncocyte cell ulcerated expansions and duct wall compression, forming sporadic papillae. IHC: express MUC5 AC and 6, CK 7 and 19, panCK. Index Ki-67 – 30 %. Conclusion: Intraductal papillary neoplasm of the bile duct, oncocytic variant (ICD O). Neoplasm confined to bile duct wall (pT1). No neoplasm growth in the resection margin (R0). No metastases (pN0) in 10 (parapancreatic) lymph nodes studied. Stage IA.
Conclusion: Differential testing for IPNBs should cover purulent cholangitis, cholangiocarcinoma, and biliary mucinous cystic tumours. Prognosis for IPNB is unclear.

PS-16-005

Acute haemolytic anemia with liver failure as initial clinical manifestations of Wilson's Disease

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Objective: Wilson's disease is an autosomal recessive disorder of copper transport. It results in accumulation of copper in the liver, brain, and other organs. Severe hemolytic anemia is an unusual clinical presentation. Since effective treatment is available for this disease, early and correct diagnosis is important. We report a case of a previously undiagnosed Wilson's disease revealed by acute intravascular hemolytic anemia and liver failure as an initial manifestation of disease.
Method: A previously healthy, 11-year-old boy, presenting with abdominal pain, jaundice, tea-colored urine, and anemia was admitted to the pediatric hospital. Clinical and laboratory investigations for suspected hematological and hepatic disorder were immediately taken. Blood sample for genetic testing for Wilson's disease was performed. The patient was treated with plasmapheresis and other supportive treatment, but unfortunately the condition turned fatal 6 days after hospitalization.
Results: Autopsy revealed shock with hemolytic anemia and respiratory distress syndrome superimposed on liver cirrhosis. Positive Orcein-Shikata and Rubeanic acid stain, ultrastructural visualization of electron-dense lysosomal deposits and liver copper content analysis, in conjuction with genetic results, confirmed the diagnosis of Wilson's disease as cause of cirrhosis.
Conclusion: Wilson's disease must be considered in case of acute hemolytic anemia associated with liver failure in young adults.

PS-16-006

PDX-1 is a reliable immunohistochemical marker for differentiation between pancreatic neuroendocrine neoplasms and pancreatic solid-pseudopapillary tumours

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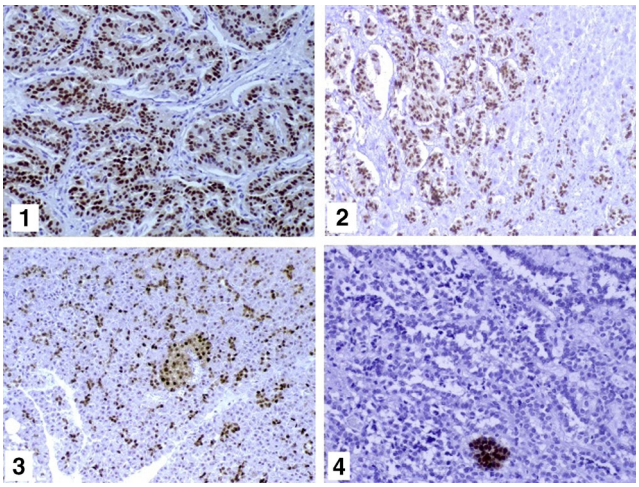
Objective: Pancteatic duodenal homeobox-1 (PDX-1) is one of the earliest transcriptional factors that plays a critical role in further pancreatic development, detected in the developing pancreatic epithelium. The role of expression of this factor in the development of tumours of various origin is not yet fully understood.
Method: Immunoexpression of PDX-1 (clone EP139, Epitomics) was evaluated in 73 pancreatic tumours (65 surgical and 8 biopsy samples) - 61 neuroendocrine tumours (pNET) (53 primary and 8 liver metastases) and 12 solid-pseudopapillary tumours (pSPT).
Results: PDX-1 expression was detected in 58 of 61 pNETs PDX-1 expression was detected in 58 of 61 pNETs (95.1 %). Reactivity was predominantly nuclear labeling in 49 (84,5 %), nucleocytoplasmic - in 9 (15,5 %) tumours, respectively (Figs.1 and 2). Nuclear expression PDX-1 was also observed in ductal cells, nucleocytoplasmic - in islet cells, and was absent in acinar cells of the pancreas (Fig.3). PDX-1 expression was detected in none of the 12 investigated pSPT (Fig.4).
Conclusion: PDX-1 is a very good marker for differentiation between primary pNET and its metastasis and pSPT. The absence of expression of PDX-1 in pSPT is further proof of non-epithelial origin of these tumours.



PS-16-007

Recurrence factors of Hepatocellular carcinoma in transplantation patients

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Objective: Liver transplantation (TPL) is utilized to the therapeutic choice for hepatocellular carcinoma (HCC). The aim of this study was to investigate the recurrence rate of HCCs after TPL and prognostic factors for recurrence.
Method: 342 patients who had received liver TPL between 1996 and 2012 in Seoul National University Hospital were enrolled and 519 HCC patients with partial hepatectomy between 1995 and 2006 were selected as a control group (non-TPL group).
Results: 69 in 342 patients (20.2 %) were relapsed and the recurrence rate was lower than non-TPL group (54.9 % 337/519, $p < 0.001$). Stratification analysis by pT stage showed pT1-2 stage TPL group had lower late recurrence rate (beyond 2 year) than non-TPL group. A univariate DFS

analysis by Kaplan-Meier analysis disclosed that tumour number, maximum tumour size, gross type, Edmondson-Steiner(ES) nuclear grade, angioinvasion, pT stage, Milan criteria ($p < 0.001$), UCSF criteria (all $p < 0.001$), and positive expression of CK19 ($p = 0.006$) were predictors of tumour recurrence. A multivariate analysis, tumour number ($p = 0.028$), maximum tumour size ($p < 0.001$) and angioinvasion ($p = 0.005$) were independent predictors of tumour recurrence.
Conclusion: TPL may have protective effect for late recurrence of pT1-2 HCCs, compared with non-TPL group and prognostic factors for recurrence were similar with previously well-known prognostic factors of HCCs.

PS-16-008
Endocrine cell hyperplasia in chronic calculous cholecystitis is associated with metaplastic changes
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Objective: In recent years there appeared information about different metaplastic changes in gallbladder associated with chronic calculous cholecystitis. These were pseudopyloric metaplasia, intestinal metaplasia with or without dysplasia. The aim of our study was to assesse the endocrine cell hyperplasia in association with these types of metaplasia.
Method: Surgical biopsy samples collected from 18 patients with calculous cholecystitis with metaplasia and from 9 patients with chronic cholecystitis without metaplasia were investigated. Immunohistochemical reaction were done with antibodies against chromogranin A, serotonin, gastrin, somatostatin and synaptophysin.
Results: It was found that endocrine cells positive for chromogranin A, serotonin, gastrin, somatostatin and synaptophysin were increased significantly in number ($\chi = 9.45$, $p = 0.002$; $\chi = 6.67$, $p = 0.009$; $\chi = 8.0$, $p = 0.005$; $\chi = 9.45$, $p = 0.002$; $\chi = 8.0$, $p = 0.005$, respectively) in most cases with metaplasia. It was detected that pseudopyloric glands prevailed in the patients with metaplasia.
Conclusion: In conclusion we may stete that endocrine cell hyperplasia was associated with metaplastic changes in gallbladder.

PS-16-009
The controversy of signet ring cell degeneretion of gallbladder mucosa
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Objective: Signet ring cell degeneration (SRCP) is a phenomenon of epithelial cells to round up and shape making signet ring forms considered to be degenerative change. It is emphasized that there is a high risk of overdiagnosis of signet ring cell adenocarcinoma in same locations. The precise mechanism for their production is still unclear, but it seems to be related to ischemia, necrosis, ulceration or provoked by inflammatory process.
Method: Routine histological, histochemical (alcian blue, PAS) and ancillary immunohistochemical (E-cadherin, Ki-67, p53) examination were done.
Results: We present a case of 76-year-old male patient who had chronic perforated pyloric ulcer and had cholecystectomy due to prominent surrounding peritonitis. Besides chronic cholecystitis, mucosa showed almost completely SRCD accompanied by papillary hyperplasia with focal low grade dysplasia. Although almost all epithelial cells expressed strong membranous immunopositivity for E-cadherin, some group of significantly atypical dysplastic epithelial cells showed high Ki-67 and p53 index associated with SRCD.
Conclusion: This rare and peculiar SRCD phenomenon is not always mucosal degeneration of non-neoplastic cells and could be associated with dysplasia.

PS-16-010
A rare variant gallbladder cancer: Adenosquamous carcinoma of the gallbladder
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Objective: Gallbladder cancer is the most common malignancy of the biliary tract, accounting for 80–95 % of biliary tract cancers. This tumour is a highly lethal disease with an overall 5-year survival of less than 5 % and mean survival less than 6 months. The most common type of gallbladder cancer is adenocarcinoma, and the incidence of adenosquamous carcinoma, associated with worse prognosis is rare.
Method: A 81-year-old female patient presented to our general surgery outpatient clinic with abdominal pain. The physical examination revealed tenderness on palpation in the right upper quadrant. Abdominal ultrasound examination showed hydropic swelling of the gallbladder. She underwent gallbladder resection with regional lymphadenectomy. Pathology analysis revealed a 10,5-cm pT3N1adenosquamous cell carcinoma of the gallbladder.
Results: Patients with adenosquamous cell carcinoma of the gallbladder most commonly showed a large mass replacing the gallbladder fossa. The bulky tumour is usually diagnosed at an advanced stage with frequent invasion of the adjacent organs, such as the liver, extra hepatic bile ducts, duodenum, stomach, colon and pancreas.
Conclusion: Here, we present a rarely seen case of gallbladder adenosquamous carcinoma.Although this type gallbladder carcinoma had a tendency for liver invasion and poor outcome, better survival can be obtained by performing curative resection. Key Words: Adenosquamous carcinoma, gallbladder cancer, neoplasm.

PS-16-011
Luschka ducts of the gallbladder occurring in adults: Report of 17 cases
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Objective: Luschka ducts (LD) of the gallbladder (GB) are rare congenital lesions, comprising varied lesion subtypes. There are few recent reports in adult patients. We aimed to report the characteristics of 17 cases of gallbladder LD as diagnosed on cholecystectomy specimens.
Method: The surgically resected GBs were analyzed for GB lesions and LD features (length, cystic dilatation, nodular pattern, epithelial mucosecretion and atypia, inflammation, and cytokeratin 20 and ROS1 immunohistochemisties). These data were analyzed with regard to the main clinical characteristics.
Results: The age varied between 24 and 86 years (median, 61 years) and, the gender ratio was 7:10 (female: male). The diagnosis was cholecystitis, acute (10) or chronic (7). 3 GB were alithiasic. GB adenocarcinoma was associated in one of the acute cholecystitis cases. The LDs were subserosal (16) or at the resection site (4, both in 3 cases). LD length varied between <1 and 25 mm. A nodular pattern was seen in 4 cases. Epithelial mucosecretion occurred in 5 cases, regenerative atypia in 6. Cystic dilatation was seen in 3 cases. Polymorphous peri-LD inflammation was more frequently mild (9 versus 4 with moderate or severe inflammation; 3 cases lacked inflammation). ROS1 and cytokeratin 20 were negative in the case with a history of colon adenocarcinoma.
Conclusion: The results of our study suggest that LD-complexes may harbor varied aspects, from duct-like, inframilimetric or cystic, to nodular complexes, being preferentially located subserosally. Epithelial atypia warrants ROS1 and cytokeratin 20 immunohistochemistries, helpful in the differential diagnosis with adenocarcinoma.

PS-16-012

Could mean platelet volume predict histological activity of chronic active hepatitis B?

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Objective: Liver biopsy is the gold-standard method to assess the severity of liver damage, but the invasive nature of this method limits its usage. The aim of the present study was to evaluate whether complete blood count (CBC) parameters such as mean platelet volume (MPV) would be useful in predicting liver histological activity in chronic hepatitis B (CHB).
Method: 136 patients with chronic active hepatitis B based on liver biopsy were enrolled retrospectively into the study. MPV, platelet distribution width (PDW) and platelet count were compared according to liver biopsy findings such as histological activity index (Knodell score).
Results: We demonstrated that MPV and PDW were significantly increased and platelet count was significantly decreased in moderately active hepatitis group compared with mildly and minimally active group (p = 0.002, p = 0.03, p = 0.006, respectively). According to treatment cut-off point of histological activity index in mildly active group, significant difference was found between MPV and PDW levels (p = 0.02 and p = 0.04).
Conclusion: We suggest that MPV might help the treatment decision before biopsy or during follow up, especially in mildly active CHB and it can be used as a new marker that can be useful to determine the activity of CHB.

PS-16-013

Amyloidosis first diagnosis from a liver biopsy

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Objective: The diagnosis of amyloidosis depends on the histologic demonstration of amyloid deposits in tissues. The most common sites biopsied are the kidney, rectal or gingival tissues in patients suspected of having systemic amyloidosis. Examination of abdominal fat aspirates can also be diagnostic. Despite the fact that a colon biopsy which took place a few months earlier was negative (Congo Red -), the first diagnosis of our patient's condition was made after a liver biopsy.
Method: A liver FNB was received from a 39-year-old woman admitted for chronic diarrhea, vomiting, hepatomegaly and ascites.
Results: Histologically, although single cell and trabecular hepatocellular arrangement was retained, there was total sinusoidal extinction by an acellular homogeneous eosinophilic material filling the sinusoids. Amyloidosis was obvious, confirmed by a positive Congo Red stain and further histochemical and immunochemical techniques.
Conclusion: Amyloid is present in more than 90 % of rectal and subcutaneous fat biopsies in systemic AA or AL amyloidosis. A negative result does not exclude the possibility of amyloidosis due to the unavoidable problem of sampling error and the variability of amyloid deposition. Despite the initial diagnosis of collagenous colitis after rectal biopsy in our patient, it was liver biopsy which finally disclosed amyloidosis as the main source of systemic distress.

PS-16-014

Polymorphism of DNA repair genes XRCC1 and XRCC3 and hepatocellular carcinoma risk in Romanian population

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Objective: Our study aimed to clarify the association between XRCC1-Arg399Gln, XRCC3-Thr241Met, and XRCC3-5′UTR polymorphism and Hepatocellular Carcinoma (HCC) risk and to find a link between their expression and the clinical outcome of HCC.
Method: A total of 50 cases with HCC were collected. These three genetic variants (XRCC1-Arg399Gln, XRCC3-Thr241Met and XRCC3-5′UTR) were genotyped by pyrosequencing method. All analyses were performed using the MedCalc statistical package.
Results: Statistical analysis results did not identified a causal next to single nucleotide polymorphism (SNP), polymorphic genotypes variants, and clinicopathological characteristics in analyzed cases. Survival correlations reflected the possible prognosis value only for XRCC3-5′ UTR(P = 0.003) in HCC, considering that wild-type gene was associated to a statistically significant longer survival compared to SNP.
Conclusion: Our data interpretation supports the assumption that DNA repair genes polymorphism vulnerable against numerous injuries with genotoxic effect may be incriminated in initiation of primary HCC, without a demonstrable direct connection between polymorphous genotype and HCC. HCC initiation and evolution modality reveals a multifactorial mechanism including genetic polymorphism which does not possess a crucial role.

PS-16-015

Primary adenoneuroendocrine carcinoma of the gallbladder

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Objective: Neuroendocrine tumours (NETs) that settle on gallbladder means less than 1 % of all gastrointestinal tract NETs and less than 5 % of all gallbladder carcinomas. It occurs more frecuently in females and reaches its highest incidence in the seventh decade of life.
Method: Preoperative diagnosis is exceptional and it takes place in less than 20 % of cases. It is clinically insidious and indistinguishable from the symptoms associated with choledocholithiasis.
Results: We present a 70-year-old patient who had previously consulted because epigastric pain, vomiting and heartburn. Abdominal CT showed a large tumour mass occupying the light of the gallbladder. Intraoperative biopsy showed a poorly differentiated malignant tumour. Subsequently, we recieved a tumoural gallbladder. Microscopically we appreciated an infiltrating neoplasia with a nested pattern, consisting of small cells with hyperchromatic nucleus and nuclear molding. Furthermore moderately differentiated glandular structures with poorly differentiated foci were seen. Immunohistochemically, small and hyperchromatic cells were positive for synaptophysin, enolase and CD56, while the glandular structures were positives for CK7 and 19. Ki67 was around 90 %.
Conclusion: NETs of the gallbladder are extremely rare and often occur with other concomitant carcinoma. Patient prognosis is poor in any case, but early detection with complete resection may improve the prognosis.

PS-16-016

Combined hepatocellular-cholangiocarcinoma with stem cell features: Clinicopathologic correlation

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Objective: A rare type of combined hepatocellular-cholangiocarcinoma (HCC-CC) with stem cell features (HCC-CC-SCF) was recently recognized and further subdivided into typical, intermediate-cell and cholangiolocellular subtypes. While subtypes of HCC-CC-SCF have been proposed for histological distinction, their clinicopathologic features, pathogenesis and prognosis remain unclear.
Method: Routine histological and immunohistochemical examination and reevaluation of clinical data on age, sex, radiological features, size, etiology (HBV, HCV, alcohol) and cirrhosis.
Results: In last three years we diagnosed three cases of HCC-CC-SCF among eight HCC-CC. Well defined hepatic mass sometimes showed

satellites, but US/CT/MR features with irregular "peripheral enhancement" in some cases were interpreted as focal nodular hyperplasia or vascular lesions. No significant differences were found between HCC-CC-SCF and HCC-CC in respect to clinical data. Although histologically and immunohistochemically variable, we concluded one case as typical and two cases as cholangiolocellular type with diffuse immunoexpression of CAM5.2, canalicular and/or cytoplasmic pCEA and N-cadherin and at least focal immunopositivity for CK7, CK19, Hep-Par1 and NCAM/CD56, but consistently negative for CK20, vimentin and CDX-2.
Conclusion: Lack of specific or suggestive clinicopathologic features requires examinations on larger series of HCC-CC-SCF. Recognition of these tumours could allow further studies on their biology and might have implications for new treatment options.

PS-16-017
Heterotopic gastric mucosa of the gallbladder presented as a polypoid mass
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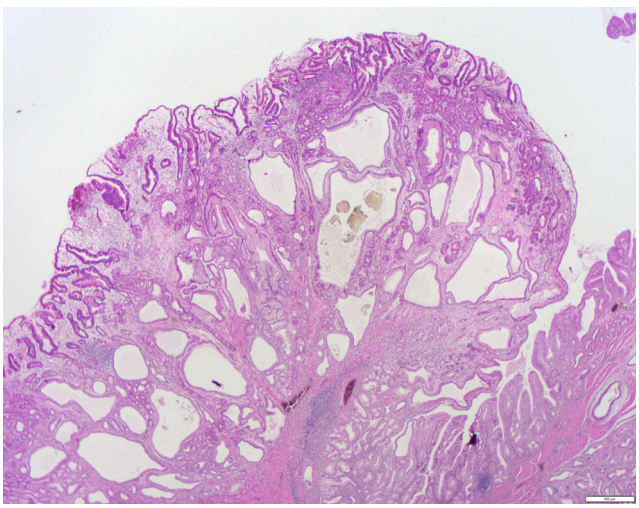
Objective: Heterotopias of various tissues have been described in the gallbladder. The most common ones include tissue of pancreas, intestines, liver, adrenal and thyroid gland and gastric mucosa. Patients are usually asymptomatic; in rare cases patients present with billiary type symptoms. Heterotopias most often are incidental finding in cholecystectomy specimens.
Method: A 39-years old Caucasian presented with biliary colic and nausea. Physical examination revealed abdominal tenderness. Abdominal multislice computed tomography (MSCT) was preformed, hyperdense area in the infundibulum of the gallbladder, measuring 2 cm in the greatest diameter was found. Laparascopic cholecystectomy was preformed.
Results: On gross examination gallbladder measured 6 × 2 cm with polypoid mass measuring 2 × 1,5 × 1 cm in the gallbladder neck. Microscopic analysis revealed polypoid heterotopic gastric mucosa, containing pyloric and fundic type glands with parietal cells. Few glands were cystically dilated and lined with columnar mucinous epithelium with foci of intestinal metaplasia and low grade foveolar dysplasia. Surrounding lamina propria was edematous with lymphocytic infiltrate. Remaining of the gallbladder had normal histologic apperence.
Conclusion: Heterotopic gastric mucosa in the gallbladder is rare entity. Because it can result in acute and chronic cholecystitis as well as carcinoma it should be taken into consideration during gallbladder specimen examination.

Heterotopic gastric mucosa of the gallbladder presented as a polypoid mass:



PS-16-019
Solitary desmoid tumour of the Pancreas: A case report
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Objective: Solitary desmoid tumours (DTs) are rare spindle cell tumours, accounting for 0,03 % of all neoplasms, occurring very rarely in extrapleural localization.
Method: We report a case of pancreatic DT in a 47-years-old male presenting with recurrent epigastric pain and obstructive jaundice. Imaging studies revealed a homogeneous 4 cm tumour in the pancreatic head, well-delimited, but not encapsulated, mainly solid, with a cystic component. Due to the clinical suspicion for cystadenocarcinoma pancreatectomy was performed.
Results: Histologically, the tumour was composed of spindle cells with regular nuclei, separated by large amount of collagen fibers and myxoid tissue. No necrosis was found and mitotic activity was 1–2 mitoses in 10 HPFs. The cystic component was due to retention cysts and ductal dilatation. Immunohistochemical analysis showed that tumour cells were positive for Beta-catenin, CD34, Vimentin, CD99, Actin, bcl-2 and negative for S-100, CK, EMA and Desmin. Proliferative index on Ki-67 staining was below 2 %. Diagnosis of benign solitary desmoid tumour was made.
Conclusion: There is limited data regarding biological behavior of DTs with extra-pleural localization, because they are quite rare tumours. Diagnosis of malignancy is based on nuclear atypia, cellularity, necrosis, high Ki-67, expression on p53, 4 mitoses in 10 HPFs and tumour larger than 10 cm.

PS-16-020
Expression of Ki67 and Bcl-2 in chronic Hepatitis C virus infection and prognostic significance in hepatocellular carcinoma
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Objective: Chronic hepatitis C virus (HCV) infection is prevalent and often causes hepatic fibrosis, which can progress to cirrhosis and cause hepatocellular carcinoma (HCC) or liver failure. HCC is one of the most common malignant tumours that carry a poor prognosis. To improve the long-term outlook for HCC, an accurate prognosis is important. We sought to examine immunohistochemical expressions of proliferative Ki67 and Bcl-2 apoptotic marker and their potential role as prognostic factors in HCV patients.
Method: Ninety formalin-fixed paraffin-embedded samples from patients with chronic hepatitis, cirrhosis and HCC receiving needle liver biopsy were investigated immunochistochemically for the expression of Ki67 and Bcl-2 and correlated with age and Knodell index.
Results: Ki67 and Bcl-2 expression was statistically significantly higher in HCC and cirrhosis compared with chronic hepatitis ($p < 0{,}001$). Knodell index was statistically positive correlated with age ($p < 0{,}05$).
Conclusion: These data suggest that HCV infection induces increased and abnormal hepatocyte proliferation which might be related to the increased risk of HCC in patients with HCV-related liver damage. High Ki67 and Bcl-2 expression might be associated with poor survival in patients with HCC.

PS-16-021
The proliferative rate of hepatic adenomas versus well differentiated hepatocellular carcinomas using Ki-67 immunohistochemistry "hot spot" digital analysis

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Objective: To investigate the utility of digital protocols for Ki-67 immunohistochemistry quantitative analysis ("hot spot" method) in the setting of well differentiated hepatocellular neoplasms.
Method: Resection cases of typical hepatic adenomas (HAs) (n = 40), atypical HAs (n = 9), and WD HCCs (n = 56), diagnosed between 1997 and 2014, were selected (re-reviewed by 3 GI pathologists). HAs were further classified by immunohistochemistry using antibodies against liver fatty acid binding protein [LFABP], glutamine synthetase [GS], B-catenin, hepatic serum amyloid [SAA], and C-reactive protein [CRP]). Ki-67 proliferative index by IHC was evaluated in all cases by digital analysis using a standardized neuroendocrine tumour "hot spot" protocol (Fig. 1).
Results: The proliferative rate of HAs (typical, median 1.2 % [range 0–7.4 %] and atypical, median 1.0 % [range 0.3–3 %]) was significantly lower than that of WD HCCs (median 4.5 %, range 0–50 %) ($P < 0.0001$). Only a few (6 %) of the adenomas (all inflammatory/telangiectatic type) had proliferative rates higher than 4 %, compared to most (51 %) of WD HCCs.
Conclusion: Ki-67 is a potentially useful adjunct marker in the evaluation of WD hepatocellular neoplasms, as "hot spot" proliferative rates >4 % are uncommon in HAs but frequent in WD HCCs.

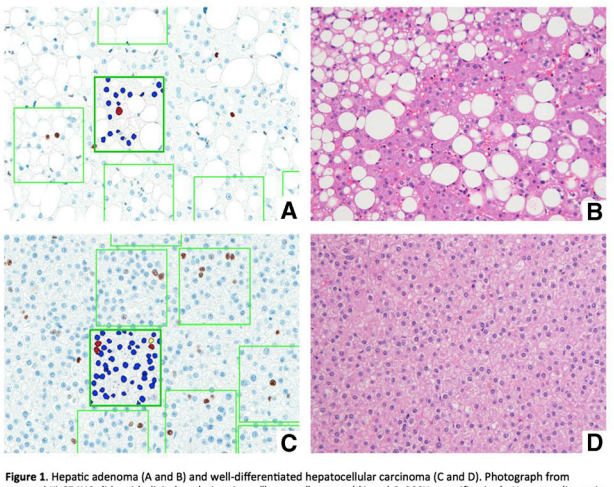

Figure 1. Hepatic adenoma (A and B) and well-differentiated hepatocellular carcinoma (C and D). Photograph from scanned Ki-67 IHC slide with digital analysis using a "hot spot" protocol (A and C, 200X magnification). Hematoxylin-eosin stain (B and D, 200X magnification).

PS-16-022
Eosinophilic cholecystitis: A report of four cases
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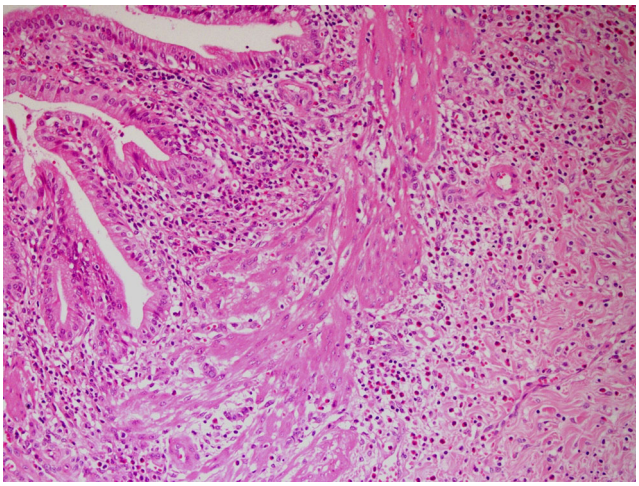
Objective: Eosinophilic cholecystitis (EC) is a very rare form of cholecystitis and is characterized histologically by a marked infiltrate composed predominantly eosinophils. Its prevalance is 0.25–6.4 %.
Method: We report four cases which were diagnosed as EC.
Results: Our cases were two females (36 and 47-years-old) and 2 males (47 and 54-years-old). All cases admitted with abdominal pain. One of them had high percentege in neutrophils in hemogram. Aspartate transaminase, alanine transaminase and alkaline phosphatase levels were high in 2 of 4 patients. These enzymes were normal in one patient. Three of four cases had gallstones in ultrasongraphic and gross examination while one of them had biliary mud. On gross examination, the gall bladders' lengths were 7.5–12 cm and wall thickness' were 2–7 mm. Histopathologically; dense infiltrates composed of eosinophils were seen. Retrospective analysis of case histories did not reveal any known etiology.
Conclusion: Histopathologically the patients with acalculous cholecystitis have a higher percentage of eosinophils than the patients with gallstones. In contrast, three of our four patients had gallstones. EC can be associated with hypereosinophilic syndrome, parasitic infestations, few herbal medicines and certain drugs. Only one of our patients had used Paliperidon which has no defiened relationship with EC yet.

Figure1: Case 1:



PS-16-023
Analysis of Collagens IV and VI expression in pancreas at chronic pancreatitis
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Objective: To study collagens IV and VI expression in pancreas at CP.
Method: Using morphological, immunohistochemical, morphometric methods, we investigated the pancreas specimens of 28 patients with CP who underwent duodenum saving resection of the pancreas head. Control group included 7 pancreas head specimens of people, died due to accident and having no pathology of pancreas. Statistic analysis included T-test. All p value ≤ 0.05 was considered statistically significant.
Results: Our research showed that collagen IV localized in basements membranes of vessels and ducts, acinar cells. Expression was higher in pancreas samples at CP. Collagen VI localized in cytoplasm of acinar cells and duct's epithelium. Count of positive cells and total positive area were more than 2-fold increasing in pancreatic tissue of patient with CP. The results of the markers expression are displayed in Table.
Conclusion: Histological examination showed collagen IV, VI expression changes statistically significant in pancreas samples at CP. The revealed changes expression connected with progressive degenerative changes and fibrosis.

Table. The marks of the expression of collagen IV, VI

Groups	Collagen IV		Collagen VI	
	Count	Area, mkm^2	Count	Area, mkm^2
Chronic pancreatitis	750,2±2,86	1093297,22±3340,36	1409,92±7,21	241506,09±21000,92
Control group	924,11±8,5	751045,11±10096,45	615,15 ±19,34	85524,08± 3433,07
p value (T-test)	**p=0,0005**	**p<0,000001**	**p<0,000001**	**p=0,000002**

PS-16-024
Nodular regenerative hyperplasia of the liver associated to hepatocellular carcinoma
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Objective: Nodular regenerative hyperplasia (NRH) is an infrequent morphologic pattern included within Non-Cirrhotic Idiopathic Portal Hypertension (NCPH). It is characterized by diffuse micronodular transformation of the hepatic parenchyma without fibrous septa. Association with hepatocellular carcinoma (HCC) is extremely infrequent.
Method: We describe the clinicopathological features of a patient diagnosed of NCPH and hepatocarcinoma submitted to liver transplantation.
Results: 40 year old man categorized as NCPH presented with oesophageal variceal bleeding in 2001 without aetiological factors for chronic hepatic disease (negativity for hepatotropic viruses, autoimmunity). Liver biopsy showed no cirrhosis. Signs of portal hypertension without vascular disease on abdominal CT and normal hepatic venous pressure gradient were found. In 2014, presented a HCC and was proposed for liver transplantation (2015). Grossly the liver showed a dysmorphic, macronodular parenchyma. Histopathologic findings were: NRH without cirrhosis, myointimal fibrosis of a venous structure of the hepatic hilum, focal nodular hyperplasia (2 × 1 cm) in segment V-VIII and grade 2/4 HCC (4 × 3.7 cm).
Conclusion: This case highlights NRH as a morphological pattern occurring in the setting of NCPH and its difficult diagnosis in liver biopsy. Assessing the utility of screening for HCC in these patients should be considered due to the possible pathogenic relationship between NRH and HCC, despite being non-cirrhotic.

PS-16-025
The histological effects of neoadjuvant chemotherapy on colorectal liver metastases and non-tumoural parenchyma: The experience of a tertiary center

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Objective: Histological assessment of colorectal liver metastases (CRLM) after neoadjuvant chemotherapy (NC) changed in the last years. Our aim is to determine the impact of NC on the CRLM and non-tumoural parenchyma.
Method: In 2012 and 2013, 176 patients underwent CRLM surgery. The medical files and histological slides were reviewed. The Rubbia-Brandt system was used. For the statistical analysis a simple probit model was employed.
Results: The mean age was 63.5 years, being 69 females and 107 males. Tumours ranged between 0.2 and 18.5 cm. NC was performed in 137 patients (77.8 %). The most frequent drug regimens included oxaliplatin (52–38 %), irinotecan (46–34 %) or both (20–15 %). Forty had also cetuximab (29 %) whereas 22 bevacizumab (16 %). Ninety-three patients (68.4 %) had no response, 29 (21.2 %) a partial response and 14 (10.4 %) a major response (MR). Forty-three had steatosis (31 %), 11 stetohepatitis (8 %) and 39 (28 %) sinusoidal obstruction syndrome (SOS). SOS was only observed in the oxaliplatin group (positive impact and statistically significant) while steatohepatitis and steatosis were equally present in the three NC regimens.
Conclusion: A small proportion of patients had a MR to NC. SOS was associated with oxaliplatin administration.

PS-16-026
Fulminant HSV-I hepatitis in two healthy young adult males

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Objective: Acute liver failure due to HSV-I hepatitis is a very rare event but a fatal outcome is not unusual. The objective of the present study is to describe clinical-pathological features of fatal herpes virus hepatitis in order to achieve an early diagnostic.
Method: We describe clinical and autopsy findings in two fulminant cases. We made also a bibliographic and published data review.
Results: Two healthy males (40 and 45 years old) underwent rapidly fulminant hepatic failure preceded by a very similar clinical presentation, consisting of flu-like symptoms followed by hepatic failure. Autopsy results show mottled and congestive liver, haphazard extensive necrosis surrounded by congestive areas and, nuclear eosinophilic inclusions. Immunohistochemistry and PCR were consistent with HSV-I liver infection. Bibliographic and data review revealed a lack of liver biopsy procedures as a diagnostic method.
Conclusion: The fatal outcome of this two events show the urgency to make an early diagnostic and to take into account an HSV-I hepatitis as a cause of fulminant hepatic failure in healthy patients. It remains a challenge the utility of early liver biopsy as a diagnostic tool since data related to this method in such patients are not reasonably studied.

PS-16-027
Noncirrotic hepatocellular carcinoma derivated from hepatocellular adenoma

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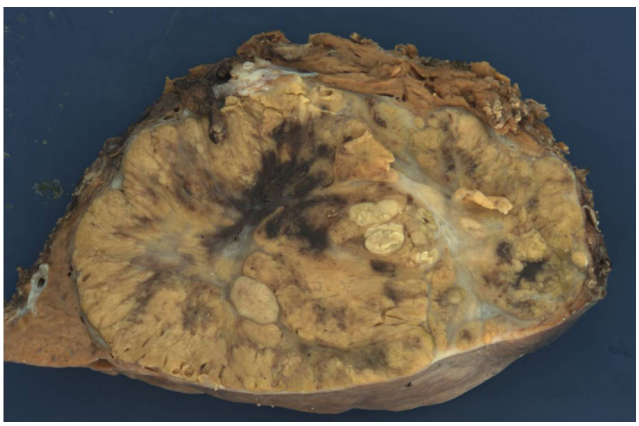
Objective: The majority of hepatocellular carcinomas arise in background chronic liver disease, particulary cirrosis. The pathogenesis of noncirrhotic hepatocellular carcinomas remains unclear. While malignant transformation reportedly occurs in <15 %of hepatocellular adenoma, the prevalence of noncirrhotic hepatocellular carcinomas arising from a preexisting adenoma is a challenge to study.
Method: We describe the case of a 68 year old woman with a Diabetes Mellitus, hypertension, Dyslipidemia, sleep apnea and kidney lithiasis, whom a routing monitoring finds out a large single liver tumour.
Results: Microscopically, the tumour was composed of well-differentiated hepatocytes with abundant eosinophilic granular cytoplasm, marked steatosis and without portal triads. It showed malignant transformation area consistent with hepatocellular carcinoma.
Conclusion: Hepatocellular carcinoma arising in the setting of hepatocellular adenoma is a rare phenomenon and has been reported in 4–8 % of cases. Advanced age, male gender, use of anabolic steroids, metabolic syndrome, and large tumour size have been cited as risk factors for hepatocellular carcinoma transformation in an adenoma.

Macroscopic image:



PS-16-028
Pigmented hepatocellular adenoma with inflammatory features and B-catenin activation

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Objective: Hepatocellular adenomas (HCAs) are benign liver tumours, currently classified in four subtypes: Type 1 (HNF-1α-inactivated HCA) caused by mutations in hepatocyte nuclear factor 1 (HNF-1α) gene; Type 2 (β-catenin-activated), with β-catenin over-expression and up-regulation of glutamine synthetase (GS); Type 3 (inflammatory), with increased expression of C-reactive protein (CRP) and serum amyloid-A (SAA). Type 4 (unclassified).
Method: The present a case of pigmented HCA, developed in a 27-year-old female, without history of contraceptive use, displaying the features of subtypes 2 and 3 of HCA according to the histological and immunohistochemical profile.
Results: The biopsy and subsequent partial hepatic resection displayed similar features. The tumour was composed by unicellular trabeculae of hepatocytes and solid areas, and it was notorious the deposition of dark brown granules of Dubin-Johnson-like pigment, strongly positive with Masson-Fontana stain. By immunohistochemistry, there was nuclear expression of B-catenin, diffuse expression of GS, and multifocal expression of CRP and SAA.
Conclusion: The present case is an example of a very rare pigmented (dark) HCA with inflammatory features and β-catenin activation. Similar to this, there is only one other case reported in the literature. β-catenin activation, considered a risk factor of malignant transformation, should be searched for in pigmented HCAs.

PS-16-029
Atypical presentation of Polyarteritis Nodosa
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Objective: Polyarteritis nodosa (PAN) is a systemic vasculitis that affects the tunica media of small and medium caliber arteries without the presence of glomerulonephritis or vasculitis or without association with anti-cytoplasmic neutrophil antibodies (ANCA) positivity. Generally involves various organs such as kidneys, skin, central and peripheral nervous system and the gastrointestinal tract. The presence of hepatic involvement by the PAN is uncommon and difficult to diagnose. The diagnosis is complicated because of unspecific serological tests and clinical features; therefore it must be based on histopathological analysis.
Method: We describe the case of a 75 year old woman with no previously known disease that required an urgent right hepatectomy due to a liver rupture with hemoperitoneum.
Results: Histologically there is an inflammatory and haemorrhagic abscess. The liver injury was consistent with nongranulomatous acute necrotizing vasculitis. The gallbladder had acute vasculitis with fibrinoid necrosis in muscular arteries of parietal medium caliber.
Conclusion: Spontaneous hepatic rupture is a rare entity with very few cases in the literature reviewed, however it has a high mortality. Early diagnosis is crucial in this disease, Therefore an extensive and exhaustive history is required, and a pathological study is essential to confirm the diagnosis of PAN type vasculitis.

PS-16-030
Giant pancreatic solid cystic desmoid tumour with 2 ectopic adrenal tissues
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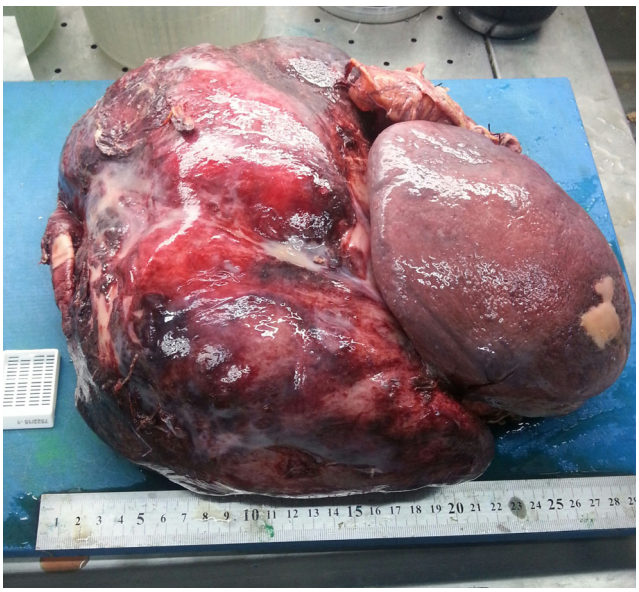
*Izmir Katip Celebi University, Ataturk Training and Research Hosp., Dept. of Pathology, Turkey

Objective: Desmoid tumours (DTs) are a rare type of benign soft tissue tumour. They are characterized by dense fibroblastic proliferation in an abundant collagenous extra-cellular matrix. Although they have no metastatic potential, they are locally aggressive with a high recurrence rate.
Method: A 19 year old woman presented with painless hard swelling of abdomen. During surgery, a giant mass measuring 37 × 26 × 12 cm within the distal pancreas invading spleen was noted. The clinical diagnosis of solid cystic pseudopapillary tumour of the pancreas was suspected.
Results: Distal pancreatectomy, splenectomy and debulking surgery was performed. Histopathologic analysis showed that the tumour had infiltrated the spleen and pancreatic parenchyma and sections of the solid areas revealed proliferation of spindle-shaped or stellate cells growing in fascicular and storiform patterns within a myxoid intercellular matrix. Cystic areas were entrapped excretory pancreatic ducts. Interestingly, there were two ectopic adrenal tissues peripherally. The histopathologic and immunohistochemical features were consistent with solid cystic desmoid tumour of pancreas.
Conclusion: Desmoid tumours of the pancreas are very rare and if they present as a solid-cystic lesion their diagnosis can be difficult. We report the case for its rarity and huge size and emphasize regular follow up since long-term prognosis is currently unkown.

A gross photo of the case:



PS-16-031
Relationship between CD4+/CD8+ T lymphocytes and necroinflammatory activity in chronic hepatitis B and C
I.-D. Caruntu*, C. Amalinei, A. Grigoras, L. Lozneanu, S. E. Giusca, R. E. Avadanei
*U.M.F. Gr. T. Popa Iasi, Dept. of Morphofunctional Sciences, Romania

Objective: Our study aimed to evaluate the degree of correlation between lymphocytes modulation of necroinflammatory process in chronic hepatitis B and C and the severity of specific lesions.
Method: We investigated 33 and 38 cases with chronic hepatitis B and C, respectively. Immunohistochemical labeling was performed by anti-CD4 and anti-CD8 antibody. The quantitative assessment was performed by counting positive cells in 10 microscopic fields with the highest density of lymphocytes, at 200 × magnification. Statistical analysis used GraphPad Prism ver. 6 (GraphPad Software Inc., La Jolla, CA, USA).
Results: In chronic B hepatitis, CD8+ T lymphocytes showed a statistically significant increase of number between mild versus moderate necroinflammatory activity ($p = 0.01$), mild versus severe ($p = 0.0007$) and moderate versus severe necroinflammatory activity ($p = 0.02$), and CD4+ T lymphocytes showed statistically highly significant differences between the three degrees of necroinflammatory activity ($p < 0.0001$).

Analogous, high degree of statistical significance ($p < 0.0001$) has been recorded in chronic hepatitis C, for both subtypes of lymphocytes.
Conclusion: Our data demonstrate the relationship between T lymphocytes and the disease severity degree, without differences between chronic hepatitis B and C. This feature suggests a similarity of the initial pathological process.

PS-16-032
Severe acute hepatitis associated with varicella-zoster virus infection
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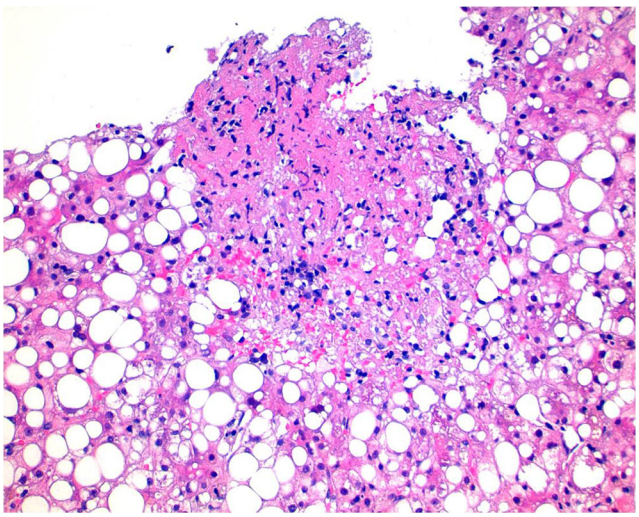
*Centro Hospitalar São João, Dept. of Surgical Pathology, Porto, Portugal

Objective: Several viruses may cause hepatic injury that can range from transient elevation of aminotransferases to acute fulminant hepatitis. We present a case of acute severe hepatitis associated with varicella-zoster infection.
Method: A 19 year-old female patient was admitted with a vesiculopustular rash involving the face, trunk and mucosas. Cushing syndrome associated with a hypophyseal adenoma had been diagnosed in this patient. Two weeks before admission she contacted with a sister with varicella-zoster infection. Laboratory tests showed leukocytosis, neutrophilia, mild trombocytopenia, rhabdomyolisis, high levels of TGO (1874 U/l), TGP (2163 U/l) and GGT (342 U/l). The diagnosis of acute hepatitis was established and a liver biopsy was performed.
Results: By histology, the liver parenchyma displayed diffuse macrovesicular steatosis and multiple nodular foci of confluent coagulative necrosis, a pattern described in the literature as "granulomatous necrosis". Widespread cholestasis with bile thrombi was observed. Viral inclusions, nuclear or cytoplasmatic, were not identified. Ziehl-Neelsen staining for acid-fast bacilli was negative.
Conclusion: Varicella is usually a self limited disease. Visceral complications can occur in 30–50 % of immunocompromised patients. Disseminated disease can course with severe acute hepatitis and it can be fatal in the absence of antiviral therapy. "Granulomatous necrosis" may be a hint for the nosological diagnosis.

"Granulomatous" hepatic necrosis:



PS-16-033
Prognostic value of angiogenic and cell proliferation immunohistochemical markers in hepatocellular carcinoma and cholangiocarcinoma
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Objective: To analyze the prognostic value of immunohistochemical expression of angiogenic and cell proliferation markers in hepatocellular carcinoma and cholangiocarcinoma, and compare them with literature data.
Method: In this study were included 110 patients with hepatocellular carcinoma and cholangiocarcinoma diagnosed between 2000 and 2012 in Fundeni Clinical Institute, Bucharest, Romania.
Results: Studied cases were represented by 28 (23.0 %) cholangiocarcinomas (15 male and 13 female, mean age- 54.11, average tumour size- 7.73 cm) and 82 (67.2 %) hepatocellular carcinoma (25 female and 57 male, mean age- 57.62, average tumour size- 4.06 cm). In 61 cases was performed immunohistochemistry for VEGF (18 cases with colangiocarcinoma and 43 cases with hepatocelular carcinoma) and in 35 cases for CD 34 (9 cases with colangiocarcinoma and 26 cases with hepatocelular carcinoma), all cases being tested for Ki67 with assessing the differences and correlations between groups mentioned above.
Conclusion: Ki67 was over expressed in intrahepatic cholangiocarcinoma and it is correlated with the survival making it a promising independent prognostic immunohistochemical marker. VEGF was expressed in about 95 % of cases with hepatocellular carcinoma and colangiocarcinoma, and CD 34 was expressed in 80 % in cases with hepatocellular carcinoma versus about 90 % of cases with colangiocarcinoma, resembling slight increase in neovascularization.

PS-16-034
Tryptase positive mast cells in colorectal liver metastases
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Objective: Our study aimed to realize a qualitative and quantitative characterization of tryptase positive mast cells (MCT+MCs) in colorectal liver metastases and to analyze their possible role as prognostic factor.
Method: Fifty patients diagnosed with colorectal liver metastases were included in the study. Mast cells were identified by using mast cell tryptase antibody and assessed at intratumoral and peritumoral levels. The quantitative data were statistically correlated with clinicopathological factors and overall survival.
Results: Within tumoural areas a small number of MCT+MCs scattered between the tumoural cells and grouped around blood vessels were identified. The number of MCT+MCs was higher at the invasion front, as compared to intratumoral zones, and their presence was associated with the inflammatory infiltrate. Non-degranulated MCT+MCs were predominantly disposed intratumoral, while degranulated type was identified mostly peritumoral. Intratumoral MCT+MCs were significantly correlated with tumour grade and N parameter from TNM staging, and significant differences were noted between peritumoral MCT+MCs and overall survival.
Conclusion: Our study offers evidences for the promoter role of mast cells in metastatic process. Moreover, mast cells presence within the inflammatory infiltrate that outline the metastatic area sustains their involvement in the activation of a local immunologic defense that can influence the survival rate.

PS-16-035
Adenosquamous carcinoma of the extrahepatic bile duct: A case report
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*Altunizade Mah. Atifbey Sokak, Istanbul, Turkey

Objective: Adenosquamous carcinoma is a tumour composed of both adenocarcinoma and squamous cell carcinoma components, especially adenocarcinoma containing significant amounts of unequivocal squamous carcinomatous elements, with keratin and/or intercellular bridges.

Method: A case of adenosquamous carcinoma in a 49 year old man from extrahepatic bile duct is presented.
Results: Abdominal computed tomography scan revealed a low density in the right segment of liver. Right hepatic lobectomy was performed, and grossly, a well defined solid mass was found measuring 8.0 x 5.0 x 2,5 cm. The histopathologic findings showed adenosquamous carcinoma with a mixture of adenocarcinoma and squamous cell carcinoma. Immunohistochemically, the squamous areas were positive for high molecular weight cytokeratins, CK5/6, p63. These markers were negative in the adenocarcinoma component. The patient died 12 months after surgery.
Conclusion: The incidence of adenosquamous carcinoma is rather common in the gall bladder, pancreas, stomach, thyroid, large intestine and liver. Primary carcinoma of the extrahepatic bile duct is a rare tumour that represents less than 1.0 % of all malignant neoplasms and less than 3.0 % of all the tumours of the gastrointestinal system.

PS-16-036
Septate gallbladder occurring in adults: Report of 20 cases
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Objective: Septate gallbladder (GB) is a rare congenital abnormality that may impact on bile streaming and stagnation. We aimed to report the characteristics of 20 cases of GB septae occuring in adults, diagnosed on surgically resected gallbladder specimens.
Method: 20 surgically resected GBs with parietal septae were selected. The main clinical and morphological features of the resected specimens were tabulated and studied for relationships.
Results: The age varied between 19 and 93 years (median, 66) and the gender ratio was 1:1. All GB showed chronic cholecystitis but one (acute cholecystitis). Lithiasis was seen in 16 GBs. All GB-septae comprised two mucosas and two muscle layers, either fusioned (8) or separated by adventitial tissue (n = 12). The septum size varied between 2–14-mm in height, ten septae being greater than 5-mm. Multiple septae were observed in 8 GBs and complete septae in 5.
Conclusion: The results of our study suggest that GB septae show a wide range of sizes from milimetric to above 1-cm. Rare cases may be alithasic or associate to acute cholecystitis.

Wednesday, 9 September 2015, 09.30 – 10.30, Restaurant
PS-17 Poster Session Electron Microscopy

PS-17-001
Ultrastructural abnormalities essential for diagnosis of Tufting Enteropathy
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Objective: Tufting enteropathy (intestinal epithelial dysplasia) is a rare congenital enteropathy related to severe intractable diarrhea with early onset due to specific abnormalities of the intestinal epithelium. We report a case with distinguished ultrastructural characteristics.
Method: Four-month old male infant was admitted in Pediatric Clinic because of protracted watery diarrhea in a period of 3 weeks and failure to thrive. After thorough clinical and laboratory examination, duodenoscopy was done. Biopsy specimens were fixated in glutaraldehyde and embedded in Durcupan resin. Semi-thin sections dyed with Toluidine Blue and ultra-thin sections treated with Uranyl Acetate and Lead Citrate were made.
Results: Light-microscopic analysis shows small intestinal mucosa with variable abnormalities of villous projections, which were flattened in parts. Focally, there was evident crowding of surface enterocytes, disorganization and focal forming of tear-shaped tufts. There was low mononuclear cell infiltration in lamina propria. Electron-microscopic analysis shows reduced number of microvilli of surface enterocytes, with structural disorganization, represented by desmosomes increased in number and length. There was evident tufts formation with disruption of brush border in their vicinity, whereas basement membrane was stratified and laminated.
Conclusion: Tufting enteropathy is a rare genetic disease for which transmission electron microscopy is a superior diagnostic tool.

PS-17-002
Scanning microscopy as diagnostic test of cancer of organs of urinary system
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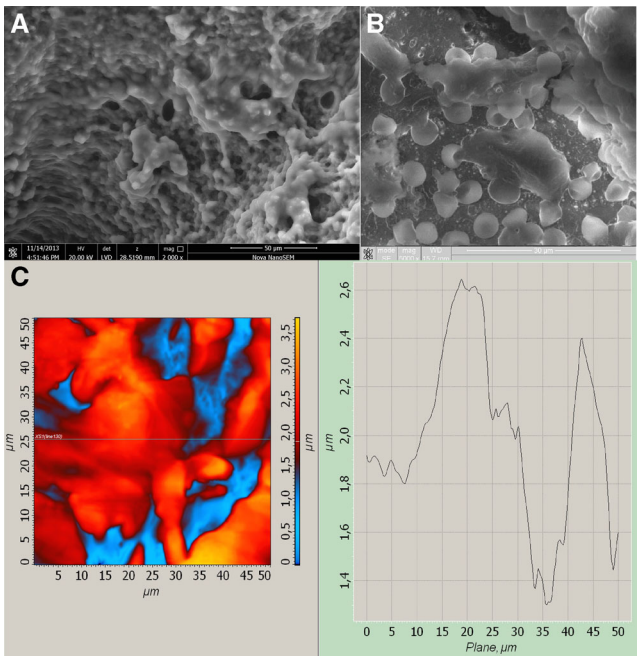
Objective: The problem of cancer of urinary system obtained particular actuality to date due to steady growth of indexes of mortality and morbidity and also with connection of difficulties of early diagnostics.
Method: The research of postoperative biopsy samples of 120 patients, who underwent surgery for cancer of kidney, urinary bladder and prostate. Scanning microscopy was carried out directly after surgery without fixations of samples.
Results: The prognostic significance of increasing of oxygen, sodium, magnesium, phosphorus in place of presence of tumour cells is revealed at use of point determination of macro- and microelements under control of electron microscopy The progressive decreasing of these elements at the distance from tumour clone was revealed. The raster and atomic power microscopy helped to reveal weak connection between tumour cells, their three-dimensional sizes were shown, the congestion of clones from several cells and passage of tumour's emboli through endothelium of blood vessels also were showed.
Conclusion: Complex use of biochemical and morphological methods allowed to enter new data in research of morphogenesis of malignant tumours of urinary system. The scanning microscopy can be used as an express-method for diagnostics of tumour growth.

Fig 1:



PS-17-003

Morphological characteristics and the presence of lipid droplets in mononuclear leukocytes of healthy persons and persons with hyperlipidemia treated with Lovastatin in vitro

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Objective: It was recently shown that lipid droplets appear in the cytoplasm of cocultured lymphocytes and monocytes incubated 24 h in vitro. We tried to determine whether the addition of lovastatin for 24 h in the culture medium affects the morphology of the cells and formation of lipid droplets in mononuclear cells taken from peripheral blood.
Method: Mononuclear cells taken from peripheral blood of hyperlipidemic and normolipidemic persons were incubated with and without lovastatin for 24 h. Subsequently cells were fixated with glutaraldehyde, embedded in EPON resins, and ultra-thin sections were made. Transmission electron microscope (Morgagni 268D) photomicrographs were used to determine morphological characteristics of cells and analyzed with coherent point grids to determine the fractional volumes of lipid droplets in the cytoplasm of mononuclear cells.
Results: After 24 h incubation cultured mononuclear cells from hyperlipidemic persons contained larger numbers of autophagic vacuoles and lipid droplets than cultured mononuclear cells from normolipidemic persons. Lovastatin treatment did not influence the number or volume of lipid droplets in all cultured cells.
Conclusion: The results do not support the role of cholesterol metabolism and lovastatin in vitro treatment in the formation of lipid droplets in mononuclear cells.

PS-17-004

Quantitative analysis of autophagy and mitochondria damage in different types of neuroblastoma

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Objective: It was suggested that spontaneous neuroblastoma cell death may occur via autophagic degeneration. On the other hand, autophagy plays a protective role in tumour cells. It is well established that mitochondrial dysfunction can trigger an autophagic response. The aim of this study was to quantify autophagic vesicles and damaged mitochondria in the cells of different neuroblastoma subtypes.
Method: Tumour tissue biopsies of neuroblastoma, ganglioneuroblastoma and ganglioneuroma were obtained from pediatric patients, fixed in glutaraldechide, embedded in EPON and thin sections were examined by transmission electron microscope (Morgagni 268D). Autophagosomes, autolysosomes, intact and damaged mitochondria were counted on photomicrographs. Results were presented as numbers of autophagic vesicles and as the percentage of damaged mitochondria in the cells of different neuroblastoma subtypes.
Results: There are statistically highly significant differences in the numbers of autophagic vesicles between all three subtypes of neuroblastoma specimens studied with more aggressive tumours having larger numbers of these structures. There are highly statistically significant differences in the proportion of damaged mitochondria between the poorly differentiated neuroblastoma specimen vs. ganglioneuroblastoma and ganglioneuroma specimens with more aggressive tumours having larger numbers of damaged mitochondria.
Conclusion: Results of this study emphasize the importance of autophagy and mitochondria damage in more aggressive neuroblastoma subtypes.

PS-17-005

Innovative approaches for study of placenta at preeclampsia

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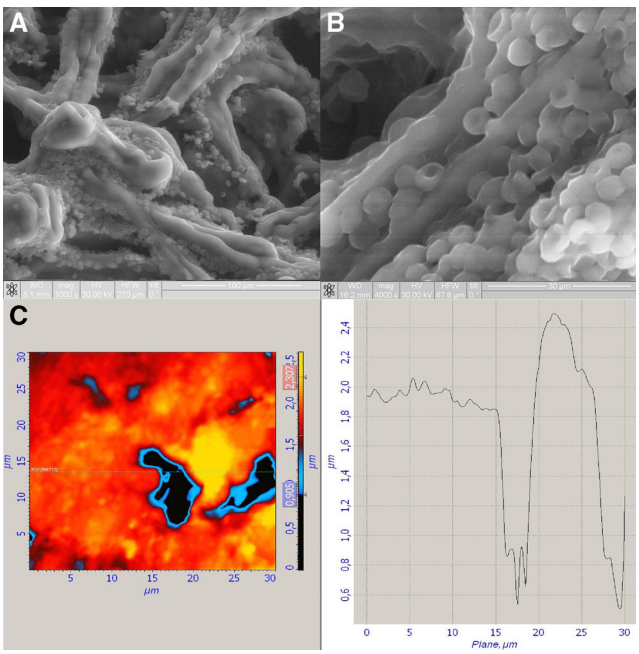
Objective: Alterations in placenta at preeclampsia may render significant influence on condition of mother and fetus.
Method: Eighty five placentas of women with preeclampsia were researched by light, transmissional and raster microscopy with elemental analysis.
Results: The number of intermediate villi was increased and the number of terminal villi was decreased. Spasm of some vessels was along the entire length, their depth was 1,2 ± 0,5 μm(1,9 ± 0,4 μm in control group). Another group of vessels were full-blooded. The decreasing of relief's drop (1,4 ± 0,2 and 1,7 ± 0,1 μm) due to sclerotic tissue was predominately inside the villi. The growth of fibrinoid occurs. Blood clots were detected in 20–25 % of vessels. Erythrocytes in capillaries and intervillous space were spiciform and deformed and had forms of normocytes, bloated disk, complete and incomplete sphere. The number of microcytes was increased. The destruction of syncytiotrophoblast with fragmental zones of necrosis and desquamation were detected. The content of oxygen, magnesium and phosphorus was decreased in endothelium cells and syncytiotrophoblast.
Conclusion: The desquamation of syncytiotrophoblast and villi, alteration of erythrocytes' forms contributes to further progression of preeclampsia, but violation of blood circulation, decreasing of content of microelements in chorion threaten the fetus and newborn.

Fig 1:



PS-17-006

Properties of esophageal neosquamous epithelium in Barrett esophagus patients treated with endoscopic radiofrequency ablation

O. Skrobic*, T. Martinovic, D. Ciric, A. Simic, P. Pesko, V. Bumbasirevic, T. Kravic Stevovic
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Objective: Radiofrequency ablation (RFA) of Barrett esophagus (BE) has been proven as effective procedure in complete eradication of metaplastic and dysplastic epithelium. Concern was given upon dilated

intercellular spaces (DIS) inside neosquamous epithelium (NSE), as it could lead to BE recurrence. We measured the intercellular spaces of NSE by comparing it to that of the native upper squamous epithelium (USE) in patients after RFA, and consecutive surgical or proton pump inhibitors (PPI) treatment.
Method: Endoscopic biopsies were obtained from NSE in patients who underwent RFA. Biopsies of NSE were compared to USE from the same patients morphologically by electron microscopy. Biopsies were fixed in glutaraldehyde, embedded in EPON and thin sections were examined by transmission electron microscope (Morgagni 268D). On each photomicrograph (magnification 2800x) the diameter of the intercellular space for each cell layer is obtained in microns by measuring the length of a line drawn perpendicularly to the neighboring membranes.
Results: Diameters of intercellular spaces of NSE were higher than those of USE in all of the specimens studied. These differences were shown to be statistically highly significant ($p < 0.01$).
Conclusion: The results of this study emphasis the presence of DIS inside NSE, and need for endoscopic follow-up despite complete macroscopic BE eradication.

PS-17-007
Generalized exfoliative dermatitis as a manifestation of chronic multifocal type of Langerhans cell histiocytosis
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*KCS Belgrade, School of Medicine, Clinic of Dermatovenereology, Serbia

Objective: Langerhans cell histiocytosis (LCH), previously known as histiocytosis X, is a rare idiopathic disorder of reticulo-endothelial system with abnormal proliferation of bone marrow derived Langerhans cells. The clinical presentation of LCH is variable and it mostly affects the skin and mucosa in the form of seborrheic dermatitis-like lesions on face and scalp along with internal organ involvement. Fortyfive-year-old male diagnosed with LCH with lung and lymph node involvement developed generalized exfoliative dermatitis - erythrodermia.
Method: Skin biopsy was fixed in 3 % glutaraldehyde, rinsed in cacodylate buffer, dehydrated in ethanol and propylene oxide, and processed for embedding in EPON. Ultrathin sections were stained with uranyl acetate and lead citrate, and examined by transmission electron microscope (Morgagni 268D).
Results: Langerhans cell histiocytosis was confirmed by electron microscope examination of skin biopsy. Specific markers of LCH, known as Birbeck granules, were found in the cytoplasm of histiocytes found in connective tissue of the skin samples. These granules possessed tennis-racket morphology with transverse striations. Intercellular edema was found between keratinocytes.
Conclusion: This case of LCH is unusual due to the generalized involvement of skin with the disease, and the skin presentation of LCH in the form of erythrodermia.

Wednesday, 9 September 2015, 09.30 – 10.30, Restaurant
PS-18 Poster Session IT in Pathology

PS-18-002
Karyometry and Ki-67 expression in minimal deviation melanomas
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Objective: Minimal deviation melanoma is a controversial entity encompassing a heterogeneous group of lesions, composed of a monotonous cell population, that were more atypical than ordinary nevi but less atypical than conventional melanomas. In a dermatopathology practice, placement of these problematic lesions into benign or malignant categories is difficult. The aim of this study was to estimate karyometric variables and Ki67 index in minimal deviation melanomas.
Method: On digital pictures, karyometric variables (nuclear area, optical density, Feret diameter, perimeter, circularity, and integrated optical density (IOD)) and Ki-67 index were estimated in deep portions of 10 cases of minimal deviation melanomas, 15 cases of nodular malignant melanomas, 10 Spitz nevi, 5 cases of cellular blue nevi, and 22 cases of compound nevi, using software ImageJ. In each case a hundred nuclei were measured.
Results: In minimal deviation melanomas, Ki-67 index and nuclear size were higher than in Spitz nevi, cellular blue nevi and compound nevi ($p < 0.05$). Differences between minimal deviation melanomas and nodular malignant melanomas were not statistically significant.
Conclusion: The results from our study suggest that karyometry and Ki-67 index, estimated in deep portions of the lesions, can be used as diagnostic tool in dermatopathology of melanocytic tumours.

PS-18-003
Fractal dimension of stromal fibrillar network: A new approach to prostate carcinoma architectural assessment
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Objective: The current method of grading prostate carcinoma uses the Gleason system, which has been shown to be influenced by inter/intra observer variability. In order to overcome this drawback, computer aid grading systems have been proposed, almost all of them targeting cellular or glandular components. We propose a new approach to Gleason pattern evaluation by tumour stroma assessment through a computational based image evaluation.
Method: From a total number of 34 cases, 299 digital images of the tumoural fibrillary network, labeled following Gleason system were acquired from Gömöri stained sections with 20x magnification. Fractal dimension, estimated through a box counting algorithm was computed on the skeleton of the black and white (binary) images obtained with a fixed threshold from the tumoural fibrillary network images.
Results: The computed fractal dimension and it's standard deviation for each Gleason pattern were 1.457/0.051 (G2), 2.450/0.069 (G3a), 1.503/0.056 (G3b), 1.504/0.052 (G3c), 1.423/0.083 (G4a), 1.547/0.055 (G4b), 1.618/0.033 (G5a), 1.590/0.079 (G5b), showing significant discrimination between different patterns.
Conclusion: Results show that stromal component assessment, even though rarely taken into consideration for diagnosis, can be a reliable tool in prostate cancer grading. This paper was published under the frame of European Social Found, Human Resources Development Operational Program 2007–2013, project no. POSDRU/159/1.5/136893.

PS-18-004
3D reconstruction of bone tissue from histologic sections in osteoporosis
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Objective: Osteoporosis is degenerative diseases and major health problem of the 20-first century. Osteoporosis is characterized by reduced bone mass and strength, and typically afflicts women in the sixth decade of life. In osteoporosis, bone biopsy is the only method that reveals the trabecular architecture. The aim of this study is to reveal usefulness of 3D reconstruction of bone tissue from histologic sections to estimate trabecular atrophy, and interruption of trabecular continuity in osteoporosis.
Method: Twenty four bone specimens were extracted from the lower limb ($n = 12$) and maxilla ($n = 12$) of patients with osteoporosis

(n = 16) and without pathological conditions (n = 8). Formalin-fixed samples of bone tissue were decalcified by formic acid and embedded in paraffin wax. Histological sections, 5 um thick, were routinely stained with hematoxylin and eosin and Masson trichrome. Integrated optical density (IOD) of decalcified bone tissue was estimated by ImageJ software. Alignment and tracing of serial sections were done by Reconstruct software.
Results: Trabecular thickness was significantly lower in osteoporotic patients compared to normal patients. In contrasts, IOD and interruption of trabecular continuity were significantly higher in osteoporotic patients compared to control group.
Conclusion: 3D reconstruction of bone tissue from histologic sections reveals increased interruption of trabecular continuity in osteoporotic bone tissue.

PS-18-005
Impact of staining method and automatization of hot-spot selection on Ki-67 index in meningiomas and oligodendrogliomas
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Objective: The Ki-67 index in meningiomas and oligodendrogliomas helps to discrimination of patients into good and worse prognostic groups. Introduction of autostainer equipment and automatization of hot-spot selection in a WSI effect changes in Ki-67 ranges that should be evaluated.
Method: The 15 cases of meningiomas and oligodendrogliomas were stained one manually with the liquid monoclonal mouse anti-human Ki-67 antigen (clone MIB-1, Dako, code M7240), and second with the ready-to-use FLEX Ki-67 antigen (Dako, code IR626) in Dako Autostainer Link. After digitalization to WSI a selection of hot-spots was done manually by an expert and automatically with an proposed algorithm based on mathematical morphology and penalty function.
Results: The comparison of Ki-67 index counted in the expert's selected hot-spots indicates an average 2.3 % higher level in automatically to manually stained specimens. Against, the automatic hot-spot selection results average 3.5 % increasing in Ki-67 level in manually stained specimens whereas only 1 % in FLEX.
Conclusion: The FLEX and autostainer's procedure effect about 3 % higher results of Ki-67 index evaluation in meningiomas and oligodendrogliomas. The automatic hot-spot selection effects a more stable results than in manually stained specimens. This work has been supported by the National Centre for Research and Development (PBS2/A9/21/2013 grant).

PS-18-006
Novel digital microscopy technology for rapid histological imaging of freshly excised tissue
D. Kosanic*, B. Rachet
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Objective: Histological imaging of freshly excised tumour tissue, without the need for freezing or fixing, offers the possibility of rapid and non-destructive histo-pathological assessment of resection margins and invasion of sentinel lymph nodes during ongoing tumour surgeries.
Method: SamanTree Medical has developed a novel digital microscopy approach, which enables rapid histological imaging of fresh tissue at high resolution (sub-micron) over a large field of view (several cm2).
Results: We present here the imaging proof-of-concept on fresh and thick tissue of animal and human origin.
Conclusion: We believe that this approach is ideally-suited for rapid intra-operative histo-pathological assessment.

PS-18-007
Systematic cancer tissue collection with associated hematological biomaterial: The CRO-Biobank experience in a clinical setting
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Objective: CRO-Biobank (the Biobank of the National Cancer Institute CRO Aviano) is a structured facility integrated in a clinical setting aimed at collecting human biological samples for cancer research purposes. Many biobanks are growing worldwide, but our challenge was to organize a collection of tissue samples with associated biomaterials: serum, plasma (with different anticoagulants), buffy coat and nucleid acid extracted both from tissue and from blood.
Method: Tissue and other biosamples are collected from patients who underwent surgery for different cancer pathologies. Tissue samples are paraffin-embedded and, when possible, OCT-embedded and stored at −80°C. Well defined tissue control methods are used: histocytology (frozen sections, FFPE mirrored samples, and cytological imprint) and molecular pathology. Molecular analyses are randomly performed as methods for DNA, RNA and protein quality checks, using appropriate positive and negative controls, with promising results.
Results: From 2009 we collected more than 10,000 blood samples (associated with tissue samples) from about 3000 patients. We optimized technical and quality processes, while also investigating ethical, legal, and IT topics. We implemented processes aimed at guaranteeing the safety of the providers, protecting patient privacy, and ensuring both the traceability and the quality of samples. We are evaluating an alternative one-step tissue biomarker and histology preservative for clinical diagnosis, molecular analysis and biobanking.
Conclusion: Our pluriannual experience allows to offer insights and useful suggestions that may serve as reference model for similar initiatives.

PS-18-009
Evaluation of synoptic pathology reporting of dutch colorectal carcinomas
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*Radboud Univ. Medisch Centrum, Dept. of Pathology, Nijmegen, The Netherlands

Objective: In 2009 the Dutch Pathology Registry (PALGA) introduced synoptic reporting (SR) in the Netherlands for colorectal carcinoma (CRC) resections. This study investigates whether SR improved the quality of gross examination and pathology reports compared to narrative reports (NR).
Method: Pathology data of all CRC patients from 2007 to 2013 was gathered using the Dutch Cancer Registry, (data from NR and SR), and linked to PALGA (SR data). Quality of CRC gross examination and PA reports was evaluated by the percentage of ≥10 lymph nodes (LN) collected and the percentage of reported circumferential margin (CRM) respectively and compared between SR and NR.
Results: Data on 84098 patients was collected, 31.5 % patients had rectal carcinoma. 64494 patients received a NR and 19604 a SR. The percentage of ≥10 LN collected between 2009 and 2013 was higher in SR (85.12 %) than NR (52.50 %) ($p < 0.001$). Furthermore, CRM was reported more often in SR (99.7 %) vs NR (86.5 %) for rectal carcinoma.
Conclusion: It appears that the percentage of ≥10 LNs collected from a CRC resection specimen increased at least partly due to SR. Additionally, SR seems to positively influence the reporting of CRM. Further analyses are necessary to study the effect of SR.

PS-18-010
Description of cells and their spatial interaction in digitalized histological bone marrow sections by scalar fields
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Objective: Analysis and description of bone marrow are demanding due to its heterogeneous cellular composition, the poor delineation and overlap of functional compartments, and highly complex immunophenotypes of several cell populations. To overcome these difficulties, we present an approach to describe objects in histological slides (e.g. cells, bone trabeculae) by a scalar field.
Method: The transformation of objects within images to a scalar field was performed by convolution of the object's centroids with differently formed radial basis functions (e.g. for direct or indirect spatial interaction).
Results: After image registration i) the scalar field, which is quite resistant to matching errors and minor morphological alterations, could be propagated through registered images; ii) the overlap of fields, which represents the spatial distance of different objects (e.g. two cells), could be calculated by the histogram intersection; iii) several well-established co-localization measurements (e.g. the Manders overlap coefficient) could be calculated; iv) the summation field of object groups could be used to identify clusters.
Conclusion: The description of objects (e.g. cells, cell clusters, bone trabeculae) as field facilitates the combination of information from serial sections, and allows automatic identification of object clusters and the analysis of different types of spatial interaction (e.g. direct vs. paracrine).

PS-18-012
Towards a Dutch National Tissuebank Portal: One portal to access all pathology archives for research
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*Foundation PALGA, Research & Registry, Houten, The Netherlands

Objective: The Dutch National Tissuebank Portal (DNTP) project aims to achieve increased, easier and improved secondary use of residual human tissue samples (FFPE blocks) from all pathology laboratories in the Netherlands.
Method: Currently, there are more than 60 million archived FFPE samples with standardized associated data which can be used for research purposes. With the DNTP researchers can request samples online through the portal from where the request will automatically be sent to the pathology laboratory where the samples are stored. After approval from a research- and privacy committee and the participating laboratory a DNTP employee will collect the samples and send them to the researcher. Pathology laboratories can request a sample to return, if this sample is needed for delayed patient care.
Results: The result will be that in the Netherlands we have established a professional research infrastructure that will provide virtual and physical access to all residual FFPE pathology samples and their associated data for research purposes. Nowhere in the world does such a web based portal exist that supports pathology laboratories and researchers in their quest of searching, requesting, registering, retrieving and returning archived FFPE samples for research from all the national pathology archives.
Conclusion: This project was financially supported by Biobanking and Biomolecular Research Infrastructure The Netherlands (BBMRI-NL), a Research Infrastructure financed by the Dutch Government (NWO 184.021.007). BBMRI-NL co-ordinates the collaboration between Dutch biobanks. It is not a biobank itself, but facilitates collaboration by harmonization and enrichment of existing biobanks.

Wednesday, 9 September 2015, 09.30 – 10.30, Restaurant
PS-19 Poster Session Nephropathology

PS-19-001
Role of complement in the pathogenesis of hypertension?
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*Universität Erlangen-Nürnberg, Inst. für Nephropathologie, Germany

Objective: Complement deposition is frequently observed in kidney biopsies of patients with hypertensive renal disease, but an association of hypertension and complement deposition or involvement of complement in the pathogenesis of hypertensive nephropathy has not been investigated.
Method: 230 archival human renal biopsies with hypertensive nephropathy and 80 control biopsies with non-hypertensive renal diseases were investigated using immunohistochemistry and semi-quantitative scores. The results were correlated with renal function. To address whether complement was only passively deposited or actively expressed by renal cells, complement deposition, C1 and C3 mRNA expression was analyzed in the 5/6 nephrectomy model of hypertension (n = 12) and controls (n = 10).
Results: Glomerular C1q and C3c complement deposition was significantly higher in hypertensive patients and rats than in non-hypertensive controls. Mean arterial blood pressure in 5/6-nephrectomy rats correlated well with the amount of C1q (r = 0.790; $p < 0.0001$), C3c deposition (r = 0,697; $p < 0.0003$) and also with left ventricular weight (C1q: r = 0.819; C3c: r = 0.621; $p < 0.002$). C3 was not only deposited but also produced by renal cells of hypertensive rats as assessed by quantitative mRNA analysis. Of note, in hypertensive patients renal function as measured by creatinine clearance correlated significantly negative with the intensity of C1q staining ($r = -0.322$; $p = 0.001$), but not with that of C3c.
Conclusion: Hypertensive nephropathy, but not other non-hypertensive renal diseases, was significantly associated with in-situ expression and deposition of complement. This finding may open new therapeutic options. Since complement activation is known to have multiple disease promoting effects further investigations are needed to identify whether it is involved in the pathogenesis or progression of hypertensive nephropathy.

PS-19-002
An unusual case of IgA-dominant glomerulonephritis
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Objective: Glomerular IgA-dominant deposition in the setting of proliferative glomerulonephritis usually indicates IgA nephropathy, and is rare in postinfectious glomerulonephritis (PIGN). IgA-dominant PIGN is an immune complex-mediated glomerulonephritis that occurs following staphylococcal infection. The typical histological pattern of IgA-dominant PIGN includes endocapillary or mesangial proliferative glomerulonephritis. By electron microscopy subepithelial "hump-shaped" deposits are shown.
Method: We report a case of IgA-dominant glomerulonephritis in 49 years old male presenting acute kidney injury, nephrotic range proteinuria and hematuria. The patient had not documented infections at the time of the presentation. He suffered from ischemic heart disease, cardiac insufficiency, mitral regurgitation, tricuspid insufficiency, septal aneurysm and hypertension. Renal biopsy was done and light microscopy revealed thickening of glomerular capillary wall and slight segmental and focal endocapillary and mesangial hypercellularity. Immunofluorescence showed strong coarse granular immunostaining of IgA, IgG and C3, lower immunostaining of kappa light chain and weak immunostaining of lambda light chain along glomerular capillary wall. On electron microscopy, subepithelial electron-dense deposits, small intramembranous deposits and some large hump-shaped deposits were present.
Results: The presented case does not entirely meet criteria of PIGN, because of lack of clinically proven infection. Moreover in the light microscopy the thickening of capillary wall was dominant, whereas mesangial or endocapillary hypercellularity was focal and segmental.
Conclusion: An unusual case of IgA-dominant PIGN should be taken into consideration, as the infection may be subclinical. In differential diagnosis the IgA nephropathy should be considered. Discriminating between postinfectious IgA-dominant glomerulonephritis and idiopathic

IgA nephropathy is of value, because of the different treatments and prognosis of the two diseases.

PS-19-003

The diagnostic challenges in Alport Syndrome: A case report

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Objective: Collagen IV-related nephropathies comprise a spectrum of phenotypes from Alport syndrome (AS) to thin basement membrane nephropathy (TBMN). It has been and still is a major clinical challenge to differentiate between TBMN characterized by nonprogressive hematuria and Alport syndrome with progressive hematuria as the main symptom.
Method: 8-year-old girl was admitted to Pediatric Department due to hematuria. The patient underwent a kidney biopsy which showed a normal gromeruli, Immunofluorescence with IgG, IgA, IgM, and C3 was negative. Electron microscopy revealed diffuse thinning of glomerular basement membrane. On the basis of ultrastructural findings TBMN was established.
Results: Four years later the girl was admitted to Pediatric Department due to hematuria and proteinuria 2g/24 h. Rebiopsy was performed. Renal tissue contained glomeruli with slight mesangial hypercellularity and mesangial matrix expansion. Immunofluorescence with IgG, IgA, IgM, C1q, C3, lambda light and kappa light chain was negative. Renal tissue for electron microscopy study contained seven glomeruli with 3 mesangial cells in mesangial area and increase in mesangial matrix. Measurement of GBM was performed. Glomerular basement membrane was not uniformly thin, and had an irregular epithelial surface. There were thick areas as well as thin, patches of complex splitting of the lamina densa (a "basket-weave" pattern). On the basis of electron microscopy study nephropathy in Alport Syndrome was diagnosed.
Conclusion: This case illustrates difficulties in the differentiate thin basement membrane nephropathy and nephropathy in Alport Syndrome. The changes in GBM usually become more marked with time, and definite diagnosis may require another renal biopsy, a few years after the first.

PS-19-004

Diagnostic and subtyping problems in patients with renal amyloidosis

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Objective: In Turkey the prevalence of renal amyloidosis is very high and it is common to evaluate only amyloid A immunohistochemistry for amyloid subtyping. In this study, consulted renal amyloidosis cases were reviewed.
Method: Between 2010 and 2015 years, 115 patients were diagnosed as renal amyloidosis. Twenty-five of them were evaluated on other centers and then diagnosed amyloidosis at our center were included in this study. Original pathology reports, clinical features, laboratory data were correlated with ancillary studies that performed in our center. In secondary amyloid subtyping non-renal organ biopsies as well as clinical features and laboratory data were used.
Results: Amyloid A positivity reported eight cases were evaluated as non-AA amyloidosis. Nine AA amyloidosis cases' mean age was 40 and follow-up was 35 months. Sixteen non-AA amyloidosis cases' mean age was 57 and their follow-up was 18 months. Two of AA and eight of non-AA cases died during this study. Misdiagnosed %12 amyloidosis cases and %32 amyloid A immunohistochemical positivity has lead to follow up and treatment problems.
Conclusion: In our country because of the AA amyloid frequency, only amyloid A identification can cause problems on follow up and treatment. This series once again demonstrate the requirement of standard and multidisciplinary approach.

PS-19-005

Prognostic evaluation of CD44 expression in renal clear cell carcinomas

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Objective: Renal cell carcinoma (RCC) is the most lethal urologic cancer. The most common type of RCC is the clear cell renal carcinoma (ccRCC). Currently, the curative treatment is surgery. However, 20–30 % of patients with ccRCC recurrence within 5 years after an initial nephrectomy. Recent reports have shown that expression of CD44 may play an important role in predicting prognosis.
Method: We investigated CD44 immunohistochemical expression in 89 paraffin- embedded ccRCC tissue samples and its correlation with tumour clinicopathological parameters and patient survival.
Results: The 55 (61,79 %) ccRCC specimens displayed a positive membranous staining reaction for CD44, while 34 (38,21 %) had a negative staining. Positive staining was defined as (1 < 25 % of epithelial cells), 2(25–50 %), 3(>50 %). For statistical analysis the stained tumours tissues were divided into two groups: in the CD44-low expression group in which included the samples(1,2) and negative cases (CD44-LEG = 68cases) and those in CD44-high expression(3) (CD44-HEG = 21cases). The CD44-HEG compared with CD44-LEG tender to have higher Tstage ($P < 0{,}0013$). Also CD44-HEG was significant associated with high nuclear grade ($P = O{,}012$) and tumour recurrence ($P < 0{,}001$) than those in the CD44-LEG.
Conclusion: CD44 may serve as a useful molecular marker because its expression is considered as poor prognostic factor for tumour recurrence and survival

PS-19-006

Leiomyosarcoma of the kidney: A rare entity with limited available information

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Objective: Among renal sarcomas representing 1–2 % of all malignant renal tumours in adults, leiomyosarcomas are the most common accounting for 50–60 %. We report a case of a 73-year-old woman with haematuria and fever. CT scan revealed a large right renal mass without any vascular or hepatic metastasis and right nephrectomy was performed.
Method: We received the right kidney measuring 19 × 8.5 × 8 cm and weighting 180 g. At the upper and middle portion of the kidney we observed an encapsulated yellowish tumour measuring 9 × 7.5 × 6 cm with a nodular external surface.
Results: Microscopically we observed a malignant tumour comprising of spindle cells arranged in interlacing bundles, whorled pattern and sheets. The cells were spindle shaped with eosinophilic cytoplasm, elongated and blunt-ended nuclei. They stained positive for Vimentin, HHF-35 and Desmin and rarely positive for EMA, CD10 and CD68. The mitotic rate was 24mitosis/10 HPF and tumour necrosis estimated <50 %. A diagnosis of leiomyosarcoma Grade 2 was made.
Conclusion: Renal leiomyosarcomas arise from smooth muscle tissue of renal pelvis, capsule or vessels, clinically and radiographically indistinguishable from more common renal malignancies. They usually have an aggressive behavior with poor prognosis. Total surgical resection, size<5 cm, low histologic grade and negative lymph node metastasis seem to be associated with better prognosis.

PS-19-007

Importance of urine cytology in Fabry disease

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Objective: Fabry disease (FD) is an X-linked disease, so a patient affected relatives should be assessed. Urine cytology may be useful as screaning test and in the evolution of the disease.
Method: We present a 49-year-old male affected from hypertension, left ventricular hypertrophy, non-nephrotic proteinuria and creatinine level 1.4 mg/dl. Microscopically, our renal biopsy presented segmental glomerulosclerosis and vacuolated podocytes, PAS+ that were all over the sample. Immunofluorescence result was negative. Ultrastructurally it presented inclusion bodies, osmiophilics, myeloid bodies mainly in the cytoplasm of podocytes. By oil-red staining in fresh tissue we objectify the lipid content of these cells, which are characteristics, very similar to those found in urine cytology and immunohistochemically identified as podocytes. Activity of alpha-galactosidase-A showed a value below normal. A genetic mutation associated FD was detected.
Results: By a familiar study we detected heterozygous mutation in the mother and sister (without clinical manifestations) and a brother with cardiac manifestations.
Conclusion: FD should be included in the differential diagnosis of proteinuria: urinary cytology may be useful in this screening and treatment response. It is necessary to confirm clinical suspicion with enzymatic and genetic study and study their relatives to detect other cases.

PS-19-008
Chronic antibody-mediated rejection: Correlations between peritubular basement membrane multilayering and transplant glomerulopathy expressed quantitatively
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Objective: The capillary lesions of chronic antibody-mediated rejection are transplant glomerulopathy (cg) and circumferential peritubular capillary basement membrane multilayering (ptcml). Correlations were sought between the two lesions expressed quantitatively.
Method: The corresponding Banff cg scores were reassessed in 61 cases with cg and microvascular inflammation. The status of ptcml was read electronmicroscopically as ptc-s with 1 or 2 layers, 3 or 4 layers, 5 or 6 layers, 7 or 8 layers or 9 or more layers, and the average ptcml level was calculated. The number of cases fulfilling the Banff criterion of severe ptcml (≥ 7 layers in one cortical ptc and ≥ 5 in two additional ptc-s) was additionally recorded.
Results: The mild (cg1) and moderate-severe (cg2-3) groups differed significantly in average ptcml level, with a cut-off of 2.9 layers/ptc between cg1 and cg2-3. The 42 % of the series that fulfilled the Banff ptcml criterion displayed a cut-off of 3.8 layers/ptc.
Conclusion: This study revealed that cases expressing cg2-3 lesions and cases fitting the Banff ptcml criteria differed in average layers/ptc cut off. ≥ 2.9 ptcml layers/ptc.

PS-19-009
Fibrillary glomerulonephritis in diabetic patients. Is there a link?: Report of two cases
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Objective: Diagnosis of Fibrillary Glomerulopathies requires Electron Microscopic examination and often poses differential diagnostic and therapeutic dilemmas. Two cases of fibrillary glomerulonephritis in patients with a history of diabetes mellitus are presented.
Method: Histochemistry, immunofluorescene and electron microscopy.
Results: Two female patients aged 65 and 43 years presented with nephrotic proteinuria. Both had a history of diabetes mellitus, the first with coexistant diabetic retinopathy, the second during her second pregnancy. Light microscope revealed glomeruli with increased size due to Congo-Red(-) mesangial matrix expansion and glomerular basement membrane (GBM) thickening. Immunofluorescence demonstrated intense IgG, C3 and κ-light-chain in the first case and intense IgG, C3, λ & κ chains in the second case, in a pattern mimicking membranous nephropathy, however more smudgy and with additional mesangial deposits. Electron microscope revealed mesangial and GBM occupation by non-branching, haphazardly arranged fibrils measuring 10–24 nm. Moreover, membranous and mesangial electron dense immunodeposits containing the same fibrillar material were shown. Based on these findings a diagnosis of fibrillary glomerulonephritis was suggested in both cases, probably on a background of diabetic fibrillosis.
Conclusion: Fibrillary glomerulonephritis is rare and its coexistence with diabetes mellitus - probably not coincidental but pathogenetically related - hampers its diagnosis and perplexes its management.

PS-19-010
Acquired cystic disease and renal cell carcinoma in hemodialysis patient with systemic lupus erythematosus: A case report
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Objective: Renal cell carcinoma diagnostics are extremely rare in patients with systemic erythematous lupus. We describe a case of renal cell carcinoma in a hemodialysis patient with acquired cystic disease and systemic erythematous lupus.
Method: A 35-year-old female was admitted for a pre-transplantation proceeding.
Results: The main disease which caused end-stage renal disease was systemic lupus erythematosus and lupus nephritis. Both kidneys were reduced in size, with multiple cyst. Based on ultrasound examination and multislice computed tomography of abdomen tumour of right kidney was diagnosed. Tumour was 22 × 25 × 30 mm in diameter, with no signs of breaking kidney capsula. After radical right nephrectomy and subsequent histopathological examination, malignancy was diagnosed as: Renal cell carcinoma cysticum et necroticum, Fuhrman grade 2, stage T1. There were a number of renal cysts lined with flattened epithelium, without atypia. Pathology assessment of the non-tumour specimen revealed a chronic diffuse and global glomerular and interstitial lesions within the class IV lupus nephritis.
Conclusion: The duration of kidney disease, less often than the dialysis, can be a more significant determining factor in the development of acquired cystic disease and systemic erythematous lupus.

PS-19-011
Immunoglobulin mediated membranoproliferative glomerulonephritis in a patient with brucellosis and nephotic syndrome
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Objective: The most frequent brucellae-associated genitourinary involvement is epididymo-orchitis. Renal involvement in brucellosis is divided into three main groups: interstitial nephritis or pyelonephritis, granulomas resulting from chronic brucellosis and renal involvement in association with brucella endocarditis. A limited number of case reports regarding glomerular involvement have been published.
Method: Histochemistry, immunohistochemistry, immunofluorescence and electron microscopy.
Results: A 39-year-old man with serologically proven brucellosis and febrile episodes since 2011, was admitted to the hospital due to brucella-melitensis bacteraemia in the course of which he developed nephrotic syndrome. A renal biopsy was performed. The main clinical differential diagnosis included a tubulointerstitial nephritis associated either with brucella

infection or with the use of antibiotics and a glomerulonephritis. Renal biopsy showed a glomerulonephritis with membranoproliferative pattern associated with immunoglobulin deposition, complemement factors and light chains. Electron microscopy confirmed this pattern. A diagnosis of glomerulonephritis with membranoproliferative pattern- immunoglobulin mediated was supported.
Conclusion: Although mild proteinuria is commonly observed during the course of brucellosis, nephrotic syndrome with biopsy-proven glomerulonephritis is quite rare. A few cases of brucella-associated glomerulonephritis have been published, four showing a membranoprolipherative pattern. The management of patients is based on the control of the infection while treatment with steroids may be useful in some instances.

PS-19-012
Renal involvement in patients with underlying hematological diseases: Indications establishing a connection
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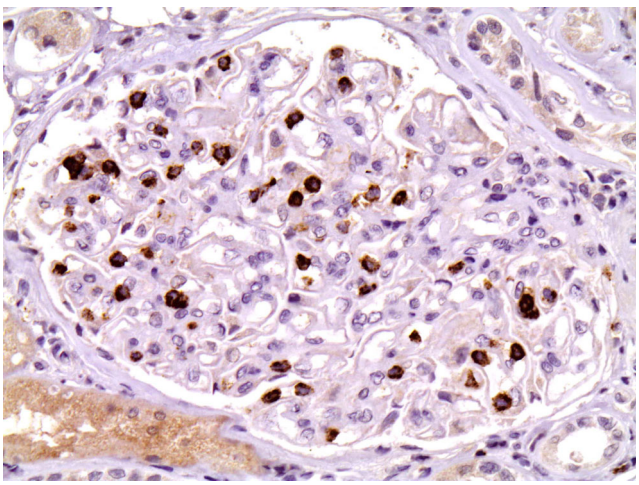
Objective: Renal involvement in patients with underlying hematological diseases may be direct or indirect. A patient with acute myelogenous leukemia and another with chronic myelomonocytic leukemia underwent a renal biopsy due to proteinuria and renal function impairment.
Method: Histochemistry, immunohistochemistry and immunofluorescence.
Results: In the first case, no glomerular pathology was established.The main finding was an interstitial infiltrate localized predominantly in the corticomedullary junction. This infiltrate could be easily overlooked as non-specific. However, immunohistochemistry revealed a myelomonocytic phenotype of the infiltrate consistent with renal involvement by the underlying acute myelogenous leukemia. In the second case, a membranous glomerulopathy was shown by means of light microscope and immunofluorescence. However, a striking finding was the presence into the glomerular and peritubular capillaries of medium sized cells with nephroid or oval nuclei, LCA, PGM1, MPO, CD43 and to a lesser extent CD15 positive but CD3,CD20, c-kit and HLA-DR negative, consistent with chronic myelomonocytic leukemia cells. Infiltration of the interstitial tissue was not observed. The possibility of a secondary (paraneoplastic) membranous glomerulopathy was raised.
Conclusion: Renal infiltrates or circulating cells may provide clues to the diagnosis of underlying hematological diseases not only in cases of direct renal involvement but also in cases of glomerulopathies arising in their background.

MPO immunoreactive cells in the glomerular capillaries in a case of membranous glomerulopathy (x 400):



PS-19-013
A case with thrombotic microangiopathy mimicing membranoproliferative glomerulonephritis
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Objective: Although their pathogenetic mechanisms are different, thrombotic microngiopathy (TMA) may be diagnosed as membranoproliferative glomerulonephritis (MPGN) histopathologically even by experienced nephropathologists.
Method: A 9-year-old boy was admitted with acute kidney injury and edema. Past medical history revealed recurrent diarrhea, hypoalbuminemia/hypogammaglobulinemia and anemia since his infancy. He had been diagnosed with protein losing enteropathy. He had undergone renal biopsies at 2 times before and had been diagnosed as MPGN. Laboratory tests revealed anemia, renal impairment (creatinine: 1.6 mg/dl, urine volume was 0,72 ml/kg/h), hypoalbuminemia, microscopic hematuria, proteinuria (3457 mg/day) and hypogammaglobulinemia. Serum C3 was low, C4 was normal. Response to steroid therapy was unsuccessful and he required hemodialysis. A third kidney biopsy revealed typical features of acute TMA superimposed on chronic features. Patient's clinical course has been significantly improved with eculizumab therapy following 5 cycles of plasma exchange. ADAMTS13 activity was found to be normal. No mutation in DGKE has been identified.
Conclusion: Good response to eculizumab treatment and beginning of symptoms in his infancy period supports the idea that it is a complement-mediated disease. The complement regulatory gene mutation tests have been performed but the results have not been reported yet.

PS-19-014
NCAM isoform switch and MMPs expressions in incipient renal interstitial fibrosis
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Objective: Considering potential involvements of several matrix metalloproteinase (MMP) types (gelatinases-MMP2, MM9; stromelysins-MMP10, MMP11; membrane-type-MMP14, MMP24) and neural cell adhesion molecule (NCAM) in tissue remodeling, we examined their expressions and assessed mRNA levels of NCAM isoforms, MMP2 and MMP9 in kidneys with incipient fibrosis.
Method: MMPs and NCAM immunostainings were applied on cryostat kidney biopsies. Real-time RT-PCR was conducted on NCAM+ renal interstitial cell, obtained by laser capture microdissection, in order to detect changes in mRNA levels.
Results: Statistically significant mRNAs over-expression of NCAM-140 kDa isoform ($p = 0.006$), and down-regulation of MMP2 ($p = 0.029$) and MMP9 ($p = 0.037$) were found in NCAM+ cells captured from incipient interstitial fibrosis. Immunomorphologically, MMP2 was focally detected as granular staining in tubular epithelial cells. MMP9 was rarely observed in interstitial cells showing an overlapping with some NCAM+ cells. However, endothelial cells of peritubular and glomerular capillaries were also MMP9 positive, especially in the cases with inflammation. In the cases associated with incipient interstitial fibrosis, MMP14 was present on particular tubular basement membranes.
Conclusion: Detected switch of NCAM140 kDa isoform with regard to its up-regulation, as well as MMP2 and MMP9 mRNA down-regulation in NCAM+ cells of incipient fibrosis, in addition to NCAM and MMP9 overlapping in some interstitial cells, could suggest regulatory roles of NCAM+ interstitial cells in incipient renal fibrosis.

PS-19-015

Tubulocystic renal cell carcinoma: A case report

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Objective: Tubuocystic renal cell carcinoma (TC-RCC) is a rare tumour entity recently included in the New Renal Epithelial Tumours and Emerging /Provisional Tumour Entities
Method: We report on a 65-year-old male patient with a 3,3 cm, partially cystic mass in the middle portion of the left kidney. Left nephrectomy was performed.
Results: Microscopically, the tumour consisted of tubules and cysts, lined by a single layer of flat, hobnail or cuboidal cells with a distinct nucleoli and brightly eosinophilic cytoplasm. Immunohistochemical analysis revealed that the tumour cells were positive for vimentin, kerAE1/AE3, ker8/18, P504S and focally for ker20.
Conclusion: The differential diafnosis of TC-RCC includes tumours with a multiloculated configuration, such as multilocular cystic renal cell carcinoma, cystic nephroma, mixed epithelial and stromal tumours, cystic oncocytoma and Xp11.2 renal cell carcinoma. Although the great majority of reported cases have behaved in an indolent manner, the biological behavior of this rare tumour has not been yet fully established.

PS-19-016

CD105 (Endoglin) expression in renal cell carcinoma

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Objective: The risk of recurrence is relatively high during the 3–5 years after radical surgery in RCCs. Most frequently used the prognostic factors are tumour grade and nuclear stage. The aim of study is investigate whether CD105 is a reliable prognostic factor to guide clinical decisions or not.
Method: Immunostaining for CD105 was performed on formalin-fixed, paraffin-embedded tissue sections from 57 patients with RCC who underwent nephrectomy in between 2003 and 2007. The microvessel density (MVD) of tumour tissue was measured and CD105 expression was evaluated.
Results: Mean age of the patients were 61.23 years (±11.277). In 54 cases microvessels of tumour were positive, three cases were negative for CD105. The mean score of CD105 expression in microvessels of the tumour was 22.653 (±12.185). Tumour cells were not expressing CD105 In this study no statistically significant correlation was found between CD105 expression and gender, age, tumour size, tumour grade or stage.
Conclusion: These findings suggest that CD105 does not associate with survival of RCC and CD105 may not be an ideal prognostic factor for patients with RCC. On the other hand nearly all of the cases expressed CD105 in tumour microvessels; this may be a novel therapeutic target for RCC but further studies with large groups are needed.

PS-19-017

A case of a rare renal cell carcinoma carrying t(6;11) translocation

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Objective: Progress in the diagnostics based on morphology and immunohistochemistry, genetic and molecular methods has led to the identification of new entities in renal tumour pathology. Therefore the International Society of Urological Pathology (ISUP) recently recommended modifications of the WHO 2004 renal tumour classification and called it ISUP Vancouver Modification of WHO (2004) Histologic Classification of Kidney Tumours. Among proposed new epithelial neoplasms is MiT family translocation renal cell carcinoma (RCC) including t(6;11) renal cell carcinoma. The transcription factors include: TFE3, TFEB, TFEC, and MiTF and form MiT subfamily. The fusion of 2 of these factors has been involved in RCC pathogenesis.
Method: 26-year-old man with no previous medical history presented with accidentally discovered cystic and solid tumour of the lower pole of the left kidney Histologically, neoplasm demonstrated biphasic morphology, composed of larger and smaller epithelioid cells, with the latter clustered around eosinofilic material, tubular, papillary formations and solid sheets of clear or eosinofilic cells with nuclear grade 3(Furhman).
Results: Immunohistochemistry revealed melan A diffuse positivity, negative reaction for HMB 45 and CD 10, while CK showed mild positive reaction of tumour cells. The case was consulted in Plzeň Biopsy laboratory where molecular genetic testing revealed TFE3 negative and TFEB positive with t (6;11) translocation, so histologic diagnosis was confirmed.
Conclusion: Present case is interesting since the t(6;11) renal cell carcinomas have been recently shown to harbor a gene fusion involving TFEB but have yet to be formally recognized entity.

PS-19-018

Structure of glomerulopathies in nephrology clinic (analysis of biopsies), period: 2000–2014

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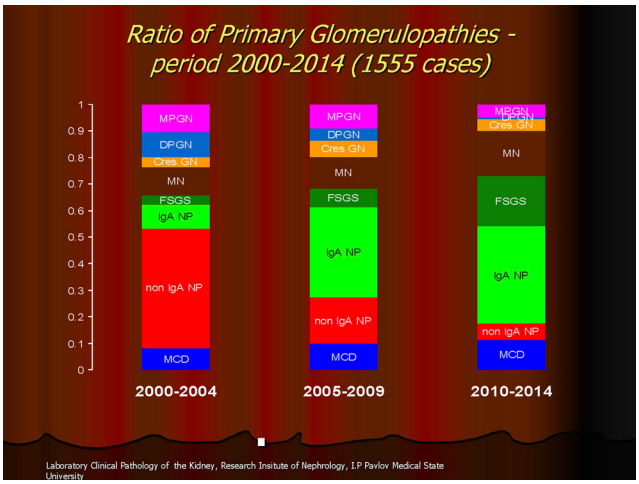
Objective: Comparative analysis of the nosological structure glomerulopaties for the period 2000–2014, subdivided into subperiods 2000–04, 2005–09 and 2010–2014.
Method: The study has been performed by the analysis of pathomorphological conclusions on renal biopsies. In accordance with Naumovic R at all. 2009, the groups of primary glomerulopaties (PGP), secondary glomerulopaties (SGP), glomerulonephritis with hereditary and metabolic pathology (GNHM), vascular nephropathy (VN), tubulointerstitial nephropathy (TN), nephropathy under different pathologies were distingiushed. PGP were subdivided on membranoproliferative glomerulonephritis (MPGN), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), minimal change disease (MCD), crescentic glomerulonephritis (CGN), acute diffuse proliferative glomerulonephritis (ADPGN), mesangial proliferative glomerulonephritis (MGN: Non IgA- and IgA-nephropathy). The systemic lupus erythematosus (SLE), amyloidosis, and vasculitis wereselected in the secondary nephropathy.
Results: During the period 2000–2014, it was revealed decreasing (from 79 to 72 %) of PGP values and increasing of SGP from 10 to 14 %. The ratio of deseases into PGP has changed due to increasing of IgA - nephropathy, FSGS, and MN. The number of patients with CGN and MCD remained unchanged over the period. Real decreasing in MPGN, DPGN was revealed. Secondary glomerulopaties, despite of increasing in the absolute number of all types, showed the changes in the ratio of nosological groups. So for 10 years the percentage of the deseases into the group was changed due to slight increasing the number of vasculitis and reducing the patients with amyloidosis and SLE.
Conclusion: Our results suggest reliable dynamics of nosological types into the groups as PGP, and SGP within 15 years which generally corresponds to the dates of other authors in similar studies.

Structure of glomerulopathies in nephrology clinic (analysis of biopsies), period: 2000–2014:



PS-19-019

Renal anastomosing hemangioma associated with end-stage renal disease: A case report

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Objective: We present a very rare example of a hemangioma variant occuring in an end-stage kidney.

Results: A 24-year-old female with end-stage renal disease due to membranoproliferative glomerulonephritis presented with bilateral kidney masses with similar radiological features. A partial right nephrectomy was performed. Grossly, 3 × 2.8 × 2 cm fleshy brown well-circumscribed tumour with a central myxoid scar was detected. Microscopically, the tumour was composed of anastomosing sinusoidal capillary vessels with a lobular architecture. Vascular structures were lined by flat or hobnail endothelial cells. There was no nuclear atypia, mitotic activity or necrosis. Immunohistochemistry showed positivity for CD31, CD34 and Factor-VIII-related protein. D2-40, Pancytokeratin and HHV-8 were negative. Ki-67 proliferation index was %1–3. The morphological and immunohistochemical findings were diagnostic for anastomosing hemangioma of the kidney. The follow-up was uneventful after 6 months.

Conclusion: Primary vascular tumours of the kidney are uncommonly seen in routine surgical pathology practice. Anastomosing hemangioma is a rare variant of capillary hemangioma that can occur in end-stage kidney. This entity should be kept in mind in clinical evaluation of renal masses in end-stage kidney and should not be over-diagnosed as malignant.

PS-19-020

Case study of a metastatic clear cell tubulopapillary renal cell cancer

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Objective: Clear cell papillary or tubulopapillary renal cell cancer (CCPRCC) is a recently described subclass of renal neoplasms with an extraordinarily good prognosis without reported agressive spread or lympnode metastasis.

Method: We present the case of a 44 years old lady without any significant previous disease. Her left kidney was removed because of a 5 cm parenchymal grayish renal tumour, which had cystic macroscopic appereance. A 2 cm big lymph node was also removed. Close follow up in 12 months up showed no relapse. Microscopically both localisation (kidney and lymphnode) contained a tumour with partly cystic, partly branching tubulopapillary pattern. Tumour cells had empty/clear cell cytoplasm and low grade nuclei. Both tumour shared similar immunophenotype: diffuse and strong cytokeratin 7, pancytokeratin, EMA, CAIX positivity; focal, mainly luminal CD10, vimentin positivity, whereas AMACR, MelanA and HMB45 were negatíve. Molecular studies are in progress.

Results: Morphological and immunophenotypical examinations resulted in the diagnosis of a tubulopapillary clear cell renal cell cancer which metastatized into regional lymph nodes.

Conclusion: CCPRCC is described as an indolent (almost benign!) low grade renal neoplasm with no metastatic cases reported until now. Our index case raises our attention of the potential malignant behavior of this kind of tumour.

Wednesday, 9 September 2015, 09.30 – 10.30, Restaurant
PS-20 Poster Session Ophthalmic Pathology

PS-20-001

Iris melanomas: Chromosomal aberrations and BAP1 expression

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Objective: Iris melanomas have a better prognosis than melanomas located in the choroid or ciliary body. Our group found that chromosome 3 loss also occurs in melanomas of the iris but it's not an indicator of poor prognosis in this uveal melanoma (UM) subtype. We want to investigate whether this chromosome 3 loss is accompanied with a loss of BAP1 expression in iris melanomas and if there is a correlation with the patients' clinical outcome. The prevalence of UM specific mutations in the genes GNA11, GNAQ, BAP1, EIF1AX and SF3B1 occur in irismelanomas was also investigated.

Method: To determine the BAP1 expression we used immuno histochemistry. For mutation analysis we will use the Ion torrent next generation sequencing method.

Results: Preliminary data show that loss of chromosome 3 resulted indeed in a loss of BAP1 expression in iris melanomas. Targeted sequencing using a multiplex UM gene panel is in progress and additional results may be presented at the meeting.

Conclusion: Negative expression of BAP1 is present in melanomas of the iris. We need more samples to draw any solid conclusions.

PS-20-002

Metastatic disease in uveal melanoma: Importance of a genetic profile?

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Objective: Mutation of SF3B1 has been identified in low-grade uveal melanoma with a good prognosis. In this study, we compare chromosomal aberrations and gene mutations between a primary uveal melanoma and its multiple hepatic and peripancreatic metastases.

Method: DNA was isolated from a large primary uveal melanoma after fractionated stereotactic radiotherapy and three distinct metastases (two liver samples and one peripancreatic lymph node) to perform single nucleotide polymorphism array and fluorescent in situ hybridization. We analyzed mutations in uveal melanoma target genes BAP1, GNAQ, GNA11, SF3B1 and EIF1AX.

Results: The primary tumour revealed no abnormalities in chromosome 3, whereas metastases showed deletion of at least 3q12.1-q24 while the

BAP1 gene was not mutated. All samples revealed the following consistent chromosomal aberrations: loss of 1p, gain of 6p a+nd gain of 8q. Subsequently, heterozygous SF3B1 and GNA11 mutations were observed. The metastases showed more genetic aberrations than the primary tumour and therefore may represent the genetic status of the tumour prior to irradiation, whereas the current primary tumour shows presumably irradiation artifacts. An early occurring mutation in GNA11 was observed in all samples.
Conclusion: The SF3B1 mutation seems to predispose for late metastatic disease in absence of a BAP1 mutation.

PS-20-003
Calcification and osseous metaplasia in ocular melanoma
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Objective: Ocular melanoma is a rare malignancy found in clinical practice, but it is the most frequent tumour of the eye of the adults. Calcification and bone formation is an even rarer feature for this pathology, only 7 cases reported so far, mostly in correlation with brachytherapy or tumoural regression.
Method: We present a case of a 59 year-old female with an aggressive tumour measuring 21 mm in diameter. Histologically, heavily pigmented, epithelioid cells (after the revised Callender classification) with clear atypical features and a mitotic index of 20–23 mitoses/mm2 were found.
Results: Within the tumoural mass we observed areas of necrosis, hemorrhage, calcification, bone formation and fibrosis. Tumoural foci infiltrating the sclera, the adjacent fibro-adipose tissue, the blood vessels and the optic nerve were also seen, but without extrinsic muscles invasion. Immunohistochemical tests showed diffuse positivity of HMB-45, Melan-A and S100 whereas Ki-67 was more than 30 % positive. Lung and liver metastasis were assessed.
Conclusion: Ocular melanoma has a distinct behavior in comparison to cutaneous melanoma and has a widely divergent prognosis. Approximately half of the patients will develop metastasis. No systemic therapy was associated with evident clinical outcome for patients with advanced disease and overall survival rate remains poor. Acknowledgement: POSDRU/ 159/1.5/S/135760 Keywords: ocular melanoma, calcification, bone formation

Wednesday, 9 September 2015, 09.30–10.30, Restaurant
PS-21 Poster Session Other Topics

PS-21-001
Immunohistochemical expression of apoptotic markers in renal tissue, in a model submitted to hemorrhage followed by volume replacement
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Objective: To identify possible apoptotic events in renal tissue, using an animal model in which was simulated acute controlled hemorrhage, a frequent condition after a clinical situation resulting from a serious traumatic event, followed by volume replacement.
Method: 18 Large White pigs underwent total intravenous anesthesia and randomly divided in three groups ($n = 6$). Group 1 and 2 were submitted to passive 25 ml/kg arterial blood bleeding followed by volume replacement with LR in group1, and HES in group2, while group3 (control) was submitted to the same conditions, except bleeding and volume replacement. Renal tissue samples were processed for immunohistochemistry, using in situ TUNEL and Cytochrome c methods. The immunoreactivity levels were compared between groups using the Kruskal-Wallis test with Dunn's post test.
Results: Higher levels of apoptotic immunoreactivity were found for the HES group when compared to control and LR groups in convoluted tubules ($p < 0.01$) and when compared to the control group in the descending limb of the loop of Henle and collecting duct.
Conclusion: These findings are suggestive of a higher degree of insult in the tubular renal cells from animals that received HES 130/0.4.

PS-21-003
Histopathology photographs in medical records under Cloud system: Treasure of islands
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Objective: The purpose of this paper is to establish the method to show the photograph of pathology report as soon as possible to a patient who lives in rural area. In the small clinic in detached island it is not easy to see the laboratory data which were checked in a large urban hospital.
Method: For the patients who live in three small islands in Japan, the establishment of medical records using cloud system to communicate with a small clinic to a large hospital in urban area was important. To use the database of patients, the Cloud system was selected. The cloud system, virtual private network (VPN), and long term evolution (LTE) were used to communicate with the medical records.
Results: Three clinics in four islands are communicating with the database in the Cloud system. After the pathologic department makes a diagnosis of the patient, the reports are sent to the database of the Cloud system. Using this system doctors can work in flex time.
Conclusion: Pathology photographs are added to the medical records in the Cloud system and they have become easy to show the cancer cells to patients in detached islands. Histopathology photographs in medical records under the Cloud system become the treasure of islands.

PS-21-004
Small Intestine mucosal injury and apoptosis following hemorrhage and volume replacement with different intravenous solutions
A. L. Ortiz*, H. Vala, C. Venâncio, C. Garcia, A. Silva, D. Ferreira
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Objective: To characterize mucosal loss (ML) and apoptotic events in the small intestine after hemorrhage and volume replacement with a crystalloid, Lactated Ringers Solution (LR), and a colloid, HES130/0.4 solution, in a pig model.
Method: %ML and apoptotic events at the epithelium of the villi were evaluated in the small intestine from pigs that underwent total intravenous anesthesia and passive controlled arterial bleeding, followed by volume replacement using LR (group1, $n = 9$) and HES130/0.4 (group2, $n = 9$). Apoptotic events were investigated by performing immunohistochemistry using Cytochrome c antibody and M30Cytodeath immunofluorescence assay.
Results: %ML was significantly higher in group1 ($P < 0.0001$). Similar moderate to intense cytoplasmic immunoreactivity was seen in both groups for Cytochrome c antibody. The median percentage of apoptotic cells in the non-detached villi epithelium was 5.94 % (1.46–31.47 %) in group1 and 6.38 % (0.36–47.48 %) in group2. No significant differences were observed between groups.
Conclusion: Results suggest that HES130/0.4 administration may more efficiently prevent the acute loss of intestinal mucosa, and, therefore, the integrity of the intestinal barrier. However, the indicators of intestinal apoptosis do not differ between HES 130/0.4 or RL administration. Funding: FCT, project COMPETE: FCOMP-01-0124-FEDER-009525; IPV, CI&DETS, FCT and QREN/FEDER (Ovislab ICT-2013-05-004-5314 ID-64757)

PS-21-005

Accidental finding of a large placental chorangioma in eutrophic neonate: A case report

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Objective: Chorangioma is a rare and benign tumour of placenta arising from chorionic tissue with a frequency of about 1 %. Chorangiomas are typically solitary and small and have no clinical significance. Large lesions are seen rarely and may be associated with maternal or fetal complication.
Method: We present an incidental finding of chorangioma during the routine macroscopic examination of the placenta of a healthy 34-year old woman at 39 week of gestation whose pregnancy was normal with a normal delivery of a female neonate with 8/9 Apgar score and birth weight of 3.150 kilograms.
Results: A gross examination of chorangioma show a polypoid, well circumscribed, purple-red, homogenous large mass, attached on the fetal surface of placenta and measuring 9 × 8 × 5 cm. Microscopic, the tumour is composed of multiple proliferating vascular chanel from capillary to cavernous size, with predominating the capillary component, lined by plump endothelial cells separated by mesenchymal stroma. Immunochistochemical stainings with CD34, CD31 and Vimentin were performed to confirm the morphological diagnosis.
Conclusion: Our case demonstrate a pregnancy resulted in a healthy, eutrophic neonate despite the maternal and fetal complications associated with large chorangiomas which include intrauterine growth restriction, low birth weight, cardiomegaly, anemia, thrombocytopenia and other abnormalities.

PS-21-006

Angiogenic factors in bone sarcomas: A nude mice xenograft model of human chondrosarcoma (grade II and III) compared to high grade osteosarcoma

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Objective: The present experience describes a nude mice model for testing angiogenic factors and chemokine expression (CXCL9, CXCL10, GRO) and their receptors at early stages of tumour growth in two xenografted human chondrosarcomas (Chs, grade II and III) and one high-grade osteosarcoma (OS), comparing the immunohistochemical expression and genomic profile.
Method: Primary grade I, II and III human Chs and an OS were implanted into the backs of nude mice. Two grade I Chs did not grow in the animals. Mice were sacrificed at 24, 48, and 96 hours; and 7, 14, 21 and 28 days from transfer. The expression of angiogenic factors was studied by immunohistochemistry, molecular biology (ELISA and qRT-PCR) and indirect immunofluorescent two-colored staining for CXCL9, CXCL10 and GRO with their receptors.
Results: 48 h after tumour implantation a peak of HIF1α and VEGF was observed in Ch grade III and OS, which showed later (96 h) in Ch grade II. Higher chemokine ligand expression was present at 48 h in all tumours. Moreover two genomic patterns have seen: early phase (angiogenic induction) and late phase (vascular remodeling). Expression of the angiogenic factors appeared later in Chs grade II than in Chs grade III and OS.HIF1α, VEGF and chemokines (ligands and receptors) displayed a strong activity in the early phases of tumoural growth. Neoplastic angiogenesis activation occured earlier in high-grade sarcomas (Ch grade III and OS).
Conclusion: HIF1α, VEGF and chemokines (ligands and receptors) displayed a strong activity in the early phases of tumoural growth. Neoplastic angiogenesis activation occured earlier in high-grade sarcomas (Ch grade III and OS).

PS-21-007

In vivo toxicity assessment of nanoparticles

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Objective: This study aims to assess the possible toxicity of nanoparticles (NPs) loaded with curcumin in Wistar rats by means of serum markers and histopathology.
Method: PLGA NPs were used (100 to 300 nm), both plain and loaded with curcumin. A total 90 adult Wistar rats were divided into 6 groups of 15 animals. Each group was administrated with a different solution (control, plain NPs, NPs with curcumin), either subcutaneously or intraperitoneally. Peripheral blood was collected and examined for CRP and IL6 levels. Specimens from the brain, liver, heart, kidney, stomach and from subcutaneous tissue were collected and examined histologically.
Results: Serum markers showed inconclusive results. Hematoxylin&Eosin sections from the heart, kidney, liver and stomach showed no pathologic findings. Sections from the subcutaneous tissue demonstrated the anti-inflammatory effectiveness of NPs loaded with curcumin. Histological examination of the brain specimens from the animals that received plain NPs showed minor lesions, including focal ischemia and reactive gliosis, in a few animals. Nonetheless the group that received NPs with curcumin showed no such lesions.
Conclusion: The present study demonstrates, not only that the clinical applicability of Nanotechnology can be envisioned, but also the significance of Pathology in the evaluation of new technologies.

PS-21-008

Generalized lymphadenopathy as the first manifestation of metastatic malignant melanoma: A diagnostic paradox

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Objective: Although more than 90 % of melanomas have cutaneous origin, there are a few cases who present with lymph node disease or metastatic viscera lesions, with no identifiable primary, described as melanomas of unknown primary site.
Method: We report a case of a morbidly obese 63-year-old male, with multiple comorbidities, who presented with neurological symptoms and extensive lymphadenopathy was revealed on clinical examination and on imaging.
Results: Excisional biopsy of a supraclavicular nodal mass followed and histopathological examination with the aid of immunohistochemistry lead to the diagnosis of metastatic malignant melanoma. Despite investigations the primary tumour site remained unrevealed and the patient received palliative chemotherapy.
Conclusion: Generally, melanomas evolve from any site of the body containing melanocytes or cells that are capable of differentiating into melanocytes, although cases without an identifiable cutaneous, ocular, or mucosal primary, claimed as melanomas of unknown primary, comprise only 1–4 % of melanoma cases per year. Extensive work-up sometimes seem meaningless. It is also stated that such patients with lymph nodal disease, despite the unfavorable sign of nodal involvement fare better survival rates than common patients with known primary and lymph nodal metastasis.

PS-21-010

Bizarre parosteal osteochondromatous proliferation

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Objective: Bizarre parosteal osteochondromatous proliferation (BPOP) is anunusual reactive process composed of bone and cartilage attached to the surface of bone.
Method: A 19-years-old woman, referring pain the last 2 years which increased in last 6 months, and a palpable mass on the surface of the distal end of the femur without any trauma. Radiogiography showed a calcified mass attached to the underlying cortex by a broad base. A lesion measured 2,5 × 1,5 × 0,8 cm, consisted of cartilage cap and bone tissue which histologically was a BPOP.
Results: BPOP was first described in 1983 as an unusual reactive process involving the small bones of the hands and feet. However, lesions in the long bones, skull, maxilla and metatarsophalangeal sesammoid have been reported. Affects patients of any age, but most are 20–30 with a slight female predominance. The lesion is benign with good prognosis but may recur locally usually 2 months to 2 years after surgery. Complete excision with the best possible margin is the treatment of choice.
Conclusion: Differential diagnosis must be made from osteochondroma, parosteal osteosarcoma, myositis, ossificans and fracture callus. Subsequent cytogenetic studies have shown a recurrent chromosomal traslocation t (1;17)(q32;q21), supporting the clonal neoplastic nature of the lesion.

PS-21-012
Activity based costing for pathology examinations and comparison with the current pricing system in Okmeydani Training and Research Hospital
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Objective: To demonstrate the real cost data of the pathology examinations by using the activity-based costing method and to contribute to the financial planning quality improvement and present tools to the control of costs of the departments, health managers and also the social security institution.
Method: All histopathological examinations that are accepted by Okmeydani Training and Research Hospital Pathology Department during August 2014 were studied and their real costs are calculated by activity based costing method. Calculated costs were compared with the Healthcare Implementation Notification system price lists.
Results: The costs of the pathology tests listed within the same pricing levels in the Healthcare Implementation Notification system list showed great differences. In this study costs of 77,4 % of the examinations costs were higher than the Healthcare Implementation Notification system price lists.
Conclusion: The prices of the pathology examination listed at different levels in the Healthcare Implementation Notification system lists do not cover the real costs. Costs that are calculated by the activity based cost system may vary according to the type of service and the service of health care institutions. However, the basic parameters of the method has shown the necessity for more accurate leveling of pathology tests. Although prices also differ between countries, The Healthcare Implementation Notification system list needs to be revised in order to reflect the costs of the levels of the examinations.

PS-21-013
Application of nanoparaffin technology in the processing of histological material
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Objective: The pathological examination is one of the longest in the list of medical tests. Most of this time is spent on preparation of the microslide. Our goal was to have developed optimal standarts of processing by applying Nano composites.
Method: 8 various types and concentration nanocomposite paraffin (nanoparaffin) were created of ultrasound supported by UP200HT device on the base of Paraffin. Carried out 96 experiments with different time intervals.One hundred ninety-two postoperative and autopsy tissue samples were used in the examination. The quality of slide were avaluted using five point score system by independent pathologists in blind methods.
Results: Nanoparaffin reduces standard time of keeping tissue samples in paraffin twice. Nanoparaffin gives chance to erase chemical agent - xylene. Nanoparaffin brings significant economic impact. The results of this project highlights that the time is spent on preparation of the slide 2,5 times decreased and 3 times decreased reagents using.
Conclusion: By reducing these two factors - time and agents spent, the cost-effectiveness of pathological examination is significantly increase.

PS-21-014
New classification of Cancer of Unknown Primary Origin (CUP) Syndrome
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Objective: Cancer of Unknown Primary origin (CUP) is characterized by metastatic tumour spread without identifiable primary tumour. Our goal was to examine incidence of this heterogeneous CUP syndrome and to create a CUP classification based on clinicopathological factors.
Method: Autopsies corresponding to criteria of CUP syndrome were selected using our database of 11046 autopsy cases (1993–2014). In type-1 ("clinical") CUPs, primary site was not found clinically but identified by autopsy. In type-2 ("clinicopathological") CUPs, primary site was not determinable either clinically, or by autopsy. Regarding type-3 ("pathological") CUPs, no tumour was suspected clinically whereas autopsy revealed metastatic spread from unidentifiable primary tumour.
Results: Altogether 3467 malignant tumours were found including 126 CUPs (types 1/2/3: 77/39/10). Cumulative incidence rate of type-1 and -2 CUPs (corresponding to conventional CUP definition) was 3.35 %. Complete incidence rate (3.63 %) declined with time (1993–2007: 4.23 %; 2008–2014: 2.66 %) due to decreasing incidences of type-1 and -3 CUPs. Histological types: adenocarcinoma~63 %, neuroendocrine~11 %, squamous~9 %, anaplastic~9 %, melanoma~5 %. Origins of type-1 CUPs: lung~47 %, pancreas~12 %, biliary~10 %, intestine~7.8 %, liver~6.5 % and stomach~6.5 %.
Conclusion: Type-2 and -3 CUPs may originate from microscopic-sized metastasizing primary tumours. Based on above classification, improvement of clinical diagnostics may contribute to decreased incidence of type-1 CUPs and transfer of type-3 CUPs into type-2 category.

PS-21-015
Fast and inexpensive self-made tissue microarray for histochemical, immunohistochemical and in situ hybridization studies: Examples with bladder cancer
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Objective: The tissue microarray (TMA), first described by Battifora (1986) and first implemented in 1998 by Kononen et al., is a powerful research and quality control toll used in many Pathology lnstitutions. Unfortunately, all the commercial aray instruments are very expensive and thus not suitable for laboratories with limited funds. We describe simple, fast and cost-effective method for constructing of manual TMA.
Method: Skin punch biopsy needle of 2-mm diameter was used for extracting cores from 60 donor blocks with normal bladder tissue and muscle-invasive bladder cancer and for injecting into recipient block. A modified metal wire was used as a stylet. Adhesive dot-grid paper was

attached to the surface of the bare paraffin block and used as guide to make array pores. The cores were then transfered to the prepared holes in the recipient block. The tissue array was sectioned using a standard microtome and used for Van-Gieson Elastica staining, HER-2 immunodectection and silver in situ hybridization.
Results: We successfully performed histochemical, immunohistochemical and silver in situ hybridization studies on a self-made tissue microarray, without any substantial tissue loss.
Conclusion: This method could be done by any pathology laboratory and represents good and reliable alternative for commercially available, expensive devices.

PS-21-016
Angiomyomatous hamartoma of an inguinal lymph node: A case study
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Objective: Angiomyomatous hamartoma is a vascular disorder of uncertain histogenesis that usually involves inguinal and femoral lymph nodes.
Method: A 7-year-old boy presented with a right inguinal mass measuring 6 cm in MRI. The patient underwent an excisional tumour biopsy. At the pathology lab we received an encapsulated multilobular cystic mass 6, 2 cm in greatest diameter, filled with blood-serous fluid. Its solid component was brown to yellow and had a soft consistency.
Results: Microscopically the tumour represented a lymph node with parenchymal replacement by fibrous tissue consisting of spindle shaped cells and containing a large number of small anastomosing vessels as well as a large amount of mature adipose tissue. No nuclear hyperchromasia or pleomorphism was observed. Differential diagnosis included lymph node hemangioma, angiomatous fibrous histiocytoma, angiomyomatous hamartoma and nodal lymphangiomyomatosis Immunohistochemically spindle cells were SMA positive, while CD34 demonstrated the vessel wall. The final diagnosis was that of angiomyomatous hamartoma.
Conclusion: Angiomyomatous amartoma is a rare process probably of hamartomatous nature which is mainly supported by the disorganized pattern of growth and its mixed components. Some authors suggest that it represents a disordered angiogenic process arising from hilar vein correlated with chronic impairment of lymphatic flow.

PS-21-017
Serosal patch technique and growth factors: A way to get more enterocytes?
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Objective: The bioengineering of the small intestine due to impairment of the intestinal epithelium is becoming an attractive field of research. We explored the possibility of the multiplication of the enterocyte mass using the serosal patch technique and growth stimulators.
Method: Sixty Mill Hill rats were divided in 4 groups of 15 animals. In the control group (Group C) the patch wasn`t created. In each of the other three groups 8 parietal and 7 visceral patches have been surgically created. Group NS was not postoperatively treated; Group G was stimulated with granulocyte colony-stimulating factor (G-CSF); Group GM was stimulated with recombined humane granulocyte-macrophage colony-stimulating factor (rHuGM-CSF). Newly formed mucosa was analyzed using light microscopy. Transmission electron microscopy was used for the assessment of ultrastructural organization of enterocytes and development of microvilli on the apical segment were analyzed.
Results: Animals in Group NS showed slow and inadequate epithelium proliferation. In the Group G, epithelium initially proliferated rapidly, but appeared atrophic after 8 weeks. Stimulation of animals in Group GM led to faster epithelization, and epithelium showed signs of advancing proliferation after 8 weeks.
Conclusion: We confirmed enterocyte multiplication by serosal patch technique, as well as greater efficiency of stimulation with rHuGM-CSF.

PS-21-018
The utility of acetone usage as a dehydrating and clearing agent in tissue processing
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Objective: We searched the utility of acetone usage as a substitute of dehydrating and clearing agents (alcohol and xylol) for a rapid tissue processing.
Method: Eighty blocks with large (2 × 1 × 0.4 cm) and small (0.5 × 0.5 × 0.3 cm) formalin-fixed tissue samples were hand-processed with acetone at 20°C (1 vs 2 h) followed by 60°C molten paraffin (varying 1–4 h vs overnight). The physical quality of the sections (disruption, folding, adhesion, cracking, thickness alterations) and the staining quality (nuclear/cytoplasmic details, uniformity) were evaluated and graded semiquantitatively as; 0: inadequate for diagnostics, 1: needs improving, 2: adequate for diagnostics. Immunhistochemical stainings were done in an automated-stainer.
Results: The best scores were achived by "2-h acetone-2-h paraffin" combination except breast and spleen samples. Shorter aceton processing resulted in disruption and loss of adhesion in sections while prolonged (overnight) paraffin infiltration caused hardening of tissues. Section quality was adequate for diagnosis in %79 of the tested samples.
Conclusion: Acetone, which is miscible with both water and paraffin, can be used as a fast, single-step dehydrating-clearing agent for many tissues without significantly altering tissue morphology and immunhistochemistry results. Fat containing tissues may require additional xylene steps. Further research is needed to reveal its efficacy as a fixation agent or its interference with molecular techniques.

PS-21-019
Pigmented villonodular synovitis: A retrospective study of 103 cases
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Objective: To review clinical and histological characteristics of pigmented villonodular synovitis (PVNS) in La Rabta's Hospital.
Method: Retrospective study of the histologically proven cases of PVNS, diagnosed between 1991 and 2014 in the Pathology Department of La Rabta's Hospital. Clinical data were reviewed for each patient and the following parameters were evaluated: gender, age at diagnosis, initial clinical symptoms and site of onset and histological features of the lesion.
Results: A total of 103 patients with histologically proven PVNS were included. The majority of patients were female (62.13 %) and the mean age at the time of diagnosis was 35.4. The knee was the most frequently affected site (75 % of the cases) followed by the hip (20 %of the cases). Pain and progressive local swelling sensation were the most frequent symptoms at onset. Diagnosis was histologically proven in all cases. Hemosiderin were detected in all cases. The cell types most frequently encountered were the giant cells, histiocytes and foam cells.
Conclusion: Our outcomes suggest that PVNS shows a female predominance, occurs mostly between 20–40 years and favors the knee and hip. Recurrence is frequent, particularly in the knee. However, only the histological study of the lesion allows establishing a definitive diagnosis.

PS-21-020

The influence of intra-abdominal hypertension on the morphological status of internal organs

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Objective: It is known that an increase of intra-abdominal pressure has a negative effect on the function of the gastrointestinal tract, respiratory, cardiovascular and urinary systems.
Method: It was an experimental research: male rats of the same age, weight, diet ($n = 100$). Among them: a control group ($n = 10$) - intact animals without affecting; comparison group ($n = 90$) - animals, which was artificially created by intra-abdominal hypertension of different degrees (15, 25, 35 mm Hg) and different exposure times (3, 12, 24 h). The method of creation of intra-abdominal hypertension - pneumoperitoneum.
Results: We made a histological examination of tissue of kidneys, liver, intestines, myocardium and lung. We got these results: lung - perivascular edema, focal hemorrhage, atelectasis foci; myocardium - fragmentation of cardiomyocytes with ischemic area, vascular congestion, focal and extensive hemorrhage in the myocardium; liver - dystrophy of hepatocytes, congestion of segments central vein; kidney - dystrophy of renal tubular epithelium, perivascular hemorrhage, congestion of the capillaries. Pathological changes in the intestine were not identified.
Conclusion: The degree of these changes depends on time and level of intra-abdominal hypertension.

PS-21-021

Trousseau's syndrome associated with lung adenocarcinoma presented as acute myocardial infarction

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Objective: Trousseau's syndrome (TS) may be encountered in a form of diverse and polymorphic spectrum of thrombotic disorders in setting of malignant disease. We suspected that TS was an underlying cause of acute myocardial infarction (AMI) in a 49-year-old man with low cardiovascular risk and suspicious lung infiltration.
Method: We represent a case of 49-year-old man with radiologically detected abnormal 15 mm shadow in right lung hilum who suddenly developed AMI. Four days later, and before diagnostic bronchoscopy, the patient died, and clinical autopsy was performed.
Results: Post mortem results revealed poorly differentiated lung adenocarcinoma in advanced stage. Blood clots were found in medium and small branches of coronary blood vessels not only in the field of myocardial infarction, but also in surrounding non-necrotic muscle. In addition to massive AMI, ischemic infarcts were found in kidney and spleen. Occlusive thrombi and thromboemboli were found in veins and arteries of medium and small caliber in visceral organs, and in venous plexuses of the pelvis.
Conclusion: Although TS is not rare, the presentation with AMI is very seldom encountered in clinical practice. For patients without clinical evidence of atherosclerosis, hypercoagulability associated with cancer as underlying cause of AMI should be considered and investigated.

PS-21-022

Adult extrarenal nephroblastoma arising in a retroperitoneal mature teratoma

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Objective: Nephroblastoma is a frequent tumour in children but rare in adults. We report an even rarer case of an adult extrarenal nephroblastoma developed in a retroperitoneal mature teratoma, with speculated metastatic gonadal origin.
Method: A 44-year-old man with a 5-month history of intermittent colicky low back pain underwent radiologic examination that revealed a large right-sided retroperitoneal cystic-solid mass. Surgical resection was performed. Grossly, a 17 cm, well circumscribed, multilocular, cystic tumour filled with green-tan fluid and containing a 6 cm solid nodular area was identified.
Results: On pathology, the solid area revealed the classic triphasic pattern of nephroblastoma (blastema, stroma and epithelial glandular structures). The cystic spaces were covered by fibrin or lined by squamous epithelium and foreign body giant cells. Immunohistochemically, blastema cells were focally positive for WT-1 and vimentin, stroma for vimentin and epithelial structures for cytokeratins AE1/3. The diagnosis of nephroblastoma arising in a setting of mature teratoma was made. Urological examination was advised, which showed a small scarred calcified area in the right testis.
Conclusion: The few reported cases of adult extrarenal nephroblastomas in teratomas developed in metastatic sites of gonadal teratomas. Literature search did not reveal cases of adult nephroblastoma in primary retroperitoneal teratoma.

PS-21-023

Primary extra-gastrointestinal stromal tumour of the retroperitoneum: Case report

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Objective: Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal tract and typically express c-kit/CD117. Rarely neoplasms with similar pathologic features are found outside gastrointestinal tract (omentum, mesentery, retroperitoneum) and are called extra-gastrointestinal stromal tumours (EGISTs). Only 58 cases of primary retroperitoneal EGISTs have been reported. We herein report an additional case of this rare entity.
Method: A 19-year-old female presented with lower abdominal pain. Pre-operative radiological evaluation with ultrasonography and computed tomography revealed a 3 × 3.8 cm retroperitoneal heterogeneous solid mass located near the left common iliac artery. She underwent surgical removal of the tumour.
Results: On gross examination, we identified an encapsulated tumour 5 × 4 × 2.5 cm and the frozen section was "negative for malignancy". Microscopically, the neoplastic cells were proliferating spindle cells, with mitotic rate of 0–1/50hpf. Immunohistochemistry revealed strong positive staining for c-kit and CD34 and the diagnosis of GIST was confirmed. Pathologic diagnosis was GIST of low malignancy potential according to Fletcher classification. The patient had uncomplicated postoperative course and did not receive adjuvant tyrosine-kinase inhibitor therapy. At 2- years follow-up she remains disease-free.
Conclusion: Primary EGISTs of the retroperitoneum are extremely rare. Immunohistochemistry for c-kit may help in the differential diagnosis of EGIST from other mesenchymal tumours.

PS-21-024

Incidence and morphological characteristics of the gastroenteropancreatic neuroendocrine tumours, diagnosed and confirmed for one year in UMHAT Dr. Georgi Stranski, Pleven

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Objective: Over 90 % of neuroendocrine tumours (NETs) in Bulgaria were reported to arise in the gastrointestinal tract. Our objective was to

study the incidence and morphological characteristics of the gastroenteropancreatic NETs, diagnosed for 1 year.
Method: The present retrospective study explores the incidence and morphological characteristics of the gastroenteropancreatic NETs, diagnosed and confirmed for 1 year period (during 2014) in UMHAT "Dr. Georgi Stranski", Pleven.
Results: Seven cases of gastroenteropancreatic NETs were diagnosed and treated for the studied period. Most common primary sites were: pancreas in 4 (57.14 %) cases and 2 in colon (28.57 %) cases. According to the morphological criteria, 2 (28.57 %) were well differentiated NETs, 3 (42.86 %) were moderately differentiated, and 2 (28.57 %) were poorly differentiated NETs. One of them was mixed adenoneuroendocrine carcinoma. All cases demonstrated immunoexpression of Chromogranin A and Synaptophysin in adition to the distinct neuroendocrine morphology. Distant site metastasis were observed in 5 (71.43 %) cases.
Conclusion: According to our results, most of the gastroenteropancreatic NETs were well and moderately differentiated. A considerable number of patients had distant metastasis at the time of diagnosis. The expression of Chromogranin A and Synaptophysin supported the morphological diagnosis of gastroenteropancreatic NET.

PS-21-027
Dantrolene variable hepatic toxicity related to oral and intravenous long term administration
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Objective: Dantrolene sodium is a muscle relaxant used in therapy of spasticity and malignant hyperthermia, because of its wery well delimited peripherall action on skeletal muscle. Its major inconvenient is still related to hepatic injury. Our study try to identify a possible relationship between dantrolene way of administration and the degree of hepatic injury, as an useful step towards the most appropriate therapeutic decision.
Method: 21 male Wistar rats were randomly assigned in three groups, control group/oral administered dantrolene group/intravenous administered dantrolene group, for 3 weeks. 5 mg/kg body weight of dantrolene, in a volume of 0,3–0,5 ml/100 g weight, in a suspension of saline solution with 0,5 % carboxymethyl cellulose was given once a day.Samples of hepatic tissue were prelevated and processed for the microscopic exam.
Results: The two groups of rats which received dantrolene presented large susceptibility for hepatic alterations; hepatic steatosis, signs of acute hepatitis revealing the toxicity of dantrolene.
Conclusion: Long term dantrolene administration requires a clinical and laboratory monitoring of the liver functions, together with individualization of doses, in order to obtain the optimal response with minimal hepatic injuries.

PS-21-028
Electro-hyperthermia induced programmed cell death in a colorectal cancer allograft
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Objective: The electric field and the concomitant heat of <42oC, generated by modulated electro-hyperthermia (mEHT), can selectively target malignant tumours due their elevated glycolysis (Warburg effect), ion concentration and conductivity compared to normal tissues. mEHT has been used as a complementary to radio- and chemotherapy. We earlier showed in immunocompromised mice that mEHT can provoke apoptosis and may promote immune cell infiltration in colorectal cancer xenografts. Here we tested the mEHT related damage, stress and immune response in cancer allografts in immunocompetent mice.
Method: We implanted Colon-26 carcinoma allografts in Balb/C mice. After mEHT treatment we used immunohistochemistry on fixed samples for detect AIF, BAX, caspase-3, HMGB1 proteins and CD3+ cells.
Results: mEHT resulted in progressive tumour damage compared to controls. The cell death response was accompanied increase of activated caspase-3 levels, without significant translocation from mitochondria into nuclei of apoptosis-inducing factor (AIF), or accumulation of Bcl-2-associated X protein (BAX) in mitochondria. Stress-associated release of HMGB1 protein and increased number of CD3 positive T cells were also observed. Additional i.p. administration of a CD8+ T-cell promoting agent resulted in a systemic tumour destruction.
Conclusion: mEHT can induce caspase-dependent programmed cell death and stress-associated release of HMGB1, which may support T cell mediated tumour immunity.

PS-21-029
Structural changes in the tissues for transplantation after sterilization with gamma and electron beam radiation
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Objective: Sterilization is an important step in the preparation of biological material for transplantation. The aim of the study is to compare morphological changes in three types of biological tissues induced by different doses of gama and electron beam radiation.
Method: Frozen biological tissues (porcine skin xenografts, human skin allografts and human amnion) were irradiated with different doses of gamma rays (12.5, 20, 35, 50 kGy) and electron beam (15, 25, 50 kGy). After melting the specimens were fixed by formalin, processed by routine paraffin technique and stained with hematoxylin and eosin, alcian blue at pH 2.5, orcein, periodic acid Schiff reaction, phosphotungstic acid hematoxylin, Sirius red and silver impregnation.
Results: The basic staining showed vacuolar cytoplasmic degeneration of epidermal cells by the lowest doses of gamma and electron beam radiation. There was damage of fine elastic fibers in the xenografts dermis at the dose of 25 kGy of both radiation types. Disintegration of epithelial basement membrane was induced by the dose of 15 kGy of electron beam radiation. Disintegration of the fine collagen fibers in the papillary dermis was induced by the lowest dose of electron beam and by the highest dose of gamma radiation.
Conclusion: Irradiation by both, gama rays and the electron beam, causes similar changes on cells and extracellular matrix, with singnificant damage of the basement membrane and of elastic and fine collagen fibers in the papillary dermis, the last caused already by lowest dose electron beam radiation. Supported by VEGA 1/0297/14.

PS-21-030
Modulated Electro-hyperthermia (mEHT) of allografted colorectal cancer: Does modulation make any difference?
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Objective: Modulated electro-hyperthermia (mEHT) can be complementary to radio- or chemotherapy in clinical oncology. We earlier showed that amplitude modulated radiofrequency (13.56 MHz) current of mEHT can be enriched in cancer cells to elevate heat and induce programmed cells death without harming adjacent non-malignant tissues. The effect of modulation, chosen to fit the time-fractal fluctuation in fractal electrophysiology, was studied in EHT treatment.

Method: C26 mouse colorectal adenocarcinoma cell line was implanted to both femoral regions of BalbC mice were treated using EHT with (mEHT) or without (EHT) modulation for which a 1/f noise source (harmonic time-fractal fluctuation) was used. Archived tumour samples were tested for morphology and for Ki67 positive proliferating fractions and CD3 positive tumour infiltrating T lymphocytes using immunohistochemistry.
Results: Both EHT and mEHT treatments caused significant tumour cell death compared to the untreated control tumours. The amount of proliferating cells was found after mEHT treatment, except when EHT and control samples were compared. The number of CD3 positive T cells showed a decreasing gradient of mEHT>EHT>untreated tumours.
Conclusion: Besides elevated tumour cell damage more efficient reduction of tumour cell proliferation and initiation of CD3 positive T cell accumulation accompany mEHT treatment in C26 colorectal cancer than after using plain EHT.

Wednesday, 9 September 2015, 09.30–10.30, Restaurant
PS-22 Poster Session Pulmonary Pathology

PS-22-001
Acute respiratory distress syndrome: Clinical diagnosis vs. autopsy findings
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Objective: To compare the Berlin definition of acute respiratory distress syndrome (ARDS) to autopsy findings.
Method: All patients with clinical criteria and/or pathohistological diagnosis of ARDS who died in the intensive care unit within a 10-year period were included in the study. Patient's clinical charts were reviewed to establish whether patients met the Berlin definition criteria for diagnosis of ARDS, histologically defined as the presence of diffuse alveolar damage (DAD). A histopathological analysis of suspicious areas within lungs from every pulmonary lobe was made.
Results: 67 patients with clinical criteria for ARDS and/or pathohistological finding of DAD have undergone the autopsy. Forty-six patients met clinical criteria as well as pathohistological criteria for ARDS, 11 patients met clinical criteria without pathohistological confirmation of DAD, and 10 patients had pathohistologically diagnosed, but clinically unrecognized ARDS. The Berlin definition clinical criteria presented a sensitivity of 82 %, positive predictive value of 80 %, and accuracy of clinical criteria was 68 %. The histopathological findings in 11 patients who met clinical criteria for ARDS without pathohistological finding of DAD were pneumonia (n = 10), and pulmonary embolism (n = 1).
Conclusion: There is stil a space for further improvement of clinical criteria for recognizing ARDS in comparison to pathohistological findings.

PS-22-002
Comparison of pathohistological findings within the lungs and the values of PaO2/FiO2 ratio in acute respiratory distress syndrome
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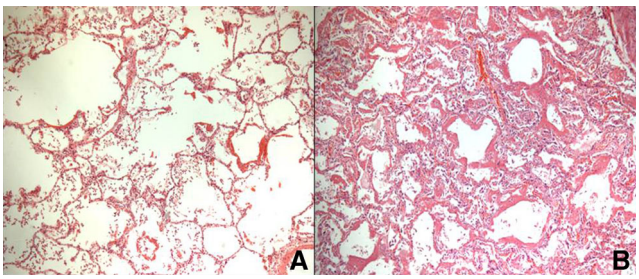
Objective: To investigate a correlation between PaO2/FiO2 ratio and stages of diffuse alveolar damage (DAD).
Method: Forty six patients with both clinical and pathohistological diagnosis of ARDS who died within a 10-year period have undergone the autopsy. ARDS was classified into: mild (PaO2/FiO2<300), moderate (PaO2/FiO2<200), and severe (PaO2/FiO2<100). Presence of hyaline membrane (estimated in grade 1 (discrete), and grade 2 (extensive)), edema, hemorrhage, microthrombosis, proliferation of type II pneumocytes, mutilating fibrosis, interstitial and organizing pneumonia was analyzed.
Results: In severe ARDS (n = 21) hyaline membrane grade 2 and edema predominated, hemorrhage and microthrombosis were present in two-thirds of patients, while proliferation of type II pneumocytes, organizing and interstitial pneumonia were present in 38, 28 and 14 % patients respectively. In moderate ARDS (n = 23) hyaline membrane grade 1, proliferation of type II pneumocytes, interstitial and organizing pneumonia were present in 83, 83, 70 and 65 % patients respectively. Edema, hemorrhage and microthrombosis were detected in less than 50 % of patients. In mild ARDS (n = 2) only hyaline membrane grade 1, proliferation of type II pneumocytes, organizing and interstitial pneumonia was found. Mutilant fibrosis was found only in 3 patients with moderate ARDS.
Conclusion: Exudative phase of DAD dominated in severe ARDS, while proliferative phase preponderated moderate and mild ARDS.

Hyaline membrane grade 1 (A) and grade 2 (B), H&E x 50:



PS-22-003
Pathohistological diagnosis of pulmonary aspergillosis: A five year experience
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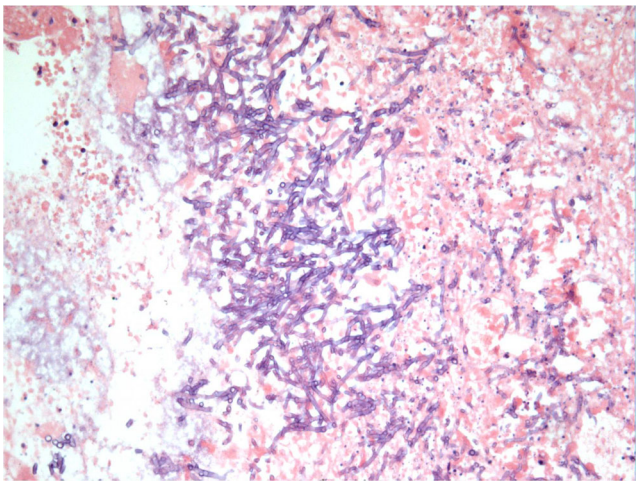
Objective: To evaluate the pathohistological diagnosis of pulmonary diseases caused by Aspergillus.
Method: Retrospective study included 38 patients with pathohistologically confirmed Aspergillus infection at our institute during the 5-year period. Biopsy materials were obtained by bronchoscopy, open lung biopsy through video assisted thoracoscopy and thoracotomy. In addition to standard HE staining, in all patients special stains (Ziehl-Neelsen stain, Periodic acid-Schiff stain (PAS) and Grocott method) were used.
Results: A total of 38 patients with characteristic clinical and radiological findings, as well as pathohistologically proven pulmonary aspergillosis were found. Aspergilloma was diagnosed at 34 (90,32 %) patients. At 3 (6,45 %) patients chronic necrotizing pulmonary aspergillosis was determined, and at 1 (3.23 %) patient invasive pulmonary aspergillosis was diagnosed. Diagnostic materials were obtained by katheter biopsy in 5 (12,5 %), bronchobiopsy in 7 (18,75 %), transbronchial biopsy in 9 (25 %), and surgical procedures in 17 (43,75 %) patients. Of 38 patients,

only in 5 patients Aspergillus infection was microbiologically confirmed.
Conclusion: Although setting of pathohistological diagnosis allows rapid diagnosis of fungal infections, there is no possibility of a final identification of pathogens. Characteristic clinical and radiological findings, as well as laboratory confirmation of the fungus is essential for the final diagnosis.

Invasive pulmonary aspergillosis- partly preserved and partly necrotic hyphae of Aspergillus fumigatus, H&E x 200:



PS-22-004
Relationship between 18F-FDG uptake on PET/CT and expression of Ki-67 and p53 proteins in patient with lung cancer: A clinocopathologic study
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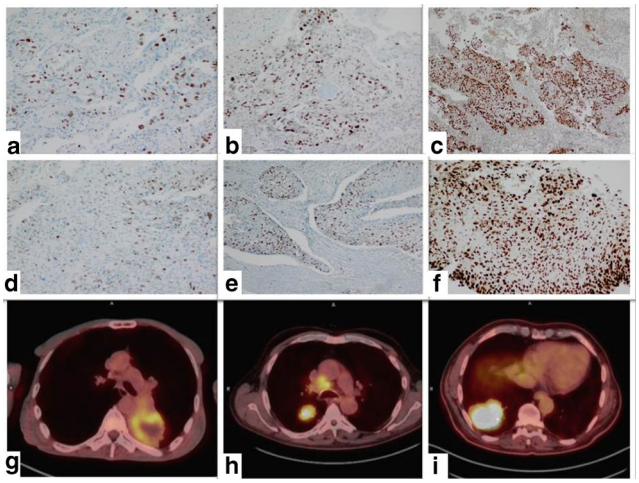
Objective: The aim of the study was to investigate the relationship between Ki-67 and P53 expression and the maximum standardized uptake value (SUVmax) on 18 F-FDG PET/CT in patients with lung cancers.
Method: The staining intensity of Ki-67 and p53 expression was evaluated by immunohistochemical method in NSCLC (31) and SCLC (13) patients. The SUVmax measurement of each primary lung cancer lesion was obtained retrospectively. We evaluated whether there is any correlation between immunohistochemical staining intensity and SUVmax measurement of primary lung lesion.
Results: We found that Ki-67 and p53 % scores were significantly higher in SCLC compared to the NSCLC (50 vs 34, $p = 0.009$ and 64 vs 50.9, $p = 0.043$, respectively). We found a significant correlation between the SUVmax values with Ki67 and p53 % values, $p = 0.0001$ (Pearson Correlation (PC) was 0.83) and $p = 0.0001$ (PC was 0.81), respectively. According to the pathologic subgroup of the lung cancer, there was a significant correlation for SUVmax with Ki-67 % (PCwas 0.96, $p = 0.0001$) and p53 % (PC was 0.84, $p = 0.0001$).
Conclusion: Our analyses showed that Ki-67 % was significantly correlated with SUVmax values in patients with lung cancer in all subtypes (adenocarcinoma, squamous and SCLC) but the regression was more prominent in adenocarcinoma and squamous cell carcinoma. Also there were significant correlation between the SUVmax and p53 % values in adenocarcinoma and squamous cell carcinoma but not in SCLC.

Figure1:



PS-22-006
In pulmonary metastases of melanoma, malignant melanocytes retain the ability of "epidermotropism"
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Objective: The presence of epidermotropism in metastatic skin melanoma is well-known, leading occasionally to confusion with a new primary melanoma. In lung melanomas, it has been proposed that the presence of malignant melanocytes within the bronchial epithelium is possibly an indication of primary disease. The aim of this study was to examine whether metastatic malignant melanocytes to the lung retain the ability of "epidermotropism" in the adjacent normal bronchial epithelium.
Method: We examined formalin-fixed, paraffin-embedded tissue sections from four cases of metastatic melanoma to the lung (three superficial spreading and one desmoplastic) and one primary squamous cell lung carcinoma. Immunohistochemistry was performed using S-100, Melan-A and HMB-45 antibodies.
Results: Microscopic examination revealed the presence of atypical intraepithelial cells in bronchi adjacent to the tumour in all three cases of metastatic superficial spreading melanoma. These cells were present focally, had similar morphology to the neoplastic melanocytes and were positive for S-100, Melan-A and HMB45. Intraepithelial melanocytes were not found in the cases of metastatic desmoplastic melanoma and squamous cell lung carcinoma.
Conclusion: Malignant melanocytes retain the ability of "epidermotropism" in metastatic sites in the lung, therefore their presence within the bronchial epithelium is not a proof of primary site.

PS-22-007
The role of lung macrophages in the postcontusional pulmonary alterations: An experimental study
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Objective: Pulmonary contusion appears to be a progressive lesion in blunt chest trauma patient. It's known that pulmonary contusion induces a local inflammatory response. The aim of this study was to present the role of parenchymal lung macrophages in postcontusional pulmonary alterations.
Method: Fifteen male Wistar albino rats underwent pulmonary contusion by dropping a weight of 500 g from a height of 45 cm (2.2 Jenergy) to the left lateral thoracic wall. The animals were divided in three groups based

on the time of autopsy: 24th, 48th and 72nd h after blunt chest trauma. Lung tissue samples were evaluated by light microscopy. Immunohistochemistry staining for macrophages was performed using the anti-CD-68 monoclonal antibody. Positive to CD-68 cells were counted in ten visual fields (40x).
Results: At the 24thh there were observed presence of the hemorrhages, atelectasis, and accumulation of neutrophils in the lung parenchyma. Lung edema with massive infiltration of macrophages (interstitial and alveolar) was the prominent histological findingat the 48thh. Proliferation of the fibroblast was visualized at the 72ndh. The quantity of the macrophages in traumatized lung had increased with the time with peak at 72nd h.
Conclusion: This experimental study confirms that pulmonary contusion is a progressive lesion. It induces an invasion of mononuclear cells into the traumatized lung, which we consider to be responsible for the postcontusional lung alterations.

PS-22-011
Primary adenoid cystic carcinoma of the trachea: A case report
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Objective: Primary adenoid cystic carcinoma is very rare type of carcinoma, representing less than 1 % of respiratory tract malignancies.
Method: We present a 61-year-old female patient with previous history of dyspnea and chest pain. Bronchoscopy revealed the lobular tumour measuring 40 mm in proximal trachea, which obstructed 70 % of its lumen. During bronchoscopy transbronchial needle aspiration was performed, and material was observed cytologically and histopathologically.
Results: Clusters of small cells with intercellular non-fibrillar hyaline matrix and extracellular hyaline globules were seen in the cytological findings highlighted by May-Grunwald-Giemsa stain. It was suspect to be an adenoid cystic carcinoma. Histomorphological characteristics showed mixed cribriform and tubular pattern of growth, with moderately uniform small cells with eosinophilic cytoplasm and round hyperchromatic nuclei, making pseudo-cystic spaces with hyaline PAS positive eosinophilic basal membrane and material in lumen of spaces. Cuboid ductal cells were surrounding small cells. In immunohistochemical studies, small cells were p63 positive and ductal cells showed positive for EMA. Final diagnosis according to clinical and pathological findings was primary adenoid cystic carcinoma of trachea.
Conclusion: Cytological diagnosis of rare adenoid cystic carcinoma of trachea can mimic pleomorphic adenoma, basal cell adenoma and carcinoma. Definitive diagnosis must be confirmed by histopathological findings before classification and therapy.

PS-22-012
What are clinicopathologic findings of lung cancer in Albanian population?
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Objective: To determine the most common histotype of lung cancer and the main clinical signs of lung cancer, in Albanian population.
Method: Retrospective study, from january 2011 up to december 2014, analyzing all histopathologic reports, and other data of the patients hospitalized in the university Hospital of lung diseases in Tirana. Methods used, were Pearson Chi-Square and Likehood-Ratio.
Results: Male to female ratio was 81 %(n = 878) to 19 %(n = 206). Age range was (16–91) with mean age 62,4 years SD ± 9,1. Spreading according to histotypes was: 36 % Squamous cell carcinoma, 32 % Adenocarcinoma, 15 % Small cell carcinoma, and 17 % others. 67 % of them have been smokers. Clinical symptoms were: hemoptysis 29 %(n = 315), cough 27 %(n = 293), dyspnea 23 %(n = 249), and chest pain 22 %(n = 227). Day hospital avarage was 7 day, and day range (1–31) with SD ± 6.4. Performance status was: 60.2 % improved, 35.2 % idem, 3.3 % dead in hospital.
Conclusion: Squamous cell carcinoma is the main histotype of lung cancer in Albanian people. Most of these patients come in late stage of diseases, so in this condition a substantial portion of lung cancer cases and deaths could be prevented by applying effective prevention measures, such as tobacco control and the use of early dedection tests.

PS-22-013
On two rare cases of idiopathic pulmonary hemosiderosis
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Objective: In 1850 Virchow first described a brown induration of the lungs in autopsy specimen. Ceelen in 1931 published the clinical course of two cases. Grill et al. in 1962 demonstrated fulminant form of idiopathic pulmonary hemosiderosis (IPH). IPH is a rare disease of children and young persons characterized with recurrent pulmonary hemorrhages of unknown cause, diffuse radiologic abnormalities, cough, haemoptysis and moderate to severe hypochromic anemia.
Results: We present 2 cases of fulminant form of IPH. Case 1 – 44 years old man admitted to the Hospital with severe respiratory and heart failure without any history of previous diseases. After cardiopulmonary resuscitation he died in half an hour. The postmortem examination revealed diffuse pulmonary hemorrhages and oedema of the lungs. Histologically the only findings are interstitial and intraalveolar hemorrhages, hemosiderosis, destruction of the elastic fibers in the alveolar walls and interstitial fibrosis. No significant pathologic changes in other organs were discovered. Case 2–18 years old soldier was found dead in the morning in the sleeping room. He has not any history or previous diseases. At autopsy the only findings were diffuse pulmonary hemorrhages.
Conclusion: The diagnosis of both cases was made after exclusion of toxic infection injuries, thromboembolism, mitral stenosis, vasculitis, thrombocytopenia and immune complexes diseases as lupus erythematosus and Good Pasture syndrome.

PS-22-014
Unusual variant of non-small cell lung carcinoma: Alpha-fetoprotein-producing hepatoid adenocarcinoma
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Objective: We experienced a very rare case of Alpha-fetoprotein-producing hepatoid adenocarcinoma of the lung. The patient was 68 year old male who presented with thoracic pain and bloody sputum.
Method: Chest CT revealed a two separated tumour masses. The largest one, 85 mm in diameter, involved mediastinal structures with consecutive tracheal dislocation, and other mass at periphery of the right upper lobe, 50 mm in diameter. Abdominal CT revealed no lesions in other sites. Right superior lobectomy with mediastinal lymphadenectomy was performed. Majority of mediastinal tumour mass was inaccessible for complete resection.
Results: Histology showed a tumour composed of polygonal large cells with clear cytoplasm and large atypical nuclei, coarse chromatin and inconspicuous nucleoli. The tumour cells were arranged in solid sheets and rare abortive gland formation. Immunostaining showed that tumour cells express: pankeratin, AFP, focally HepPar-1 and HCG. The differential diagnosis included: poorly differentiated hepatoid carcinoma of the lung and yolk-sac tumour. Postoperative level of serum AFP was elevated (1762 ng/ml). In situ hybridization was performed: there was no overrepresentation of 12p in the tumour, which excludes a germ-cell tumour.

Conclusion: Diagnosis of alpha-fetoprotein-producing hepatoid adenocarcinoma of the lung, was established. Following diagnosis, the patient received four cycles of concurrent chemotherapy (gemsar+cisplatin). After second cycle, level of serum AFP decreased (67 ng/ml). Repeated chest CT showed almost complete regression of the mediastinal mass.

PS-22-015

IgG4 related disease-like changes in tumour induced obstructive pneumonia

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Objective: The authors report a retrospective study describing relatively frequent, however, so far underestimated changes mimicking IgG4 related disease in the lung parenchyma of patients with non-small cell lung cancer (NSCLC).
Method: A series of 19 cases of obstructive pneumonia identified in resection specimens from patients treated by lobectomy for NSCLC or carcinoid was evaluated. Immunohistochemistry for IgG and IgG4 was performed. Number of IgG and IgG4 positive cells in high power field was quantified. IgG4/IgG ratio was calculated.
Results: From 19 cases of obstructive pneumonia, 4 cases had more than 50 % IgG4 from IgG+ plasmocytes. Absolute number of IgG4+ plasmocytes in these cases was more than 60. Only in one case these changes were found on larger area, in rest of cases there was only small focus in close proximity to the tumour.
Conclusion: IgG4 related disease-like changes can be found in obstructive pneumonia. Diagnosis of IgG4 related disease from core cut biopsy should be, therefore, established only in cases where the diagnosis of malignancy is ruled out. The rare cases of coincidence of true IgG4 related disease and NSCLC have been described, however, as the presence of similar changes is relatively frequently associated with malignancy, underdiagnosis of tumour lesion has fatal consequences.

PS-22-016

Comparative study of cytology and histology of primitive lung cancers: Study of 981 cases

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Objective: The objective is assessing the sensitivity of the cytology and histology in the diagnosis of lung cancers.
Method: Our work is a retrospective study involving 981 cases of bronchial aspiration coupled with bronchial biopsies collected during 5 years. Immunohistochemical (IHC) study was conducted by CK 20, CK7, CK5-6, TTF1, chromogranin, synaptophysin and CD45.
Results: Of the 981 cases, 168 malignant cases were confirmed by histology and 167 malignant cases were confirmed by cytology. The median is 66 years. The sex ratio (H/F) was 8/1. The sensitivity of the cytology was 99.4 %, the specificity was 100 %, the positive predictive value was 100 % and the negative predictive value was 99.9 %. 82.73 % cases were confirmed by the first biopsy, 11, 30 % cases by the 2nd biopsy, 1,78 % cases by the 3rd biopsy, 1,78 % cases by the 4th biopsy, 2,28 % cases by 5th biopsy. The cyto-histological correlation is excellent for small cell carcinoma (SCC) (97 %); low to non SCC (35 %), for squamous-type (36 %) and for adénocarcinoma (28 %). 19, 64 % cases required an IHC study and helped in 96, 97 % to define the histological type.
Conclusion: Although the cytological classification, there is still reluctance on the part of some clinicians about the reliability of cytological diagnosis in the lung cancer.

PS-22-017

Immunohistochemical study of experimental oxidative stress impact on antioxidant markers in lung vascular structures

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Objective: The imbalance between the oxidants/antioxidants represents the dominant feature of oxidative stress, causing different types of lung injuries and affecting the lung normal functions. Our study assesses 2 markers of the oxidative stress, by immunohistochemical monitoring of Mn-SOD/EC-SOD in pulmonary vasculature after bleomycin administration.
Method: To produce oxidative stress, 14 male Whistar rats weighting 235 ± 10 g were randomized in two groups, control and bleomycine trated (a single dose of endotracheally administered bleomycine, 2,5 U/kg body weight dissolved in 0,25 ml saline 0,9 % NaCl). While SOD level was determined in blood, prelevated lungs, preserved in formaldehyde until embedded in paraffin, were sectioned and immunostained for Mn-SOD and EC-SOD.
Results: The significant augmentation of EC-SOD level in blood is also correlated with a highly vascular EC-SOD expressed in lung, consequent of bleomycine-induced lung injury response in rats, at the same time, low lewel Mn-SOD was detected in blood and in all the examined blood vessels.
Conclusion: Extensively expressed EC-SOD in lung vasculature after bleomycin administration compared with MN-SOD low level may be accorded to its higher lung distribution together with its more considerable involvement in the defense in this type of oxidative stress.

PS-22-022

Nuclear size and Ki-67 index of squamous dysplasia and squamous cell lung carcinoma in bronchoscopic biopsy

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Objective: Squamous dysplasia may be precursor of squamous cell carcinoma of the lung. These lesions may cause a diagnostic dilemma in small biopsy specimens. The aim of this study was to estimate karyometric variables and Ki-67 index of squamous dysplasia and squamous cell lung carcinoma.
Method: At Institute of Pathology of Niš, formalin-fixed, paraffin-embedded bronchoscopic mucosal samples from 10 patients with moderate squamous dysplasia and 10 patients with squamous cell lung carcinoma were retrieved from pulmonary pathology archives. Serial histologic sections of 4 μm thickness were prepared for staining with hematoxilin and eosin and analyzed using image analysis system ImageJ. Immunohistochemical staining was performed by streptavidin-biotin method, and Ki-67 activity was quantified with plugin Cell counter.
Results: All measured nuclear variables: nuclear area, Feret diameter and perimeter were found to be significantly different between squamous dysplasia and squamous cell lung carcinoma ($p < 0.01$). The values of nuclear variables of squamous cell carcinoma were significantly larger than in squamous dysplasia. Similarly, Ki-67 index was significantly larger in squamous cell lung carcinoma compared to moderate dysplasia ($p < 0.01$).
Conclusion: Morphometric image analysis may be helpful ancillary tool in distinguishing moderate squamous dysplasia from squamous cell lung carcinoma in bronchoscopic biopsies.

PS-22-023

Alveolar adenoma of the lung with CD34 and CD10 positive stroma: Differential diagnosis in a biopsy

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Objective: Histological differential diagnosis of alveolar adenomas of the lung includes lymphangioma and sclerosing pneumocytoma. In biopsies additional tumours have to be excluded.
Method: A 44 years old patient presented with a tumour in the right pulmonary hilus in a routine thoracic x-ray. A CT-guided biopsy taken from paramediastinal/lung revealed a tumour consisting of two components: a tubular epitheloid and mesenchymal population. Because of a dominating spindle cell component and the primarily lacking preexisting lung parenchyma in the biopsy, the tumour could not be classified exactly in spite of TTF1 positivity of the tubular component in the biopsy, nor potential semimalignant behavior could be excluded. Lobectomy with lymphadenectomy was performed. Comparative immunostainis of biopsy and resection specimen.
Results: Intraoperatively the tumour was clearly situated in lung parenchyma and sharply circumscribed. Preliminary diagnosis was sclerosing pneumocytoma, which was excluded because of lack of TTF1 positivity of the stromal component and lack of sclerosis and papillae. Final diagnosis was alveolar adenoma of the lung in the resected right upper lobe. There were some unusual details: only little cyst-formation in the center of the tumour, strong immunopositivity for CD34 and CD10 of the stromal cells. This stromal component was the reason for further differential reflections in the biopsy: solitary fibrous tumour, which was excluded by histomorphology in the resection specimen and adenoleiomyomatous hamartoma, which should express smooth muscle actin and is not expected to be as homogeneously arranged as this tumour.
Conclusion: In rare tumours precise clinical information including the exact organ context of a lesion is essential for a correct diagnosis in biopsies to avoid over-therapy.

Table 1: Comparison and figures 1 and 2:

specimen	staining	Clone	result epithel	result stroma	comment
biopsy	TTF1	8G7G3/1	nuclear pos	neg	
	Ki67	30-9	<1%	<1%	overlaying blood cells positive
	alpha Fetopr.		neg	neg	supposed situation in the mediastinum
	CD99	H036-1.1	neg	neg	
resection specimen	TTF1	8G7G3/1	nuclear pos (+++)	neg	
	Ki67	30-9	<1%	5%	
	CD99	H036-1.1	neg	neg	
	pancytokeratin	AE1/AE3	pos	neg	
	EMA	E29	pos in situ, neg desquamated cells	neg	
	CK7	OV-TL 12/30	pos in situ, neg desquamated cells	neg	
	actin (SMA)	1A4	neg	neg	vascular network
	desmin	D33	neg	neg	
	podoplanin	D2-40	neg	neg	few lymph vessels peripherally
	CD31	1A10	neg	single cells	
	CD34	OBEnd/1	neg	pos (+++) cytopl-membr	
	CD10	56C6	pos (++)	pos (+++) cytopl-membran	
	S100	S100PAB	neg	pos	some stromal cells
	bcl2	SP66	neg	some single cells	
	bcl2	CL 124	neg	neg	some lymphocytes
	GFPA	EP672Y	neg	neg	
	CD5	SP19	neg	neg	some overlaying lymphocytes
	PAS-D		single cells	neg	
	PgR (progesteron)	1,00E+02	neg	neg	
	EGFR	3C6	membranous pos (++)	diffuse weakly pos	

table 1 – comparison biopsy – resection specimen
fig 1 biopsy

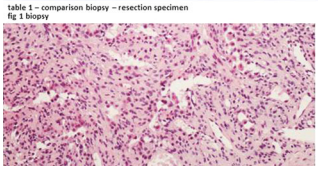
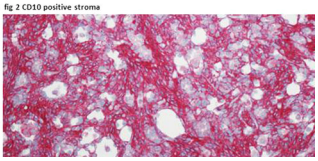


fig 2 CD10 positive stroma



PS-22-024
Phenotypic profile of high-grade non-small cell lung carcinomas in small biopsies and in postoperative material
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Objective: Most of patients with lung carcinoma are inoperable, thus, the diagnosis relies on small tissue biopsy (oligobiopsy) and cytologic smears. The aim was to compare the phenotype in poorly differentiated non small cell lung carcinoma (NSCLC) present in oligobiopsies and in surgical resection samples.
Method: The postoperative tissue material of poorly differentiated NSCLC was obtained from 123 patients, however, only in 39 cases a tissue from surgical resection was available. Squamous cell carcinomas amounted to 46 % of studied tumours followed by adenocarcinomas (24 %), large cell (14 %) and adenosquamous carcinomas (5 %). The rare histological subtypes and mixed carcinomas made the remaining 11 %. The histopathological diagnosis was based on the routine hematoxylin & eosin staining.
Results: The results of immunohistochemical stainings (IHC) in the whole tissue sections and oligobiopsies were compared by means of statictical parameters. The analysis is shown in the Table 1.
Conclusion: The results in whole tissue sections showed high concordance with IHC staining in oligobiopsies. The highest compliance was found for CK7 and CK5/6, whereas the lowest for TTF1, Napsin A and mucin stainings. The immunohistochemical phenotype of small oligobiopsies correlates with the profile presented by the whole tissue sections. The project was supported by National Science Centre UMO 2011/01/N/NZ4/01710.

Table NSCLC:

Antibody	R – Spearman	Kappa
p40	0,803	0,78
p63	0,634	0,769
CK 5/6	0,786	0,84
CK 7	0,886	0,896
TTF1	0,554	0,524
Napsin A	0,628	0,443
mucicarmin	0,52	0,48

PS-22-025
Bronchiolar epithelium adaptation to stimuli: Vimentin and high weight molecular cytokeratin expression may relate to carcinogenesis
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Objective: Terminal Respiratory Unit (TRU) inflammation has been recognized as a carcinogenic pool for bronchial-pulmonary carcinomas after adult stem cells carcinogenesis. An immunohistochemical study was developed to verify the behavior of TRU epithelial cells in bronchiolitis.
Method: A series of surgical biopsies concerning broncholitis classified as Chronic Bronchiolitis (CB) - 11 cases, considering lymphocytic infiltrate along with smooth muscle cells hyperplasia; 15 cases of Respiratory Broncholites (RB) and 14 cases of Broncholitis Obliterans (BO), was compared with preserved morphology (BPM)- 5 cases, obtained after surgical drainage of spontaneous pneumothorax due to heterogeneous infant pleural scars. The immunohistochemical panel considered TTF1, CK5.6.18, and vimentin was applied to all cases.
Results: The BPM cases presented TTF1 expression and negativity for vimentin and CK5.6.18 had 1 positive case. Vimentin and CK5.6.18 basal / epithelial cells expression was correlated progressively with BO, CB and RB, representing 8/14,4/11 and 2/15 positive cases for vimentin and 8/4, 5/11, and 7/15 positive cases for CK5.6.18, respectively.
Conclusion: These results are important to understand TRU carcinogenesis potentiality indicating bronchialization of bronchiolar epithelium, where adenosquamous carcinomas and pleomorphic carcinomas may develop: basal cell metaplasia with CK5.6.18 expression

represents bronchial basal cell phenotype, maintaining TTF1 expression and epithelial-mesenchimal transition is represented by vimentin overexpression.

PS-22-026

Technical advantage of preparing FISH ALK/ROS1 on previously immunostained slides

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Objective: EML4-ALK fusion gene define a tumour group of adenocarcinomas responsive to targeted therapy. ALK FISH is currently considered to be the gold standard for selection of crizotinib anti-ALK treatment. When a laboratory is confronted with scarce material on a FFPE sample, to maybe overcome this issue we describe a feasible method of FISH on immunostained slides.
Method: Choosing an adequate immunostained negative slide is essential for a good visualization of the signals. Removal of the cover slip in xylene may require 1 or 2 days. FISH protocol as currently described is then applied, followed by a break-apart probe specific to the ALK locus according to the manufacturer's instructions. FISH-positive cases were defined as >15 % split signals in tumour cells (At Shaw et al).
Results: The slides present little or no autofluorecence in immunostained negative slides. One hundred neoplasic cells are currently counted, with over 15 % presenting spliced signals, to be considered as ALK positive.
Conclusion: Chromogen labeling with diaminobenzidine (DAB) may lead to autofluorescent effects hampering FISH analysis. Routine negative immunostained slides of the studing case can be considered with a rigorous quality testing. By this method, FISH ALK, MET and ROS1 are feasible on previously immunostained slides.

PS-22-027

Pulmonary congenital cystic adenomatoid malformation typeI presenting as a single cyst of the middle lobe in an adult

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Abstract: Congenital cystic adenomatoid malformation (CCAM) of the lung presents mainly in neonates, is rare in children beyond infancy, and has not been very rare in adults. Cases of CCAM have been previously described in adulthood, more often type I with multiloculated cystic lesions. We report a case of type I CCAM presenting as a single, expansive cystic mass in the middle pulmonary lobe in a 42-year-old female, revealed by persistent cough. Computed tomographic scan showed a single cyst with air fluid level, occupying the lateral segment of the lobe. The patient underwent a middle right lobectomy without complications Histologically, the cystic wall consisted of vascularized fibrous tissue lined by cuboidal or columnar respiratory epithelium with focal gland-like appearance. Rare smooth muscle bundles and elastic fibers were present. The diagnosis was CCAM, type I, according to the modified Stocker's classification. In conclusion when CCAM type I consists of a single large cyst, the differential diagnosis includes lung and bronchogenic cysts. The exact localization of the disease and the histological examination can be crucial for the correct diagnosis.

PS-22-028

Immunohistochemistry and molecular profile of Reactive Pneumocytic Lesion (RNL), Atypical Adenomatous Hyperplasia (AAH), and Adenocarcinoma In Situ (AIS): A comparative study

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Objective: The aim of the present study is to compare the immunohistochemical (IHC) markers and molecular profile currently available for the diagnosis and prognosis of these lesions.
Method: We studied 33 lung tissue samples with the diagnosis of RNL (six cases), AAH isolated (19 cases), and associated with AIS (eight cases). Invasive lung adenocarcinoma was present in 15/33 (45 %) specimens. We performed IHC analysis: ki67, p53, bcl2, EGFR, cyclinD1, CEA, p16, NFkB-p65, ubiquitin, TTF1, C4.4A, survivin. And molecular status of EGFR, KRAS by DNA sequencing; and ALK rearrangements by FISH.
Results: 6 cases of RNL; were weakly positive for cyclinD1 (6/6), TTF1 (6/6), p16 (4/6) CEA (1/6) and EGFR (1/6). 19 cases of AAH were positive for TTF1 (19/19), cyclinD1 (19/19), p16 (14/19), CEA (13/19), EGFR (4/19), and p53 (1/19). Both groups shown Ki67 Expression < 3 %. 8 cases of AIS were positive for TTF-1 (8/8), CEA (5/8). p16 (3/8), survivin (3/8), EGFR (3/8), C4.4 (2/8), p53 (2/8), cyclinD1 (2/8), and bcl2 (1/8). Ki-67 was positive in >5 %. Molecular findings shown EGFR alteration in 2/26 cases of AAH associated to AIS.
Conclusion: The IHC study of CyclinD1, CEA, and EGFR have proven to be useful. And the molecular alterations suggest that AAH and AIS are related.

PS-22-029

Oxidative stress, inflammation and epigenetics in pathogenesis of chronic obstructive pulmonary disease during chronic nicotine exposure of rats

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Objective: Chronic obstructive pulmonary disease (COPD) is a highly prevalent disease characterized by chronic bronchitis, largely irreversible remodeling of the small airways and emphysematous destruction of the alveoli. COPD often results from prolonged exposure to irritant such as cigarette smoking or inhaled particulates. The current study aimed to understand the intricate mechanisms by which chronic exposure to nicotine can lead to the pathogenesis of chronic lung inflammation that may promote COPD.
Method: Rats were allocated into two groups: “Control”, which received saline injections, “Nicotine” which received nicotine injections (2, 5 mg/kg) for 6, 12, 18 and 24 weeks.
Results: Overall, the rats treated daily with nicotine showed a significant increase in the extent of lipid peroxidation, the activities of antioxidant enzymes, and mRNA expression of COX-2 and MMP9 in pulmonary tissues, compared to control rats. The histopathological findings revealed significant morphological alterations with a growing interstitial infiltration of mononuclear cells and macrophages. Beyond 18 weeks of nicotine treatment, we observed emphysematous appearance with pulmonary microvascular leakage (edema, fibrin) and hemorrhage.
Conclusion: Taken together, these data support the pathogenic role of nicotine due to its oxidative potential that change the appearance and function of lung cells; promotes inflammatory lung processes and leads emphysema lesions like-COPD.

PS-22-030

Bronchial basal cells express TTF1 in pulmonary adenocarcinomas

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Objective: Bronchial and bronchiolar epithelium adaptation to tobacco may become an outstanding way of previewing carcinoma development/carcinogenesis after basal cells, cylindrical and mucous cells hyperplasia/metaplasia with intermingled immunophenotype in between bronchioles and bronchial expression.

Method: The immunoexpression of ten well differentiated epidermoid carcinomas(3) and adenocarcinomas(7: acinar 3; solid 2; mucinous 1; and papillary/micropapillary 1) was compared with either bronchial and bronchiolar cells. The following panel was applied: CK7, TTF1, Ck8.18, and CD10 for adenocarcinomas, VIM for EMT, CK5.6 and p63 for epidermoid differentiation, CD56 for NE cell type, and Ki67.
Results: For epidermoid carcinomas, bronchial epithelium metaplasia had high CK5.6 and low p63 expression with vimentin negativity; one case had bronchial TTF1 basal cell positivity; in bronchioles, CK5.6 was relevant with lower expression of p63. In adenocarcinomas, vimentin was expressed in all cases, but not in one acinar case with desmoplastic stroma, where bronchioles expressed vimentin. Bronchial epithelium had TTF1 expression in adenocarcinomas and negativity in epidermoid carcinomas.
Conclusion: As a small series, it seems that vimentin expression is relevant in adenocarcinomas carcinogenesis with TTF1 bronchial expression while in epidermoid carcinomas, CK5.6 keeps being a confident marker, relevant in bronchioles where it is usually absent. There was not a specific immunophenotype for adenocarcinomas.

PS-22-031
Inflammatory myofibroblastic tumour of the lung with sarcomatous transformation: Case report
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Objective: Inflammatory myofibroblastic tumour is a rare solid tumour that occurs as myofibroblastic cell proliferation associated with inflammatory cells. Although benign, it is a tumour of intermediate biological potential due to a tendency for local recurrence and small risk for distant metastasis. Very rare inflammatory myofibroblastic tumours may undergo sarcomatous transformation.
Results: A 61-year-old, previously healthy woman was reffered to our hospital due to fatique and shortness of breath for the last 3 months. The x-ray image showed a mass lesion in the right lung, located to the lateral segment of the upper lobe. Contrast enhanced chest CT scan and chest MRI showed solid expansive mass, 4 × 2,2 cm in diameter, which was primarily referred as mesothelioma. At that time, she underwent surgical procedure. The tumour mass measured 4 × 3,7 × 1,7 cm and on cut section had hard rubbery texture. Histologically and immunohistochemically inflammatory myofibroblastic tumour with sarcomatous component was diagnosed. No further adjuvant therapy was considered necessary. The symptoms returned 2 months later. Control chest CT scan showed relapse and disease progression. Patient died the following day due to respiratory failure. An autopsy was not performed.
Conclusion: We presented a case of inflammatory myofibroblastic tumour of the lung with sarcomatous transformation with very unfavorable course and outcome.

PS-22-032
Hard to think, good to say - Pulmonary Langerhans' cell histiocytosis: A case report
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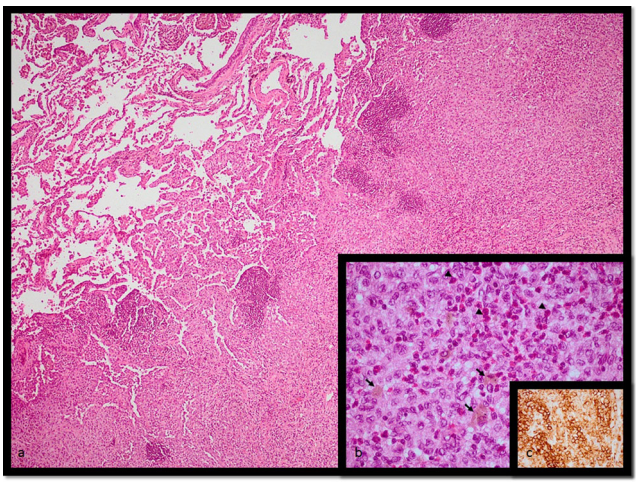
Objective: The purpose of this work is to report a rare case of pulmonary Langerhans' cell histiocytosis (PLCH), in a patient with high suspicion of metastatic disease of malignant melanoma.
Method: A 40 year-old man, with background of treated pulmonary tuberculosis in childhood, malignant melanoma excised in 2004, smoking habits and recreational drug consumer, that have been found multiple micro-nodular infra-centimetric lesions, in a thoracic radiography. The computed tomography (CT-scan) reveled multiple lesions at both lungs, some with cavitation. After signaling with harpoon by CT-scan, a surgical biopsy was made.
Results: Surgical specimen of atypical pulmonary resection with 11,5 × 4,0 × 2,1 cm, marked with harpoon. The section surface showed three white-gray speculated nodules with greater dimensions between 0,6 and 0,4 cm. Histologic examination showed an infiltration of eosinophils, lymphocytes and Langerhans' cells. Brown pigment deposits were observed. These cells stained with CD1a and S100 protein and did not stain with Melan A and HMB45.
Conclusion: The PLCH is a rare condition. A few cases have been reported, mostly associated with smoke. In this case, a surgical biopsy was performed, which resulted in the diagnosis of PLCH based on eosinophil infiltration and positive staining for CD1a and negative for Melan A and HMB45. S-100 protein would be positive in both cases. A good clinical correlation with a qualified biopsy interpretation is decisive for the correct diagnosis.

a: PLCH - Densely cellular nodule with delicate stellate extensions along the adjacent alveolar walls (original magni_cation, 40x H&E). b: Langerhans' cells with indistinct borders, (arrow heads) infiltration of eosinophils and (arrows) brown pigm:



PS-22-033
Pulmonary Langerhans Cell Histiocytosis "De Novo" after transplantation
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Objective: A Pulmonary Langerhans cell histiocytosis is presented in a 40 year-old woman after bilateral lung transplantation for emphysema without any signs of Langerhans cells proliferation in the explanted lungs.
Method: We retrospectively performed a S100 protein, CD1a and Langerin immunohistochemical analysis with no signs of Langerhans cells proliferated in her own lung tissue. We performed also a molecular profiling analysis comparing the receptor pulmonary tissue and the Langerhans cells that showed these cells were originated in receptor clones.
Results: A "de novo" monoclonal origin in stem cells, probably from bone marrow is suggested. The reason she did not developed disease in their native lungs is unknown.
Conclusion: Our case supports the view that the abnormalities that originate this kind of disease must be present in precursor dendritic cells outside the lung. A probably additive effect between tobacco antigens and local factors must be present to develop Langerhasns cell proliferation.

PS-22-034

Immunohistochemical and clinicopathological analysis of primary salivary gland-type lung carcinomas

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Objective: Salivary gland-type lung carcinomas are rare neoplasms, comprising less than 1 % of all lung tumours. Adenoid cystic carcinoma (ACC) and mucoepidermoid carcinoma (MEC) are the two most common subtypes. The aim of the present study was to evaluate the cases for histologic and immunohistochemical findings and survival.
Method: Thirteen cases diagnosed in resection specimen were reviewed histopathologically in the study. Survey data was available in 9 patient.
Results: The mean age was 52.8 ± 20.4 years-old (range = 12–73). There was slightly more frequent in men (92.3 %). The mean size was 37.3 ± 31.7 mm (range = 7–135). MEC was diagnosed in 76.9 % of patients and ACC was diagnosed in 23.1 %. Most MEC tumours were high-grade (60 %). Pleural invasion was seen in 15.4 % and perineural invasion was in 46.2 % of patients. Five patients had lymphovascular invasion. Lymph-node involvement observed in three patients. Immunhistochemically, all cases were positive for cytokeratin7 and negative for cytokeratin20. P63 was positive in 11 cases. TTF-1 was found pale and focally-positive in two case.
Conclusion: It is important to recognize these tumours because of their clinical behavior and treatment. İmmunohistochemical analysis have a limited importance in the diagnosis. Further series are possibly required to understand for prognostic significance.

PS-22-035

Pulmonary Langerhans' Cell Histiocytosis: Histopathological features

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Objective: To analyze histological characteristics of Pulmonary LC Histiocytosis.
Method: The investigated material included open lung biopsy samples taken from 14 patients at the mean age of 23.2 years. The intensity of the histological lesions was semiquantitatively measured, differentiating three intensity grades: mild, moderate, intense.
Results: In most cases the interalveolar septa were focally and intensively thickened. The inflammatory infiltrates in the septa were intense in 8 moderate in 4, and mild in 2 specimens. Lymphocytes prevailed, followed by macrophages, eosinophil granulocytes, and plasma cells. The lumen of the alveoli was occupied by a few macrophages and lymphocytes, sparse plasma cells and few eosinophil granulocytes. The alveolar cells were focally cuboid in six cases. Poor peribronchial infiltrates of lymphocytes and plasma cells were found in eight cases. Histiocyte aggregates with a stellate border were detected in all specimens, most frequently localized peribronchiolarly (14/14), perivascularly (6/14), in the interlobular septa (4/14). The aggregates were predominantly composed of Langerhans' cells (abundant in 14/14 cases), followed by eosinophil granulocytes (sparse in 8/14), lymphocytes (moderate in 8/14 cases), and plasma cells (sparse in 6/14). The histiocytes were CD1a and S 100 positive.
Conclusion: Histiocyte aggregates were registered in all biopsy samples; the histiocytes were CD1a and S100 positive.

PS-22-036

Non-Hodgkin's malignant lymphoma in lung: Discussion a case

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Abstract: Sixty-two year old woman with weakness, loss of appetite, loss of weight and back pain attended to our hospital. Thoracic CT examination revealed out 2 × 1.5 cm sized mass in the right hiler region adjacent to the right pulmonary artery and superior vena cava. Consolidation-atelectasis area was observed in the right pulmonary upper lobe. Patient underwent bronchoscopy and 5 specimen the largest of 4 mm diameters were taken. At the Sections of bronchial biopsy, atypical cells showing differences in size and shape which have, scattered, single, large, multilobulated nucleus, under the bronchial epithelial surface. CD20 immunohistochemical study showed CD20, Bcl-6, CD79a, and Ki-67 positive staining. CD-15 and CD-30 did not show any immunraectivity. Between these cells CD3 positive staining cells with dense mature looking also observed. These cells showed a rosette-like sequences among the tumour cells. This histomorphological and immunohistochemical findings were associated with non-Hodgkin's malignant lymphoma (large B-cell lymphoma w.th rich T cells). The patient diagnosed with malignanat non-Hodgkin lymphoma. Patient treated with chemotherapy. The patient is in remission for 4 years.

PS-22-037

Aberrant pulmonary neuroendocrine tumour nomenclature in daily pathology practice: Limited tissue is an issue

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Objective: Pulmonary carcinoids (PC) and high-grade neuroendocrine carcinomas (NEC) should be diagnosed according to nomenclature of the WHO 2004/2015 classification. Here we analyze the diagnostic nomenclature established in daily practice in the Netherlands.
Method: Pathology report conclusions of PC/NEC were selected from the Dutch Pathology Registry (2003–2012) through queries on anatomic location, diagnosis and keywords (e.g. carcinoma + endocrine). After screening (JLD & RJS), conclusions were excluded if inconclusive, described non-lung, non-PC/NEC, small cell cancer or autopsy cases. Clustering was performed for sampling method (non-surgical biopsies & cytology versus resection) and diagnosis. Retrieved diagnoses were compared with the WHO 2004 nomenclature.
Results: 3849 conclusions were eligible: PC (N = 2005, 52 %), NEC (N = 1788, 47 %) and neuroendocrine tumour n.o.s. (N = 56, 1 %). In 8 % (N = 157) of PC and 21 % of NEC (N = 377) diagnosis deviated from advised nomenclature. This occurred more often on biopsy and cytology (PC N = 108, NEC N = 292) than on resection specimens (PC N = 49, NEC N = 85).
Conclusion: In 8 % of PC and 21 % of NEC, mostly diagnosed on biopsy/cytology specimens, the retrieved final diagnosis did not comply with WHO nomenclature. Further research is needed to examine if this is due to personal preferences or to difficulties in applying current classification to limited material.

PS-22-038

When is it an immunologic lung disease?

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Objective: The lung is frequently involved in autoimmune and allergic diseases. Acute onset diseases can be more easily diagnosed, because of the features such as epithelioid cell granulomas and lymphocytic interstitial pneumonia (LIP) in hypersensitivity pneumonia/ extrinsic allergic alveolitis (HP/EAA), or lymphocytic interstitial pneumonia combined with granulomas or DAD in collagen vascular diseases. Chronic diseases are more difficult to diagnose, because of the morphological overlap with many other diseases.

Method: Out of the consultation cases of one of the authors, 145 cases diagnosed as autoimmune diseases/collagen vascular diseases (AD/CVD) and another cohort of 140 cases diagnosed as hypersensitivity pneumonia (HP) were selected and evaluated for features of chronic/subacute AD and HP.
Results: In most cases UIP combined with LIP was pointing to an immunologic disease. Other characteristic features were epithelioid and histiocytic granulomas, which enabled an even more specific diagnosis.
Conclusion: Understanding the course of an AD is a requisite to interpret the morphology. AD with high levels of autoantibodies tend to deposit antigen-antibody complexes and activate complement. This all can be evaluated by histopathology and allows a specific diagnosis even in the absence of clinical information.

PS-22-039
Evaluation of ALK expression in non-small cell lung cancer: A tissue microarray analysis
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Objective: The oncogenic form of anaplastic lymphoma kinase (ALK) gene represents a unique opportunity for diagnostic and therapeutic purposes in several malignancies, including non-small cell lung cancer (NSCLC). This study aimed to examine the expression levels and clinical significance of ALK in a series of NSCLC samples assembled in tissue microarray (TMA).
Method: We respectively reviewed 140 samples of NSCLC, including 64 (46 %) adenocarcinoma (ADC), 62 (44 %) squamous cell carcinoma (SCC) and 14 (10 %) large cell carcinoma (LCC) for expression of ALK using immunohistochemistry, and then immunostaining patterns were correlated with clinicopathological parameters.
Results: Expression of ALK showed a significant difference between SCC with ADC ($P < 0.001$) and LCC samples ($P < 0.001$). The highest level of ALK expression was found in ADC cases with poorly differentiated and high nuclear grade ($P = 0.005$ and $P = 0.005$, respectively). Also high level of expression of ALK was more often observed in ADC cases with poor prognosis compared to good prognosis ($P = 0.013$).
Conclusion: These findings suggested that ALK can be considered as a promising target in tailoring therapy in patients with ADC of the lung.

PS-22-040
A case report of complete consolidation of the right middle lobe due to the endobronchial fibroma
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Objective: To present a case of endobronchial fibroma that caused consolidation of the right middle lobe.
Method: A 49-year-old male patient came forward his physician for fever, cough and occasional chest pain 6 months before admission. CT scans of the chest revealed intraluminal polipoid lesion appearing in right lobar bronchus, traction bronchiectasiae of distal airway branches, consolidation of the right middle lobe and pleural effusion. On admission, patient had no symptoms. Percussion and breath sounds were decreased in the right lower lung field. Bronchoscopy revealed a node in right main bronchus, impossible to remove this way. Pathohistologic examination of the byopted material gave no diagnosis and lebectomy of the right middle lobe was made.
Results: Macroscopic exam after lobectomy showed smooth, luminous, whitish stalked node 2,5 cm in length, attached to lateral segmental bronchus. Histopathological examination revealed a polyp lined by respiratory epithelium with underlying stroma made of bundles of spindle-shaped cells inside of abundant hyalinised connective tissue. Background lung parenchyma showed bronchopneumonia and bronchiectasiae.
Conclusion: Endobronchial fibromas are usually completely removable bronchoscopically, but sometimes lobectomy may be required.

PS-22-041
Histologic repartition of pulmonary tumours in Lebanon: A 5-year single institution experience
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Objective: To compare the current histologic distribution of lung cancer in Lebanon to the worldwide trends, according to the 2004 WHO Classification.
Method: 1760 patients with a pulmonary pathology exam at Hôtel-Dieu de France University Hospital between July 2009 and July 2014 were included.
Results: 676 out of 1760 investigated patients (38.4 %) had a lung tumour. 665 (98.4 %) tumoural cases were malignant, with a mean age at diagnosis of 63.8 years and a Male/Female (M/F) Sex Ratio of 1.7. Among the malignant tumours, 86.2 % were epithelial tumours with a mean age at diagnosis of 64.8 years and a Sex Ratio of 1.9. Other malignant tumours consisted of metastatic tumours (10.2 %), lymphoproliferative tumours (2.1 %) and mesenchymal tumours (1.5 %). Most common carcinoma subtypes were adenocarcinoma (48.0 %), squamous cell carcinoma (23.0 %) and small cell carcinoma (13.3 %). Carcinoid tumours were the only carcinoma subtype with an M/F Sex Ratio below 1 (0.7). Salivary gland tumours were the carcinoma with lowest mean age at diagnosis (45.5 years).
Conclusion: The histologic repartition of lung tumours in Lebanon is similar to that in developed countries. We believe this resemblance is due to common smoking habits, known to be responsible for the increase of lung adenocarcinoma at the expense of other subtypes.

PS-22-042
Morphological pattern and necrosis percentage in pulmonary metastasis of colorectal carcinoma to validate treatment: First approach for grading
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Objective: Colorectal carcinoma liver metastasis morphology validates chemotherapy effectiveness for liver resection. L Rubia-Brandt tumour regression grading was adapted to pulmonary metastasis to understand either morphology and establish a follow-up program.
Method: Colorectal carcinoma 42 pulmonary metastasis (2014-March 2015) were evaluated by the following parameters: number of nodules per resection (solitary, two or more and more than one resection); morphology (microglandular pattern, macro-microglandular and mucin production) and necrosis percentage (0-absent; 1- < 25 %; 2-25-50 %; 3-50-75 %; 4->75 %) with total paraffin inclusion.
Results: Variable number of lymphocytes completed intermingled scarce stroma without fibroblastic collagen deposition. Of the 42 cases, 30 had an only metastasis, 6 presented more than one and 6 patients had already been submitted to various resections. One case had mucin production, 19 presented macro-microglandular pattern and 13 were microglandular. Concerning necrosis, 7 cases were over 75 %; 2 in grade 3, 8 cases in grades 1 and 2 each and 7, had no necrosis; the 6 cases with various surgical resections, showed overlapping of two contiguous grades.
Conclusion: Although small is an elucidative series of pulmonary parenchyma interference with colorectal carcinoma metastasis morphology, that differs from liver metastasis. The presented grading is suitable to be explored in larger series with chemotherapy protocol and patients follow-up registration.

PS-22-043

Retrospective evaluation of children with congenital pulmonary airway malformation: A single center experience of 20 years

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Objective: We aimed to evaluate clinical and pathologic findings of children with congenital pulmonary airway malformation (CPAM) from a single center during 20 years.
Method: We reviewed the 19 children with CPAM, who were diagnosed and treated between 1992 and 2011.
Results: There were 9 boys (47.4 %) and 10 girls (52.6 %) with a mean age of 3.26 ± 4.3 years (1 month- 13 years). Most newborns were presented with respiratory distress, while there were recurrent pulmonary infections in older children. The subtype of CPAM led to surgery was type I in 4 cases (21.1 %), type II in 8 cases (42.1 %), type III in 5 cases (26.3 %); and type IV in 2 cases (10.5 %). In 13 cases (63.4 %). A 1-month old child with type I CPAM had multiple lesions affected 2 lobes and only a newborn with type II CPAM, lesions located bilateral. There was no type 0 cases in this series. All cases were treated with lobectomy and there were no complications.
Conclusion: In the present study, a realistic comprehensive picture of CPAM in a central children's hospital has been provided. In addition the possible reasons of its different percentages according to the current literature was discussed.

PS-22-044

Particular components of the translation machinery drive lung cancer formation

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Objective: Regulation of mRNA translation occurs at the initiation step requiring the interaction of eukaryotic initiation factors (eIFs). Dysregulation may lead to abnormal gene expression possibly resulting in carcinogenesis. We evaluated pulmonary cancer eIF protein expression profiles.
Method: The protein expression levels of eIFs and members of the mammalian Target of Rapamycin (mTOR) pathway were determined by Western Blot analysis on 18 xenograft mouse models, representing the main entities of lung carcinomas. Immunohistochemistry (IHC) for the eIF subunits 2α, 3c, 3h and 4e was performed on tissue micro arrays (TMAs), containing primary lung cancer and metastasis cases of a total of 603 patients.
Results: Western Blot analysis of xenograft tumours revealed a significant up-regulation of eIF3j, 4E-BP1, Akt and phospho-Akt compared to control. We observed an expression of phospho-mTOR, eIF3a, eIF3b, eIF3c, eIF3k, eIF4g, phospho-4b and phospho-4e-BP1 compared to no signal in controls. IHC revealed up-regulation of eIF2α, eIF3h and eIF4e as well as variable expression patterns of eIF3c.
Conclusion: Our findings indicate a major contribution of eIFs to lung cancer. Specific eIF subunits are differentially expressed in various lung cancer entities potentially explaining their biological behavior linking eIFs to mTOR and other signaling cascades.

PS-22-045

Granulomatosis with polyangiitis-a lung resection after a pneumotorax

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Objective: We present a case of 44-year-old female complaining of nose and ears problems, headache, fever, chest pain, fatigue, dry cough.
Method: A computed tomography showed multiple cavity formations in the right lung. A transthoracic biopsy was taken and the patient was diagnosed with granulomatosis with polyangiitis. A month later the patient presented with pneumothorax to the right. A surgery was performed - a segmentectomy.
Results: Macroscopic - a cavity with size 60/55/28 mm, with thick walls, inner uneven surface, with whitish deposits. Histology - a wall of cavity composed of connective tissue with massive infiltration of mononuclear cells; in the interior of the cavity - zones with "geographical" type necrosis; infiltration of eosinophils and neutrophils in part of the necrotic zones; vasculitis. In the surrounding lung parenchyma - areas with microabscesses, hemorrhages, bronchiolitis obliterans, macrophage pneumonia. Morphological picture of granulomatosis with polyangiitis - eosinophilic form.
Conclusion: We present a rare case of lung resection after a pneumothorax in granulomatosis with polyangiitis. Usually this disease is diagnosed on a small biopsy specimens and in very rare occasions - we have the possibility to have a bigger specimen.

PS-22-046

Mucoepidermoid carcinoma of the lung: A case report

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Objective: Mucoepidermoid carcinoma (MEC) is a rare tumour of the lung that accounts for 0.1–0.2 % of all pulmonary tumours. MEC most often arise from the parotid or submandibular salivary glands.
Method: A 78-year-old female patient was found to have an abnormal shadow in the lung field. Chest CT showed a lobulated mass shadow measuring 30 mm in diameter in the trachea region. The clinical impression was malignancy. A lung biopsy of the mass was done and sent for histopathological examination.
Results: Histologically, the tumour is characterized by a combination of mucus-secreting cells and squamous cells. The cells lack significant mitotic activity, nuclear pleomorphism, and cellular necrosis. Immunohistochemical examination revealed that tumour cells were positive for PAS, with a keratin profile of CK7+, CK20-, CK5/6+, and were determined to be primary lung cancer. The Ki-67 expression was about 10 %. The diagnosis was low-grade mucoepidermoid carcinoma.
Conclusion: Patients with low grade MEC generally have a good prognosis, with a 5-year survival rate of 95 % and adjuvant treatment is considered unnecessary. However, effective treatment measures for high grade tumours have not been established and these cases reportedly have had poor prognosis.

PS-22-047

Invasive pulmonary aspergillosis in neutropenic patients: A clinical underestimated diagnosis

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Objective: Aspergillus species are producing rare but lethal invasive mycoses. Their incidence has risen dramatically in the last decades, more than tenfold. Neutropenic patients usually have a massive infiltration of the pulmonary parenchyma with high risk of vascular invasion and poor outcome, therefore prompt recognition of aspergillosis has major importance for their evolution.
Method: We present three cases of invasive pulmonary aspergillosis in HIV negative patients with neutropenia (caused by non-Hodgkin's lymphoma - two cases; chronic obstructive pulmonary disease with bronchopneumonia - one case).
Results: In all cases, aspergillosis was not diagnosed prior death, but it was suspected during autopsy and confirmed on microscopic

examination with special stains (PAS, Grocott). All patients had pulmonary invasive lesions (mistaken for tumour lesions in first two cases and for a bacterial abscess in the third case) and died due respiratory failure and septic shock.
Conclusion: This emphasizes the importance of a high level of medical suspicion for aspergillosis in immune suppressed patients, since the disease associates a very high mortality without proper treatment. It also sustains the importance of necroptic examination in patients with uncertain diagnosis to identify significant unsuspected causes of death. *Dutulescu and Pop are first authors in equal proportion.

PS-22-048
Comparison of biopsy analysis with cytologic examination in lung malignancies: A brief report
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Objective: The aim of the study was to asses diagnostic efficacy of biopsies with cytological procedures in lung malignancies.
Method: It was performed a retrospective study, analyzing a group of 18 cases of 56–92 years old, male and female patients with lung malignancies reported in our department between January 1st 2012 and Mars 31th 2015 who underwent simultaneous lung biopsy and cytological procedures. The histopathologic types of tumour were establish based on microscopic examination in HE stain and imunohistochemical stain.
Results: Squamous cell carcinoma was the most frequent type of lung malignancy accounting for a third of the cases, followed closely by adenocarcinoma representing 27.7 %. 13 cases had positive diagnosis of malignancy both in biopsies and cytology; 4 cases were positive for malignancies in biopsies and negative in cytology while one case was diagnosed as malignant based on cytology. Biopsy positive for malignacy Biopsy negative for malignacy Positive cytology 13 1 Negative cytology 4 0
Conclusion: Lung biopsy provides most often the definitive histological diagnosis, but accompanying cytological procedures can increase diagnostic yeld.

PS-22-049
Tumour infiltrating lymphocytes in ten cases of lung adenocarcinoma
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Objective: Inflammatory infiltrate has a variable distribution among lung adenocarcinomas. The objective of the study was to assess tumour infiltrating lymphocytes (TILs) in 10 cases of lung adenocarcinomas in relation to stromal reaction, necrosis, cyclin d1 activity and peritumoral macrophages.
Method: We investigated 10 cases of lung adenocarcinoma which showed on routine hematoxylin and eosin stain the presence of TILs. Necrosis and amount of stromal reaction were taken into account. By immunohistochemistry we assessed semiquantitatively the prevalence and distribution of CD3+ and CD8+ lymphocytes within tumour and along the invasive margins. Also, CD 68+ macrophages and cyclin d1 were evaluated.
Results: We found that TILs are mainly CD3+ lymphocytes, CD8- more than CD8+, and they infiltrate stroma more than between neoplastic cells. Peripheral distribution of macrophages is common while stromal infiltration was associated with increased TILs and presence of necrosis. Cyclin d1 was positive more at the periphery of tumour.
Conclusion: Tumoural margins exhibit nonspecific inflammation in adjacent tissue and increased proliferation on tumoural side. TILs present variable distribution within tumour, they appear trapped in tumoural stroma and suggest ineffective immune response. Aknowledgements: CERO - Career profile: Romanian Researcher, POSDRU/159/1.5/S/135760

PS-22-050
Pulmonary epiteloid henangioendothelioma presenting with an agressive course: A case report
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Objective: Pulmonary epithelioid hemangioendothelioma (PEH) is a rare, low to intermediate grade vascular tumour of the lung. Marked nuclear atypia, mitotic activity (>1/10 HPF), tumour necrosis and a spindle cell component predict more aggressive course.
Method: We report a 54 year old male patient lung nodules presented with a clinical history of approximately 4 months of hip pain. A computed tomography of the chest showed a multinodular process involving the right upper lobe, lingula as well as additional nodules in the left lobe. Bronchoscopic biopsies were taken which did not yield a definitive diagnosis. A thoracotomy was performed. Histologically, tumour cells were arranged in clusters and trabeculae set in a fibrous to dense hyalinized and myxoid stroma. Tumour cells show moderate nuclear pleomorphism, atypical mitoses (3/10 HPF) and cytoplasmic vacuoles. Pleuropulmonary involvement, intraalveolar growth pattern, extensive lymphovascular dissemination, foci of tumour necrosis and secondary lung parenchymal infarction were present. Immunohistochemical staining showed positive results for CD31, CD34 and FLI-1. He underwent chemotherapy but died becouse of disease progression after 3 months.
Conclusion: In conclusion, the diagnosis of PEH can be a diagnostic pathological challenge and must be distinguished from a variety of other benign and malignant lung disease.

PS-22-051
MDM2 and HIF1alpha expression levels in different histologic subtypes of Malignant Pleural Mesothelioma (MPM): Correlation with pathological and clinical data
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Objective: Malignant pleural mesothelioma (MPM) is an aggressive tumour with poor prognosis and limited treatments. To date prognostic and tailored therapeutic biomarkers are lacking. The study analyzed the expression levels of MDM2 and HIF1alpha in different histologic subtypes from chemonaive MPM patients.
Method: Biopsies of MPM patients from four Italian centers were centrally analyzed. MDM2 and HIF1alpha expression levels were investigated through immunohistochemistry and RT-qPCR. A pathological assessment of necrosis, inflammation and proliferation index (Ki67 immunostaining) was also performed. Molecular markers, pathological features and clinical characteristics were related to overall (OS) and progression free survival (PFS).
Results: Sixty MPM patients were included in the study (32 epithelioid and 28 non-epithelioid). Higher levels of MDM2,HIF alpha, necrosis and proliferation index were significantly associated with sarcomatoid/biphasic subtypes, while higher levels of inflammation were significantly associated with epithelioid subtype. MDM2 expression levels were significantly correlated with HIF1alpha, necrosis and Ki67. Univariate analysis showed a significant correlation of non-epithelioid histology, high levels of necrosis and proliferation index with shorter PFS.
Conclusion: Sarcomatoid/biphasic and epithelioid mesotheliomas show different MDM2 and HIF1alpha expression levels and are characterized by different levels of necrosis, proliferation and inflammation. Further

studies are warranted in order to confirm prognostic and predictive role of these markers.

PS-22-052

Targeted next-generation sequencing of cancer genes in mucinous and colloid adenocarcinoma of the lung: A retrospective analysis of 54 cases

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Objective: To explored the mutational and pathological profiles of mucinous lung adenocarcinoma (ADC) with the aim of identifying tumour characteristics of potential prognostic and therapeutic interest.
Method: A retrospective series of 54 surgically resected mucinous lung ADC (collected from 2003 to 2013 at three Institutions) was characterized by means of targeted Next-Generation Sequencing (NGS) as compared to pathological characteristics.
Results: 50 cases were invasive mucinous (IMA, 32 pure and 18 mixed) and 4 were colloid (CPA) ADC. The most frequent mutations (all >50 % of cases) with clinical significance were clustered in the receptor tyrosine kinase AKT-mTOR (KRAS, EGFR, PDGFRA, PIK3CA, RET, KDR, HRAS, APC) and the p53/DNA repair (TP53 and STK11) pathways. Interestingly, EGFR mutations were not in the "conventional" hot-spots. CPA, as compared to IMA, had a higher content of extracellular mucin ($p = 0.03$) and more frequent CDX2 expression ($p = 0.02$). IMA cases with mixed pattern were associated to a higher risk of vascular invasion ($p = 0.01$), positive nodal status ($p = 0.001$) and advanced clinical stage (p = 0.006), and with lower rates of TP53 ($p = 0.03$) and PDGFRA ($p = 0.02$) mutations.
Conclusion: Our data claim that mucinous ADC have peculiar pathological and molecular characteristics which might imply a specific clinical management, different form conventional lung ADC.

PS-22-053

Pulmonary localized non-amyloidotic light chain deposition disease: Clinicopathological, molecular, and proteomic study of 3 cases

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Objective: Light chain deposition disease (LCDD) is a rare entity. The lungs are unusually affected. We study three patients with localized pulmonary LCDD.
Method: Morphological-histochemical study was performed. IHC: Abs against amyloid-A, kappa/lambda light-chains, and transthyretin. B-cell clonality: IGH, IGK, and IGL (BIOMED-2 protocols). Targeted quantitative proteomic based method Selective Reaction Monitoring (SRM) was performed for targeted protein analysis.
Results: 2 female and 1 male (age range: 47–68 yrs). CT-scan: widespread cysts with nodules diffusely distributed in both lungs (cases #2 and #3), and one solitary nodule (case #1). Histology: extracellular large nonamyloid (Congo red-negative) amorphous deposits (IHC: kappa light-chain) associated with a mild-moderate infiltrate of small B-lymphocytes, and mature plasma-cells (ISH: kappa light-chain restriction). Case #3: lymphoma BALT/MALT-type associated with LCDD. Electron microscopy: dense granular deposits without fibrillary characteristics. Lung PCR: all cases exhibited IGK clonality. SRM proteomic: all cases were positive for kappa light-chain but negative for other components of amyloid (APOE1 and P-protein). No extrapulmonary disease, bone marrow plasma-cell proliferation, or serum/urine monoclonal protein was found.
Conclusion: LCDD may primarily affect the lung, as a rare cause of cystic-nodular disease. The diagnosis is based on pathological/molecular findings. Our cases are related to local B-cell/plasma-cell clonal proliferation.

PS-22-054

Is proliferation index (Ki-67) valuable in classification of pulmonary neuroendocrine tumours?

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Objective: Pulmonary neuroendocrine (NE) tumours are separated four histologic categories by the number of mitoses and the presence of necrosis. In our study, we applied Ki-67 to NE tumour cases and correlate mitotic activity and Ki-67 index.
Method: We reviewed the clinical data of 59 patients who underwent complete resection (31 typical carcinoid tumour (CT), 3 atypical CT, 19 large cell neuroendocrine carcinoma (LCNEC), 6 small cell carcinoma (SCC)) and analyzed Ki-67 proliferation index. Other immunohistochemical (synaptophysin, chromogranin and TTF-1) and clinicopathological (diameter, mitosis, necrosis, lymphovascular invasion, lymph node metastasis) features were also reviewed.
Results: Ki-67 proliferation index was 1.4 ± 2.3 in CTs whereas the index was 72.8 ± 19.9 in high grade NE carcinomas ($p < 0,001$). The mean Ki-67 indices in the typical CT, atypical CT, LCNEC and SCC were respectively 0.9 ± 1.1, 9.0 ± 1.4, 68.9 ± 20.8 and 84.8 ± 10.2. The difference between typical and atypical CT and also between atypical CT and LCNEC were statistically significant ($p < 0.001$). Statistically, the results of mitotic indices of four NE tumour subtypes were similarly significant.
Conclusion: Although Ki-67 is not part of the current WHO diagnostic criteria for classifying pulmonary NE tumours, our findings provide evidence for the routine use of Ki-67 index together with mitotic activity to optimize separatation of pulmonary NE tumours.

PS-22-055

Morphological characterization of clinical phenotypes in idiopathic pulmonary fibrosis patients

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Objective: Idiopathic pulmonary fibrosis (IPF) is an irreversible lethal fibrosing interstitial disease. Disease severity is determined by its rate of functional decline, slow or rapid, but the basis for this difference is not understood. The aim of the study was to characterize different morphological changes and correlate them to the rate of decline, slow or rapid.
Method: Clinical and functional data were analyzedin 59 IPF patients followed long time before lung transplantation. The %predicted FVC change/year was used to define slow (<10 %) or rapid (>10 %) decline. Twenty-seven patients underwent lung transplantation and different histological alterations (inflammation, fibrosis, vasculitis, diffuse alveolar damage) were quantified by morphometric analysis.
Results: 63 % patients were slow and 37 % rapid. 23 % (11 slow, 3 rapid) developed acute exacerbation (AE) during follow up. Pathology in 27 explanted lungs showed vasculitis, diffuse alveolar damage and innate and adaptive inflammation in rapid and AE (3 times higher than in slow). Inflammation was related to length of symptoms before diagnosis ($r = -0.65$ $p < 0.01$) and rate of FVC decline ($r = 0.8$ $p < 0.0032$).
Conclusion: Slow and rapid decliners are clear phenotypes of IPF with different lung pathology and outcomes. Phenotype identification could be very important in order to recognize outcomes and individualize treatments.

PS-22-057

Fluorescence Lifetime Imaging Microscopy (FLIM) applied to pulmonary pathology

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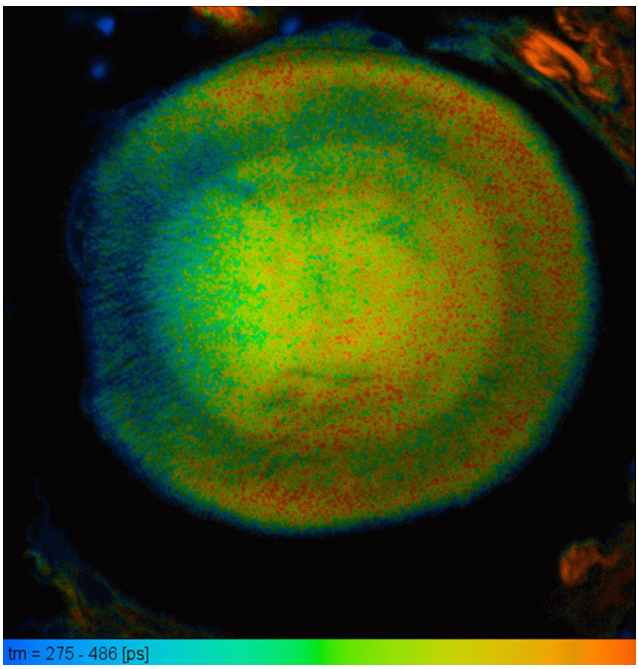
Objective: Fluorescence lifetime imaging microscopy (FLIM) measures the exponential decay rate of fluorescence and creates a virtual image of histologic or cytologic preparations without any staining by attributing virtual colors to different lifetimes of the cellular components. Fluorophores detectable by FLIM remain in sections of paraffin embedded tissues. Therefore, FLIM provides valuable complementary information in material from the archives. The aim of this study was to investigate its utility for pulmonary pathology.
Method: Unstained and dewaxed sections of 60 cases of lung specimens were examined with a confocal microscope using a pulsed laser at 405 nm, and a time-correlated single-photon counting equipment for FLIM.
Results: The lifetimes of a certain molecule or tissue varied between cases, but the lifetimes between different components (hemoglobin, elastin, smooth muscle and collagen) were highly correlated among all cases, thus permiting the creation of highly contrasted images without any staining. The storage time of the blocks and autolysis increased only slightly the lifetimes of hemoglobin, but not of other components. We obtained detailed histologic images in cases of alveolar proteinosis, corpora amylacea, pneumocystis pneumonia and hyaline membranes.
Conclusion: FLIM applied to routinely processed lung specimens from the files has shown to provide reproducible images and valuable additional information in unstained sections.

Corpus amylaceum, unstained section:



Wednesday, 9 September 2015, 09.30 – 10.30, Restaurant
PS-23 Poster Session Thymic and Mediastinal Pathology

PS-23-002
Case report of a Thymoma type AB2 according to Masaoka
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Objective: Generally thymomas type AB are regarded as mixture of type A and type B thymomas, but have not been studied in detail. Many architectural patterns and differences have been described in these types of tumours.
Method: A 65-year old female patient admitted to our hospital with symptoms of chest pain and dysphagia. On radiographic evaluation an expansive mediastinal mass measuring >3,4 cm was found and excision of the mass was considered. A whitish, compact mass measuring 3 × 2, 5 × 1,5 cm was received for rapid biopsy and the result was consistent for thymoma. We also received multiple other tissue specimens measuring 3 × 2 × 0,5 cm, which involved a small lymph node and fatty tissue. An immunohistochemical study was performed with bcl2, p53, ki67, CEA, EMA, AE1/AE3 and TTF1.
Results: The lesion, in central location, was composed of spindle-like cells (A element), while at the periphery a mixed epithelial and lymphocytic population (B2 element) was noted. The neoplasm was well delineated with a fibrous capsule. Focal microinvasions of the former were spotted, with definite invasion of capsule and with no extracapsular extension of the surrounding fatty tissue.
Conclusion: The above mentioned morphological and immunohistochemical findings were consistent with a thymoma type AB2.

PS-23-003
Eosinophilic granuloma of the rib: Two case report with long term follow-up
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Objective: The monosystemic unifocal osseous form of the Langerhans cell histiocytosis (LCH) is known as eosinophilic granuloma (EG). The term eosinophilic granuloma was first introduced by Lichenstein and Jaffe in 1940. Eosinophilic granuloma is one of the rarest causes of all osseous neoplasms and accouts for less than 1 %. It most often affects the skull and jaws which is characterized by either single or multiple lytic- bone lesions. It primarly occurs in older children and young adults, with a male prepandarence with a male to female ratio of 2:1.
Method: Here we present two cases with an isolated eosinophilic granuloma of the rib with long term follow-up which were treated with surgery alone.
Results: Postoperative follow- up showed complete cure of the disease in both patients. Discussion focuses primarly on differantial diagnosis, treatment, and appropriate follow- up for these patients.
Conclusion: The rib is rare site and most common in adults. The prognosis is exellent when disease is confined to the skeleton, expecially if it is a solitary lesion, with the majority of such lesions spontaneously resolving. However, where symptoms persist, other treatment options may be considered such as excision and currettage, steroid therapy, chemotherapy, radiofrequency ablation.

PS-23-004
T-cell lymphoblastic lymphoma revealed by an intestinal intussusception
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Objective: We report a case of intestinal T-cell lymphoblastic lymphoma (T-LBL) and points out the importance of the immunohistochemestry in the differential diagnosis of lymphoma of the gastro-intestinal tract.
Method: 19 year old man without medical history was urgently admitted in an array of acute intestinal obstruction. Imaging showed an ileo-ileal telescoping of ileal loop and its mesentery with asymmetric regular wall thickening. Resection of the small intestine carrying the tumour area was performed. Gross showed three whitish tumours. Histopathologically, the muscularis propria had abundant atypical lymphoid infiltrate in diffuse pattern. Atypical lymphoid cells expressed CD3, CD99 and TDT. CD56 was negatif.

Results: In this case, the histological and immunohistological findings concluded to multiple metastasis of a T-LBL in the small intestine. The chest tomography showed later an expensive primary mass in the anterior mediastin.
Conclusion: T-LBL is a rare type of non-Hodgkin's lymphoma, with an overall incidence of 0.1 per 100, and predominantly occur in male adolescents or young adults. A mediastinal mass was present in 80 % of the patients. An acute intestinal obstruction can be the first and unique sign of a T-LBL.

PS-23-005
A survey of mediastinal primary and secondary tumours in an oncological institute: Preliminary data from a pathologist perspective
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Objective: Our purpose was the evaluation of mediastinal tumours and of diagnostic procedures in an oncological Institute.
Method: We report preliminary data for the year 2012, based on a pathology database search. Surgical cases derived from mediastinotomy or VATS; cytological samples derived from transbronchial needle aspiration (TBNA) and/or from endoscopic ultrasound- assisted fine needle aspiration (EUS-FNA); seven second opinion cases of Thymic Epithelial Tumours were included.
Results: All our patients were adults. In the period considered, 44 mediastinal neoplasias were found among 11375 histological cases, 38 malignant (most of them primary), 9 secondary and 6 benign. Among cytological cases (27) 12 were malignant (10 lung carcinoma metastases and 2 lymphoma cases). In 13 cases the material was not sufficient or necrotic; one case was not diagnostic and one was negative. In 5 cytologically malignant samples, the cells were sufficient for predictive molecular biological assays. Primary tumours of all embryological derivations were encountered, thymic epithelial tumours, both in topic and ectopic location, being the most numerous, followed by B-cell lymphomas.
Conclusion: The heterogeneity of mediastinal neoplasias requires different diagnostic procedures, according to the compartment/s involved and to the presumptive tumour stage. A relevant improvement was provided by mininvasive diagnostic techniques.

PS-23-006
An unusual case of Thymic MALT-type lymphoma
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Objective: The purpose of the study was to characterize an unusual lymphoid proliferation occurring in the thymus of a 59-years old woman without clinical and laboratory findings of Myasthenia gravis or other autoimmune diseases.
Method: The thymus, removed by mediastinotomy, contained a 2 × 1.5 cm nodule that was investigated by morphology and immunohistochemistry on formalin-fixed, paraffin embedded tissue. The Biomed protocol-2 was applied for the clonality analysis of B-cell receptor.
Results: Histologically, the lesion consisted of medulla with marked thymic follicular hyperplasia (FH) and prominent Hassall's bodies; the cortex was atrophic. Uninvolved thymic remnants were present in the adipous tissue at the periphery. The hyperplastic follicles were surrounded by lymphoid cells with clear cytoplasm, reminiscent of an enlarged marginal zone and suggestive of an early mucosa associated lymphoid tissue (MALT)- type lymphoma. The thymic epithelial network appeared well preserved by CK19 immunostaining. Clonality analysis was decisive in confirming the diagnostic suspect by showing monoclonal rearrangement of IGH gene.
Conclusion: Thymic Malt lymphomas are very rare and frequently the proliferation destroys the epithelial network leaving only epithelial remnants and/or rare lymphoepithelial lesions. We suggest that this case of thymic florid FH represents an early phase of a thymic MALT lymphoma.

Wednesday, 9 September 2015, 09.30–10.30, Restaurant
PS-24 Poster Session Uropathology

PS-24-001
Reporting Gleason's grading 3+3 on needle biopsy: Are all the same?
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Objective: The aim of our study is to compare the concordance with the final Gleason score in the radical prostatectomy and follow-up, of patients diagnosed Gleason 3+3.
Method: We reviewed our needle biopsies Gleason 3+3 of patients surgically treated and made 2 groups 1. Gleason 3+3 reported with confidence (carcinoma >5 % or >1 core affected) 2. Gleason 3+3 reported following ISUP recommendations (1 core, <5 % of cancer).
Results: Group 1. 13 patients (mean 63 y), PSA 6.5 ng/ml. 12/13 >10 mm of carcinoma in the sample. Total cores: 6 (4–8). Gleason score prostatectomy was 3+3 in 7 patients, 3+4 in 6. 1/13 had positive margins. PSA <0.04 ngr/ml in last follow-up. Group 2. Eleven patients (mean 64 y), PSA 8.8 ngr/ml. 9/11 <1 mm of carcinoma with 2/11 cases >1 mm in the sample. Total cores: 8 (6–15). Gleason score at prostatectomy: 3+3 3 cases, 3+4 6 cases, 2 cases 4+3. 3/11 had positive margins. Four cases increased PSA in last follow-up.
Conclusion: ISUP recommends reporting small carcinomas as Gleason score 3+3. This can represent a sampling problem of a more aggressive carcinoma. When Gleason score 3+3 is reported with confidence (group 1) final grading is more concordant (54 % group, 27 % group 2) with no cases Gleason 4+3; and less positive margins in prostatectomies (7.6 % group 1, 27 % group 2).

PS-24-002
The prostate cancer detection rate on the second prostate biopsy
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Objective: The aim of the study is to identify the prostate cancer detection rate in patients who had second prostate biopsy (reTRUS) out of the patients who had negative primary biopsy (TRUS).
Method: From January 1st to September 24th 2012 all patients who unterwent prostate neddle biopsy (12 specimens) at Naesvted Hospital were investigated. Age, volume of prostate, serum-PSA, cancer type, Gleason Score, number of re-TRUS and number of patients with cancer in re-TRUS were identified.
Results: A total number of 2818 patients had performed TRUS and of these 679 patients (24 %) had prostate cancer. Of 2139 patients 709 underwent re-TRUS and of these 271 (33 %) had prostate cancer in the re-TRUS. The reasons for re-TRUS were elevated serum-PSA in 560 patients of which 184 (33 %) had cancer, suspicion on rectal digital examiniation in 70 patients of which 36 (52 %) had cancer, suspicion of cancer in TRUS in 42 patients of which 28 (66 %) had cancer and familiary disposition in 37 patients of which 20 (54 %) had cancer.
Conclusion: A high number of prostate cancers were found in re-TRUS in patients with high serum-PSA, suspect rectal digital examination, obs.pro-diagnosis in TRUS and with familiar disposition.

PS-24-003

Tryptase and chymase in prostatic adenocarcinomas

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Objective: Mast cells play some roles in tumour progression via increasing angiogenesis. Some proteases such as tryptase and chymase are stored in the mast cell granules. The roles of mast cells have been demonstrated in various biologic processes in the many tumours. The aim of this study was toinvestigate the relationship of tryptase and chymase in prostatic adenocarcinomas (PA).
Method: This study was conducted on a total of 51 paraffin-embedded prostatic adenocarcinomas samples, which were histopathologically diagnosed at the Department of Pathology of medicine Hospital between 2012 and 2014. Paraffin-embedded PA samples 3 μm in thickness, were then cut. The slides were stained with tryptase and chymase.
Results: MCC was observed that tumoural areas more acumulate than nontumoural areas (respectively; mean:18,63 ± 16,268, mean: 15, 47 ± 16,268). MCT was more acumulated than MCC in tumoural and nontumoural areas. MCT was observed that nontumoural areas more acumulate than tumoural areas (respectively; mean: 49,12 ± 19,499, mean: 46,53 ± 18,575).
Conclusion: Mast cells may important of PA. Chymase might more important than tryptase.

PS-24-004

HER2, EGFR, pAKT-Thr308 and MIB1 immunoexpression in urothelial bladder carcinomas

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Objective: Several investigators have suggested the possibility that expression of both EGFR and HER2 could be utilized for molecular targeted therapy in urinary bladder cancer. We tried to evaluate the expression of HER2 and EGFR in urinary bladder cancer.
Method: We collected 41 paraffin-embedded urothelial caricinoma tissue blocks from 35 patients. HER2, EGFR, MIB1 and phospho-AKT1, 2, 3 at Thr308 expression was studied using tissue microarrays. The immunohistochemical results correlated with conventional clinicopathological parameters.
Results: The majority of the infiltrative tumours were of high grade ($p = 0.007$) and >2 cm in gratest diameter ($p < 0.001$). This study revealed EGFR and HER2 overexpression in 26.8 and 56.1 % of the cases respectively. HER2 expression was observed mainly in high grade tumours ($p = 0.023$) with high MIB1 proliferative index ($p = 0.009$). EGFR expression was associated with tumour size and HER2 expression ($p = 0.044$). pAKT-Thr308 expressed in a large percentage of cells in all cases and was associated with tumour infiltration ($p = 0.012$).
Conclusion: pAKT-Thr308 is commonly overexpressed in urothelial carcinomas independently the tumour grade or size. We have noticed positivity of EGFR and HER2 in a considerable amount of the cases. HER2 is overexpressed in high-grade tumours with high mitotic index but HER2/EGFR coexpression is not associated with adverse prognostic parameters.

PS-24-005

The effect of histopathological parameters and prognostic factors to biochemical recurrence in radical prostatectomies

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Objective: Preoperative PSA levels became very important in addition to many histological parameters such as Gleason score, extraprostatic extension, involvement of vesiculoseminalis, status of lymph nodes and surgical margins in predicting prognosis of prostate cancer. In this study, we aimed to investigate the relationship between biochemical recurrence and preoperative PSA level, Gleason score, tumour volume, surgical margin status, extraprostatic extension and other histopathological features in prostate cancer.
Method: A total of 117 cases diagnosed with prostatic adenocarcinoma and treated by RP were included in this study. The relations between all of the histopathological parameters were studied in addition to the preoperative PSA levels, biochemical recurrence and follow up time up to recurrence.
Results: Preoperative PSA, Gleason score, tumour volume, extraprostatic extension, perineural invasion, positive surgical margins, vascular invasion, necrosis, vesiculoseminalis involvement, ganglionic involvement and high grade tertiary pattern was found to be related to recurrence. Age, high grade prostatic intraepithelial neoplasia, intraluminal mucus, collagenous micronodules and foamy cytoplasmic change was unrelated to prognosis.
Conclusion: Our findings support that reporting histopathological features such as Gleason score, tumour volume, extraprostatic extension, tumour positive surgical margins, perineural and vascular invasion, necrosis, vesiculoseminalis involvement, ganglion involvement and tertiary pattern can be helpful in predicting prognosis in prostatic adenocarcinomas.

PS-24-006

Sarcomatoid variant of urothelial carcinoma of the urinary bladder: A study of 27 cases

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Objective: Sarcomatoid variant of urothelial carcinoma is a rare neoplasm of the urinary bladder, defined as a biphasic tumour consisting of malignant epithelial and mesenchymal components, with an incidence ranging 0.2–4.3 %.
Method: Twenty-seven cases of sarcomatoid variant of urothelial carcinomas (~0.5 % of all urothelial carcinomas) were retrieved from the authors' affiliated pathology archives. The cases were analyzed for the tumour stage, grade, microscopic and immunohistochemical characteristics.
Results: The study included 18 male and 9 female patients, with the mean age of 67.2 years. All tumours were high grade. Invasion of the muscularis propria (pT2) or perivesical fatty tissue (pT3) was present in 23/24 (95.83 %) cases. The most common epithelial component was urothelial carcinoma with focal areas of glandular (8/27 = 29.6 %), squamous (7/27 = 26 %) and neuroendocrine (3/27 = 11.11 %) differentiation. Rhabdomyosarcoma (6/27 = 22.22 %) was the most frequent mesenchymal component followed by chondrosarcoma (3/27 = 11.11 %), osteosarcoma (2/27 = 7.04 %) and fibrosarcoma (1/27 = 3.70 %). Immunohistochemically epithelial elements expressed cytokeratins, whereas stromal elements reacted with vimentin or specific markers corresponding to the mesenchymal differentiation. Areas of neuroendocrine differentiation expressed synaptophysin and chromogranin A.
Conclusion: Sarcomatoid variant of urothelial carcinoma is a rare, high grade variant of urothelial carcinoma that presents at advanced stage in the majority of the patients.

PS-24-007

Pleomorphic giant cell carcinoma of the urinary bladder: Report of two cases

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Objective: In this report, we present the clinicopathologic features of two cases of the pleomorphic giant cell variant of urothelial carcinoma. This is

a rare variant of bladder cancer recognized by the WHO classification of urologic tumours in 2004.
Method: Two patients (78,F; 64.F) underwent transurethral resection because of the malign neoplasm of the bladder. Biopsies of the bladder were examined by histomorphologically and immunohistochemically.
Results: Both of two tumours included marked pleomorphism, aggregates or sheet of mononucleated and multinucleated giant cells, high mitotic counts, multifocal necrosis and focal minimally squamous differentiation. Tumours were positive with CK7, CKAE1/AE3 (pan-cytokeratin) and EMA but negative with CK20, p63, inhibin, β-HCG, PLAP, and Melan-A. Tumours were reported as pleomorfic giant cell carcinoma of urinary bladder.
Conclusion: Pleomorphic giant cell carcinoma is a rare aggressive variant of urothelial carcinoma with appearance similar to giant cell carcinoma of the the lung and rarely the pancreas, prostate, gallbladder and intestine. It has been mentioned in the 2004 WHO classification of urinary bladder tumours but fully described in 2009 by Lopez-Beltran et al. This tumour has a very poor prognosis but there are available limited data on the pathological and immunohistochemical characteristics and the clinical significance in the literature.

PS-24-008
HER2 overexpression in urinary bladder cancer and its relationship to gene amplification and tumour cell polysomy
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Objective: Beside HER2 gene amplification, polysomy 17 can also lead to elevated HER2 protein level, therefore, it is reasonable to investigate the correlation of both UroVysion FISH test (9p21 deletion, polysomy 3, 7, 17) results and HER2/polysomy 17 status with the prognosis in urinary bladder transitional cell carcinoma (TCC).
Method: Non-amplified/non-polysomic (NANP), low polysomy 17 (LP17), high polysomy 17 (HP17) and HER2 amplified groups were created from 72 TCCs by HER2/Chromosome17 FISH. Novel UroVysion test scoring system (UVyScore) with five categories (UVyS 0-IV) was created using preoperatively voided urine cytology.
Results: HER2 overexpression rate was 54 % (staining heterogeneity~58 %) by immunohistochemistry. HER2 gene amplification: 10 % (combined with HP17 in each cases). Polysomy 17: 40 % (18 % LP17; 22 % HP17), 62 % of these tumours overexpressed HER2 protein. HER2 overexpression: no correlation with grade, stage, survival. HP17 and HER2 amplified TCCs showed significantly higher grade and stage, significantly worse OS and PFS compared with NANP and LP17 tumours. UVyS III-IV: significantly shorter OS, PFS. UVyScore: independent prognostic factor (OS, PFS).
Conclusion: Polysomy 17 and intratumoral HER2 status heterogeneity are common features of TCCs, while HER2 amplification is a rare and late carcinogenetic event. HER2 FISH results and the novel UroVysion scoring system have strong predictive value on survival.

PS-24-009
Significance and outcome of cytologic atypia and mitotic index in prostatic adenocarcinomas
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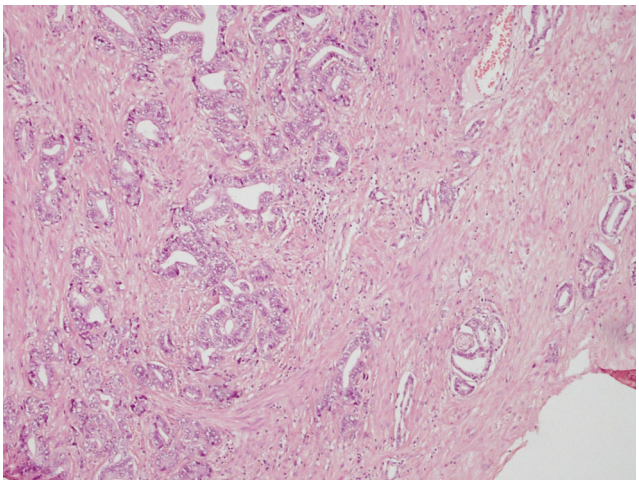
Objective: The Gleason grading system measures architectural differentiation and disregards cytological atypia (CA) and the cell proliferation index. Several studies have reported that nuclear grade and mitotic index (MI) are prognostically useful.
Method: This study included 232 radical prostatectomy (RP) specimens. CA was determined on the basis of nucleomegali (approximately 20 μm); vesicular chromatin; prominent nucleoli (even at low power), and irregular thickened nuclear membranei. The proportion of area of CA was recorded in each tumour in 10 % increments. The MI was defined as the number of mitotic figures in 10 consecutive high-power fields (HPF).
Results: In univariate analysis, significant differences included associations between failure and Gleason score, extraprostatic extension, positive surgical margin (SM), the presence of high pathologic stage, CA ≥ 10 % of tumour area, MI ≥3/10 HPF, and preoperative prostate-specific antigen. In a Cox regression model, a positive SM, the presence of a CA with ≥10 % of tumour area, and an MI of ≥3/10 HPF were independent predictors of BPR after RP.
Conclusion: The results of our study showed that, in addition to the conventional Gleason grading system, CA and MI are useful prognostic parameters while evaluating long-term prognosis in prostatic adenocarcinoma.

Figure 1: Prostate adenocarcinoma with cytologic atypia, H&E, x200:



PS-24-010
Solitary testicular metastasis from colon adenocarcinoma: An extremely rare case report
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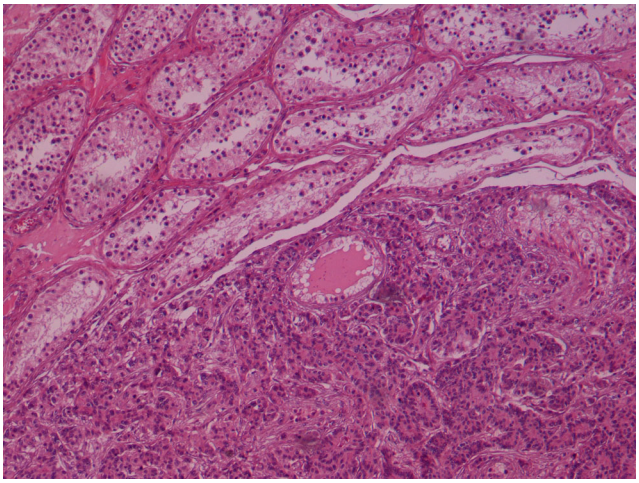
Objective: The prevalence of testicular metastasis from colon cancer has been reported to approximate 8 % of all testicular metastatic lesions. Less than 30 cases of colon metastasis to the testicle have been reported either at autopsies or as isolated case reports of advanced metastatic disease.
Method: We report a case of a 58 year old man who presented with a 2 month history of a painless right testicular mass 3 years after undergoing a ileo-hemicolectomy for a stage IIIB sigmoid colon adenocarcinoma. Physical examination and ultrasonography revealed a solitary testicular mass measuring 1,7 × 1 cm. A right radical orchidectomy was perfomed.
Results: On microscopic examination an infiltrative adenocarcinoma was found. The tumour exhibited an interstitial growth pattern with preservation of tubules and there was vascular invasion.The immunohistochemical study showed that the tumour cells were positive for CKAE1, CKAE3, CK20 and CDX2 and negative for Vimentin, PLAP, CD30, AFP, HCG. The morphology of the tumour and the immunohistochemistry were consistent with metastatic colon adenocarcinoma.
Conclusion: Testicular metastatic disease is uncommon particularly from colon cancer. Although rare, metastasis to testes should be considered as a differential diagnosis especially in older men with symptoms suggesting the present of a non-testicular malignancy.

Metastatic colon adenocarcinoma of the testis (H-Ex100):



PS-24-011

Xanthogranulomatous cystitis

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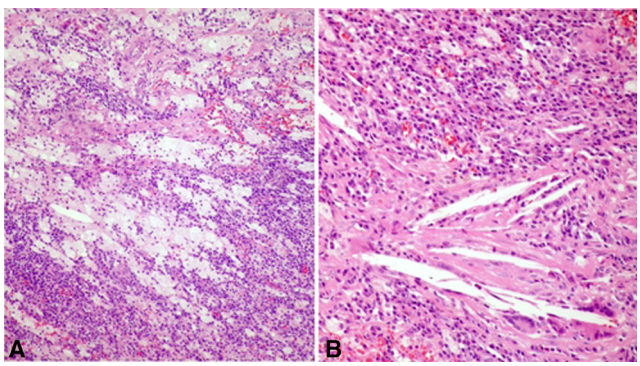
Objective: Xanthogranulomatous change has been reported to occur at many different sites, including the colon, ovary, pancreas, salivary gland, appendix, gallbladder, endometrium, brain and kidney. However, it is rarely reported in the bladder. Xanthogranulomatous cystitis is a rare benign chronic inflammatory disease of unknown etiology.
Method: We report a case of xanthogranulomatous cystitis.
Results: A 38-year-old woman was presented with 1 week history of lower abdominal pain. She had not experience any fever and did not have any lower urinary tract symptoms. A physical examination was unremarkable. Ultrasonography and cystoscopy revealed a nodular mass of 32 × 30 mm protruding from the anterior bladder wall. Partial cystectomy was performed. A histological examination of the specimen was consistent with xanthogranulomatous cystitis. The bladder muscularis propria was replaced by sheets of foamy histiocytes and chronic inflammatory cells (Figure A). Multinucleated giant cells and cholesterol clefts were also identified (Figure B). Michaelis-Gutmann bodies, which characterize malacoplakia, were not observed. There was no evidence of malignancy.
Conclusion: Xanthogranulomatous cystitis can mimic a tumour by way of its clinical and radiologic presentation. Definitive diagnosis is by microscopic analysis and exclusion of similiar process, such as malacoplakia. This report should enhance our knowledge in diagnostic pathology.

Foamy histiocytes (A) and multinucleated giant cells (B):



PS-24-012

Atypical basal cell hyperplasia of the prostate combined with conventional adenocarcinoma: A case report

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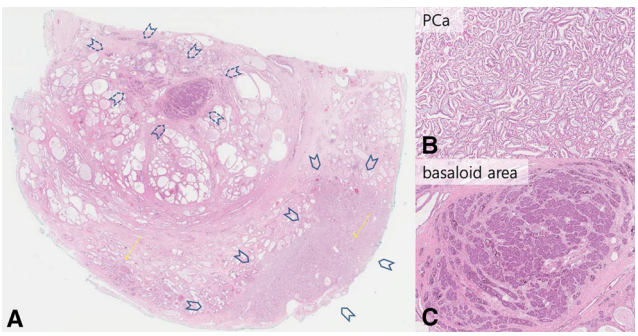
Objective: Basal cell hyperplasia of the prostate is a relatively common finding in specimens removed from patients with urinary obstruction due to benign prostatic hyperplasia. This condition was thought to be arising from basal/reserve cells and characterized by multi-layering cells within the glands. Basal cell proliferative lesion revealed a wide spectrum, ranging from benign condition to malignant tumours.
Method: Basal cell proliferative lesion revealed a wide spectrum, ranging from benign condition to malignant tumours.
Results: However, the criteria defining malignancy within this entity is ill-defined and the diagnosis of basal cell proliferative lesion is sometimes challenging.
Conclusion: We present a case of tumour-like proliferation of atypical basaloid cells which was incidentally found in a prostatectomy specimen that otherwise contained a conventional acinar adenocarcinoma.

Microscopic finding:



PS-24-013

High expression of CXCR4 is associated with lower biochemical recurrence rate in prostate adenocarcinoma

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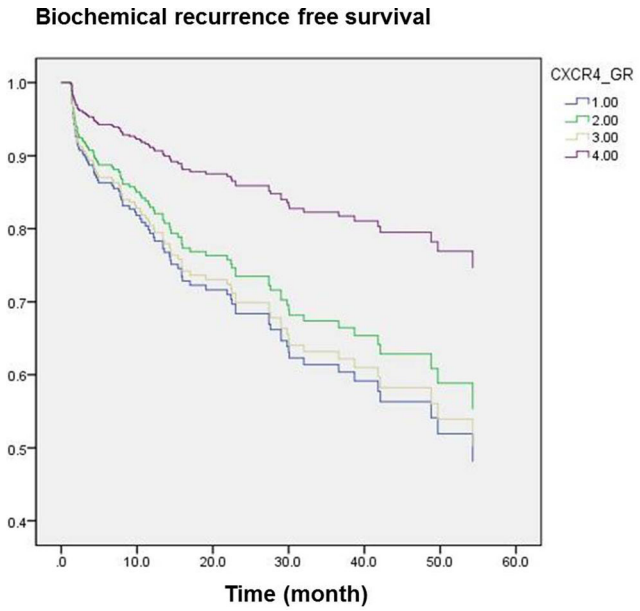
Objective: SDF-1/CXCR4/CXCR7 axis is associated with progression of prostate adenocarcinoma. The purpose of this study is to evaluate the effect of CXCR4 and CXCR7 expression on the clinicopathologic characteristics of prostate adenocarcinoma.
Method: Immunohistochemical stain of CXCR4 and CXCR7 was done in tissue microarray slides containing 365 Korean prostate adenocarcinoma samples.
Results: Both CXCR4 and CXCR7 expression were higher in tumours with Gleason grade ≤7 than those with Gleason grade ≥8. And they were also higher in tumours without biochemical recurrence (BCR) than those with BCR. BCR was associated with age (OR, 0.87–0.97), Gleason grade (OR, 2.0–4.5), surgical margin involvement (OR, 1.2–3.0), and tumour volume (OR, 1.0–1.1). However it was not associated with pre-operative PSA level, extraprostatic extension, CXCR4, or CXCR7 expression. Tumours with high CXCR4 expression were associated with lower BCR rate than those with low CXCR4 expression. However, CXCR7 expression was not associated with BCR rate. The expression of CXCR4 and CXCR7 was positively correlated ($r = 0.61$, $p < 0.01$).
Conclusion: High expression of CXCR4 was associated with lower BCR rate in prostate adenocarcinoma. However, CXCR7 expression was not

associated with BCR rate. Expression of CXCR4 and CXCR7 was positively correlated.

Biochemical recurrence free survival curve:



PS-24-014

Chromophobe renal cell carcinoma: Can be graded?

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Objective: Grading of Chromophobe renal cell carcinoma (ChRCC) is not recommended, however, previous studies have proposed a grading scheme and prognostic factors in order to distinguish the more aggressive ChRCC. We considered different variables that could help us to classify them.
Method: We reviewed 48 ChRCC using the following variables: size, Fuhrman grade, chromophobe tumour grade, perineural/vascular invasion, the presence of necrosis, stage, mitotic activity, programmed death ligand-1 (PD-L1) expression and these findings were correlated with clinical follow-up. The presence of necrosis, increase nuclear atypia and increased mitotic activity defined the high grade.
Results: 21 cases (44 %) were categorized as high grade and 27 cases (56 %) were low grade. Recurrence occurred in two patients, both of them with high grade tumour and metastases in others 2, one low grade and one high grade, the last one dying from disease. No one of these tumours appeared PD-L1 expression, only one case was positive, a high grade tumour (presence of necrosis) without adverse disease after 10 years.
Conclusion: Despite the numerous grading systems proposed, in our serie of ChRCC the most useful variables that correlated with adverse outcome were the size and the presence of necrosis.

PS-24-016

Coexistence of renal cell carcinoma and papillary adeonocarcinoma of the esophagus

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Objective: Renal cell carcinoma is sometimes accompanied by a second malignancy. However, the coexistence of this neoplasm and esophageal adenocarcinoma has not yet been reported.
Method: A 65-year old Caucasian female presented with gross haematuria. CT scan of the revealed around tumour 3,8 × 3 × 2,2 cm in the upper pole of the left kidney. Cystoscopy was normal and cytologic urine examination showed clusters of clear cells. As the patient was also complaining of difficulty in swallowing a gastroscopy was performed and a tumour of the lower esophagus was detected. Cytologic examination was consistent with adenocarcinoma.
Results: The kidney neoplasm was a clear cell renal carcinoma infiltrating its capsule, but not involving the renal pelvis, the blood vessels and the ureter. Histopathologic and immunohistochemical examination of biopsies from the esophageal neoplasm revealed a papillary adenocarcinoma. It was surgically removed and the patient underwent adjuvant treatment for both neoplasms. After 6 months she showed no evidence of disease.
Conclusion: According to the literature this case is the first one reporting the coexistence of renal cell carcinoma and adenocarcinoma of the esophagus.

PS-24-018

Prostatic adenocarcinoma with paneth cell-like appearance and a mucinous component

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Objective: We report a case of prostatic adenocarcinoma with a mucinous component and Paneth cell-like neuroendocrine differentiation.
Method: A 65 year-old man presented with PSA 9.76 ng/ml with no previous history. Digital examination was negative. Prostatic needle biopsies revealed adenocarcinoma Gleason score 7. The patient underwent radical prostatectomy.
Results: Microscopically prostatic adenocarcinoma Gleason score 8 was diagnosed, invading both lobes, showing perineural invasion and free surgical margins. There was extracellular mucin production with mucin pools formation accounting for less than 25 %.There were also glandular structures and small isolated clusters of round to pyramidal cells with Paneth cell-like morphology containing eosinophilic cytoplasmic granules. Immunohistochemistry (Chromogranin A, Synaptophysin, Serotonin) supported the neuroendocrine differentiation.
Conclusion: Paneth cell-like changes are detected in 10 % of prostatic adenocarcinomas. Neuroendocrine differentiation is considered to be an unstable phenotype and its prognostic significance is controversial; the latest studies refer a favorable prognosis. Pathologists should report any neuroendocrine component in an otherwise conventional prostatic adenocarcinoma, regarding its possible association with resistance to hormone therapy and probable modulation of the therapeutic approach. It is currently thought that the degree of neuroendocrine differentiation increases in response to Androgen Deprivation Therapy, so the patient may benefit from treatment options such as Somatostatin and peptide analogs.

PS-24-019

Small Cell Carcinoma (SCC) of the urinary bladder: Report of three cases

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Objective: Small cell carcinoma of the bladder represents less than 1 % all bladder primary tumours. It has an aggressive behavior and a poor prognosis.

Method: Three male patients (68, 69 and 74 year-old) presented to our hospital with ematuria, disuria and lower abdominal pain. The first patient had a personal history of papillary urothelial carcinoma. The second patient had undergone BCG intravescical injections for an invasive urothelial carcinoma. The third patient had no previous history. All three patients underwent transurethral resection, in the last two patients followed by a radical cystoprostatectomy and a regional lymphadenectomy. In all cases imaging studies ruled out metastatic disease.
Results: Microscopically neoplastic cells were organized in sheets and nests. They showed nuclear crowding and molding, scant cytoplasm inconspicuous nucleoli and finely stippled cromatin. Geographic necrosis, frequent mitoses and invasion of the bladder's muscle were present. The third patient had a coexistent urothelial carcinoma in situ. Immunoistochemistry showed positivity for CKAE1/AE3 (focally dot-like), Synaptophysin, Chromogranin A, CD56 and negativity for TTF-1, LCA, p63.
Conclusion: Although morphology is crucial, immunoistochemistry confirms the diagnosis of SCC offering assistance to the differential diagnosis from lymphoma, lymphoepithelioma-like carcinoma, plasmatocytoid carcinoma and poorly differentiated urothelial carcinoma. Clinicopathological correlation is important to exclude metastatic neuroendocrine carcinoma.

PS-24-020

The value of P53 and MDM2 over-expression, alone and simultaneously, to predict five-year survival of patients with renal cancer who underwent radical nephrectomy during 2007–2009 in Hasheminejad Kidney Center, an Iranian experience

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Objective: Little is known with certainty about the role of p53 or MDM2 in predicting prognosis and survival of renal cancer. The present study aimed to determine the value of P53 and MDM2 over-expression to predict 5-year survival of patients with renal cell carcinoma in Iran.
Method: Ninety one patients with kidney cancer referred to Hasheminejad Kidney Center between 2007 and 2009 and underwent radical nephrectomy were included. Immunohistochemical staining of formalin-fixed, paraffin-embedded tumour samples were performed. The 5-year survival was determined by the telephone following-up.
Results: Totally, 4.4 % of all samples were revealed to be positive for P53. Also, 20.8 % of all samples were revealed to be positive for MDM2. The patients were all followed for 5 years. According to the Cox proportional hazard analysis, positive P53 marker was only predictor for patients' 5-year survival that the presence of positive p53 increased the risk for long-term mortality up to 2.8 times (HR = 2.798, 95 %CI: 1.176–6.660, $P = 0.020$). However, the presence of MDM2 could not predict long-term mortality.
Conclusion: The simultaneous presence of both P53 and MDM2 markers in our population is a rare phenomenon and the presence of these markers may not predict long-term survival in patients who undergoing radical nephrectomy.

PS-24-021

The usefulness of break apart FISH of TFE3 gene in the diagnosis of Xp11.2 renal cell carcinoma: The experience of consultation service

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Objective: I investigated the usefulness of TFE3 gene break apart FISH in the diagnosis of Xp11.2 renal cell carcinoma in the consultation service in my hospital.
Method: I collected six cases of renal tumours suspected of Xp11.2 renal cell carcinoma between January and April, 2015. The age of patients ranged from 12 to 49 years with a mean age of 20 years. The sex ratio was equal. Six tumours were obtained from 2 biopsied and 4 surgical resected materials. The immunohistochemistry of TFE3 protein and the break apart FISH of TFE3 gene was performed for all tumours. The cut-off value for FISH was more than 10 %.
Results: Regarding immunohistochemistry, five tumours showed positivity for TFE3 protein with more than 2+ intensity and the positive range of 2 to 90 %. One tumour was negative. With regard to FISH, three tumours were considered to be positive. One tumour was unsuccessful for FISH. Two tumours were negative.
Conclusion: The break apart FISH of TFE3 gene is available in the final diagnosis of Xp11.2 renal cell carcinoma.

PS-24-022

Villous adenoma of the urinary bladder: Case report

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Objective: To present a case of an infrequent lesion of the urinary bladder.
Method: A 70-year-old man was surgically treated at the Clinic for Urology of the Clinical Center of Vojvodina due to an exophytic round lesion of the urinary bladder. Hematuria and irritative bladder symptoms were present. The clinical diagnosis was urothelial carcinoma in situ. After the adequate preparation of the patient, transurethral surgical excision of the lesion was done.
Results: Having performed a thorough histological examination with routine Hematoxylin and Eosin staining, the diagnosis of villous adenoma with low-grade dysplasia was given. Microscopically, it showed papillary-villiform architecture covered with columnar epithelium with intracellular acid mucin.
Conclusion: Villous adenoma is a rare benign neoplasm of the urinary bladder, typically with a papillary-villiform growth pattern, that is histologically indistinguishable from similar neoplasms of the colon and rectum. This kind of neoplasm is mostly seen in middle-aged and senile males with hematuria and irritative bladder symptoms. Prognosis of this neoplasia is good and the transurethral resection is the only necessary treatment. It should be considered as an important lesion because of malignancy potential. Excision and histological analysis of the entire change is recommended in order to exclude the existence of focus adenocarcinoma.

PS-24-023

An unusual case of extramammary paget's disease of glans penis

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Objective: Paget's disease (PD) of the penis is an uncommon condition which may be associated with underlying in situ or invasive malignancy. We are describing a case of PD of the glans penis related to the urothelial carcinoma of the penile urethra which presented 5 years after a completion urethrectomy.
Method: We describe the clinical history, gross description and the histology of the penectomy specimen. We also describe the clinicopathologic features of urothelial carcinoma of the penile urethra associated with paget's disease of glans penis, including the immunohistochemical features.
Results: Grossly; a cystic lesion was present within the glans. Histology showed this cystic space to be lined by urothelium displaying carcinoma in situ and possible invasive foci. The glans penis showed proliferation of atypical large vacuolated cells and cell clusters in all layers of the

stratified squamous epithelium. These neoplastic cells showed positive immunoreactivity for CK7 and CK20, as did the cells lining the underlying cystic lesion.
Conclusion: In our opinion the appearances were those of extramammary paget's disease (EMPD) of the glans penis, secondary to recurrent urothelial malignancy. EMPD is rare. The most common site for EMPD is the vulva but penis was involved in this case. In cases of male genital EMPD, usually the scrotum and penis are both affected but in this case only glans penis was involved. EMPD is less often related to underlying malignancy (15 %) compared to mammary PD. This case was related to underlying urothelial malignancy. The underlying malignancy in this case was, in our opinion, recurrent although may have been due to field-effect.

PS-24-024
Minimal prostate cancer in tru-cut biopsies: Challenges in practice
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Objective: Prostate cancer (PC) is the second most common malignancy in males worldwide. In the era of widely accessible PSA assay, tru-cut biopsies often offer small foci suspicious for cancer that need further evaluation.
Results: For a period of 5 years, a total of 842 patients were evaluated, 67 % were diagnosed with PC and 33 % had benign finding. Of these patients, only 28 (3.3 %) fulfill the requisites of minimal PC according to the published criteria. Age varies between 52 and 85, PSA level - 4.3 to above 100 nmol / ml. After strict application of histological criteria, in 7 (25 %) of the patients the diagnosis of cancer was rendered without additional immunohistochemical (IHC) study. In the remaining group, PC was signed-out only after a standard panel of IHC was applied - p63, HMWC and AMACR, with or without ERG. Gleason grade was asssigned to each case, complemented by Ki67 proliferative activity to provide additional information on the clinical significance of the process.
Conclusion: Diagnosis of minimal PC is a challenge in biopsy practice due to limited amount of tissue and wide variety of imitators, requiring additional evaluation by IHC. The clinical relevance of such finding often appears to be greater than expected.

PS-24-025
Lymphocyte rich papillary renal cell carcinoma: A case report
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Objective: We report a case of lymphocyte rich papillary renal cell carcinoma (PRCC) in a 72-year-old female with 1 month history of occasional abdominal pain. A 4,2 cm in diameter left renal mass was discovered during ultrasound exam. Radical nephrectomy was performed. On gross examination, tumour was on the lateral part of the kidney measuring 4,2 × 4, × 2 × 4 cm with extensive necrosis and hemorrhage.
Method: Histological sections have been assessed using hematoxylin-eosin stain. Immunohistochemical analysis was performed for following antibodies: CK7, CK20, vimentin, RCC, CD10, TTF-1, Ki-76, CD3 and CD20.
Results: Histological examination revealed fibrovascular papillae covered by atypical epithelial cells with large nuclei, prominent nucleoli and eosinophilic cytoplasm. The stalks of the papillae were infiltrated with abundant CD3 and CD20 positive lymphocytes, forming secondary follicles with germinative centers. Extensive hemorrhage and necrosis were found. Immunohistochemically, tumour cells were vimentin and CD 10 uniformly positive, CK7 was focally strongly positive, CK20 focally weakly positive, TTF-1 and RCC were negative. The proliferation index using the Ki-67 was 35 %.
Conclusion: PRCC may have various histological appearances; including tumour associated acute and chronic inflammation. To the best of our knowledge so far, PRCC with abundant lymphocytes forming secondary follicles have not yet been described.

PS-24-026
Renal biopsy in Radiofrequency Tumour Ablation (RFA): A six years experience with 89 cases in a single institution
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Objective: RFA is the elective technique to treat small renal masses. The aim of this study was to review our casuistry and evaluate the clinicopathological features as the diagnostic performance prior to ablation.
Method: A retrospective study of patients who underwent RFA in our Hospital between 2009 and 2014. Renal biopsies(CRB) were performed in each patient before RFA. We analyzed: age-sex-laterality, tumour-size, number/size of CRB, diagnosis (histological type/grade) and clinical follow-up.
Results: 89 patients underwent CRB before RFA. Average age was 70 years (33–89), 32 women (36 %) and 57 males (64 %). Mean tumour size 2,7 cm (1,2–5,5) and left predominant laterality47 (53 %). CRB average was 1,6 (1to5) and mean size 1 cm (0,2–2, 7). Final diagnosis: 51 (57,3 %) malignant: 28 (31,4 %) CCRCC, 16 (18 %) PRCC, 6 (6,7 %) CRCC and 1 (1,1 %) mucinous tubular carcinoma. Benign: 23 (26 %) RO and 2 (2,2 %) AML. In 13 (14, 6 %) only normal tissue observed. Predominant Führman grade CCRCC was 1 (67,9 %) and PRCC was type 1 (93,7 %). Immunohistochemistry was applied in 37 cases (41,6 %). Biopsy was conclusive in 85.4 % of the cases. In follow-up six cases had a re-ablation by tumour persistence. No tumour recurrence/metastasis was observed in RFA treated patients.
Conclusion: The pre-RFA biopsy has high diagnostic yield. The number of cores is not as important as localize by ultrasound the area to perform biopsy on representative tumour. Our single-center results on CRB before RFA have a higher diagnosis performance than previously reported.

PS-24-027
BORIS expression in testicular germ cell tumours
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Objective: Testicular germ cell tumours (GCTs) of adolescents and adults are the most common malignancies occurring in males between 20 and 40 years. GCTs account for 90 to 95 % of all primary testicular tumours and are divided into two major groups, seminomatous and nonseminomatous (NSGCT). BORIS (Brother of the Regulator of Imprinted Sites, a paralogue of the transcription factor CTCF) is a member of the cancer-testis antigen gene family, although aberrantly expressed in various malignancies and cancer cell lines. Our objective was to examine BORIS expression in various testicular GCTs.
Method: The expression of BORIS was analyzed in 48 pure seminomatous and the different components of 48 mixed germ cell tumours by microarray-based immunohistochemistry.
Results: In this study BORIS expression was confirmed in both pure seminomas and nonseminomatous tumours, where >50 % of pure seminomas demonstrated strong positivity. Among nonseminomatous tumours, yolk sac tumour component showed highest positivity.
Conclusion: The expression of BORIS in various testicular GCTs and their different components may indicate its role as a key biomarker. The role of BORIS in pathogenesis, developmental capacity and differentiation of testicular GCTs into their various subtypes remains largely unknown and should be further analyzed.

PS-24-028

Evaluation of prostatic core biopsies in five-year period (2010–2014): Single center experience

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Objective: Prostatic diseases are common pathology with annual growth all over the World. We made a retrospective analysis of 2249 core biopsies received at our institution in 5-year period in order to evaluate presence of prostatic cancer (PC) annually and to detect diagnostic difficulties in reaching right diagnose.
Method: A standard procedure of paraffin embedded section, stained with H&E was routinely used. In 310 cases suspicious for cancer additional immunohistochemical staining with monoclonal antibodies against AMACR, CKHMW and p63 was performed.
Results: 1960 cases out of 2249 were diagnosed as benign prostatic hyperplasia and 253 as PC. There was annual rise for prostatic cancer continuously in all 5-year period. (1,12, 6,98, 5,67, 7,69 and 27,68 % for 2010, 2011, 2012, 2013 and 2014, respectively). Immunohistochemistry succeeded to confirm prostatic cancer in additional 13 cases. Other cases showed basal cell hyperplasia (8 cases), atypical adenomatous hyperplasia (AAH) (8 cases), atypical small acinar proliferation (ASAP) (4 cases) and high grade PIN (2 cases).
Conclusion: There is an increased number of annual performed biopsies as well as presences of PC in core biopsies in 5-year period. Immunohistochemistry is a useful tool in diagnosing PC.

PS-24-030

Outcome of BCG therapy in superficial bladder cancer management: Tunisian experience about 180 cases

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Objective: Bladder cancer represents the first urological adult's cancer in Tunisia. BCG therapy is one of the most used therapeutic means in preventing recurrence and progression of nonmuscle invasive bladder tumours. The aim of this study was to evaluate the effectiveness of BCG therapy following the BCG protocol used in the urology department of our hospital.
Method: This was a retrospective study including patients with nonmuscle invasive bladder cancer treated by BCG therapy over a period of 3 years (2008–2011). The regimen used consisted of a once weekly instillation of BCG for 6 weeks followed by 12 monthly instillations.
Results: There were 180 patients with a sex-ratio of 9:1 and a mean age of 67,32 years. The recurrence rate was 31,66 % (57 patients) after BCG therapy. Among these 57 patients, 35 (61,4 %) progressed either in stage (4 patients), in grade (5 patients) or in both stage and grade (26 patients). Side effects, classified according to the WHO, were mainly IIB (45 patients). Analytical study did not identify any clinical or anatomopathological factor predicting the failure of BCG therapy.
Conclusion: The efficacy of our BCG protocol in reducing the potential for recurrence and progression of superficial bladder tumours was confirmed by our study.

PS-24-031

Prognostic value of Gleason Score determined preoperatively in the prostate cancer diagnosis

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Objective: In clinical practice Gleason score, which is the sum of the primary and secondary tumour grade, is used for this purpose. Since the biopsy technique provides a relatively small part of the tumour, the question of the reliability of the results obtained remains, which is the consequence of standards for sampling application quality. Therefore, the objective of this paper was testing of the reliability of Gleason score determined preoperative for making the final diagnosis after making a postoperative PH diagnosis.
Method: The study included 60 patients in whom, in addition to age, PSA level, staging, High Grade PIN (pre and postoperative), tumour grade (pre and postoperative), Gleason score determined (pre and postoperative).
Results: In patients aged 64.25 +/−7.355 (C.I.95 % 62.35–66.15) PSA level amounted to 14.62 +/− 9.93 (C.I.95 % 12.05 to 17.18), preoperative tumour grade was 1.77 +/− 0.43 (min = 1, max = 2) and postoperative 2.32 +/− 0.81 (min = 1, max = 3) ($p < 0.001$), Gleason preoperative 5.28 +/− 0.98 and postoperative 6.30 +/− 1.64, Spearman's coefficient of rank correlation was 0.87 ($p < 0.001$).
Conclusion: The results suggest that preoperative Gleason score determination is significant for assessing the prostate cancer differentiation, as well as that for reliable determination of staging a radical prostatectomy is necessary.

PS-24-033

Primary borderline mucinous tumour of the testis: A case report

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Objective: We present a very rare case of mucinous borderline tumour of the testis. According to our knowledge, mucinous testicular tumours are reported in less than 30 cases. It was postulated that ovarian –type epithelial tumours of testis derive from occult ovarian tissue, Müllerian remnants or monodermal teratoma.
Method: Routine histological and histochemical examinations were performed.
Results: Testicular tumour was diagnosed in 46-year-old man complaining dull arching scrotal pain and right testicular swelling of few years duration and umbilical hernia. Gross examination showed unilocular cystic tumour measuring 105 × 80 × 75 mm with smooth gray surface. Sections revealed honeycombing and calcifications within cystic wall but without obvious residual testicular tissue. Luminal surface showed smooth and focal papillary excrescences and the content was brownish mucin. The tumour compressed tunica albuginea with no infiltration of epididymis and spermatic cord. Microscopic examination revealed highly atypical papillary mucinous epithelium with no stromal infiltration but only mucinous pseudoinvasion in foci. There was a microfocus of chondroid change which can lead to consideration of teratomatous origin of the tumour. Cystic wall showed fibroxanthomatous inflammation with foci of sclerocalcification and cholesterol crystals.
Conclusion: Distinguishing borderline mucinous testicular tumour from carcinoma is of great importance and could represent a significant diagnostic challenge.

PS-24-034

Different gene expression profiling in renal cell neoplasms. Plexin B1 and Uromodulin are downregulated in renal tumours

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Objective: Advances in the understanding of the genetics have lead to the recognition of distinctive types of renal. Renal oncocytoma is a benign neoplasm that sometimes is difficult to distinguish from chromophobe cell renal carcinoma. Our aim is to define the differential expression profiling of renal neoplasms.

Method: Gene expression array was performed in three cases of clear cell renal carcinoma, three oncocytomas and five non-neoplastic renal tissues. To verify microarray data, we performed RT-PCR in 14 new cases of several renal neoplasms.
Results: 610 genes were significantly overexpressed in carcinomas, and 264 in oncocytomas. Cell cycle, signal transduction, extracellular matrix, cell adhesion and apoptosis were the main biological processes affected in carcinomas. On the other hand, 586 sequences were downregulated in carcinomas, 397 in oncocytomas, including signal transduction and cell cycle control related genes. Uromodulin expression was lost in every kind of renal neoplasms but not in papillary. Otherwise, expression of Plexin B1 is repressed in CCRCC, chromophobe and papillary renal carcinomas.
Conclusion: Oncocytomas and carcinomas presents different molecular pathways, although some changes, like angiogenesis or immunological response are similar. Plexin B1 and Uromodulin could be useful targets for the development of new in vitro diagnosis and therapeutical methods.

PS-24-035
Leydig cell tumour of the testis: A small case series
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Objective: Leydig cell tumours are the most common sex cord-stromal tumours of the testis. The aim of this paper is to report a series of Leydig cell tumours diagnosed in our center in a period of 23 years.
Method: We retrospectively analyzed the cases of testicular Leydig cell tumours diagnosed between 1991 and 2014.
Results: Three patients with Leydig cell tumours were diagnosed. The patient's age was 36, 78 and 37 years respectively. The main symptoms/signs were: scrotal mass (all cases) and gynecomastia (one patient). Hormonal profile was performed in two patients. Tumour diameter was 15 mm, 67 mm and 110 respectively. Pathological examination confirmed benign Leydig cell tumour in the first case and Leydig cell tumour with histological criteria for malignancy in the second case. The third case, with some particular or atypical clinical and histological features (nuclear pleomorphism, multinodularity, abundant lipochrome pigment, necrosis, inflammation, fibrosis, calcification, osseous and adipose metaplasia) was signed out as testicular "tumour" of the adrenogenital syndrome in a 37 years-old patient having two brothers known with adrenogenital syndrome. All cases were managed surgically (orchidectomy).
Conclusion: Leydig cell tumours of the testis are very rare tumours that can be challenging from pathological point of view, especially in the absence of clinical information.

PS-24-036
Vascular Endothelial Growth Factor (VEGF) expression in prostate carcinoma
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Objective: Vascular endothelial growth factor (VEGF) is involved in angiogenesis being expressed in many solid tumours, including prostate cancer. The aim of the study was to evaluate the expression of VEGF in prostate carcinoma.
Method: Immunohistochemical expression of VEGF was analyzed on three groups, each of 20 primary diagnosed prostate carcinomas: localized, locally advanced and with distant metastases. For each tumour was determined the VEGF staining score taking into account the percentage of VEGF - positive cells and the staining intensity. Cases with staining score ≤ 3.37 were considered to have low staining score, and those with score > 3.37 high staining score. The relationships between VEGF expression and some pathological factors were analyzed.
Results: 22/59 tumours (37.3 %) had high VEGF staining score (>3.37): 1 localized carcinoma (4.5 %), 8 locally advanced carcinomas (36.4 %) and 13 metastatic carcinomas (59.1 %) (p 0.001); of these, 10 (45.5 %) were moderate differentiated adenocarcinomas, 12 (54.5 %) poorly differentiated adenocarcinomas and none well differentiated tumour (p 0.090).
Conclusion: VEGF expression tends to correlate with the extent and not with the differentiation of the tumour.

PS-24-037
Stromal fibrillary component/vascular network relationship in different Srigley system patterns of prostate adenocarcinoma
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Objective: The study aims to assess the correlation between stromal fibrillary component (SFC) and vascular density (VD) in Srigley architectural patterns of prostate carcinoma.
Method: 680 digital images of prostate adenocarcinoma labeled following both Gleason and Srigley systems were acquired with X20 objective from serial sections, one stained using Gömöri technique for SFC and one immunomarked with anti-CD34 antibody for vessels. The SFC amount and VD were determined and compared. Srigley patterns were divided in: "Solid" group (Srigley-I, Srigley-III, Srigley-IV) and "Necrotizing" group (Srigley-II with subdivisions: Gleason3a, 3c and 5a).
Results: SFC and VD values had a direct, ascending correlation for all determinations ($p < 0.001$), but also for "Solid" ($p = 0.005$) and "Necrotizing" ($p < 0.05$) groups. SFC mean values had an ascending trend in both Solid ($p < 0.0001$) and Necrotizing ($p < 0.01$) groups. VD mean values had an ascending trend in Solid group ($p < 0.0001$) but a descending trend in Necrotizing group ($p < 0.0001$) towards Gleason5a pattern.
Conclusion: Intratumoral vascular network is adapting to the intratumoral interstitial space excepting Gleason5a areas where VD is reduced by the excessive SFC amount generated around "comedo type" tumoural areas. This paper was published under the frame of European Social Found, Human Resources Development Operational Program 2007–2013, Project no. POSDRU/159/1.5/136893.

PS-24-038
Ki-67 in nested variant of urothelial carcinoma and Von Brunn's nests: A clinical and immunohistochemical study
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Objective: Nested variant of urothelial cell carcinoma (NVUC) is an extremely rare, advanced-stage, high recurrence and mortality rate neoplasm. Because of its bland cytology it is difficult to differentiate this variant from Von Brunn's Nests (VBN). Our aim is to verify if Ki-67 is a reliable marker to differentiate these entities, as suggested in recent studies.
Method: 12 NVUC diagnosed between 2000 and 2014 in Marqués de Valdecilla Universitary Hospital were stained with Ki-67 and results were compared with the proliferation rate of 12 VBN. Clinical follow up was performed in NVUC cases.
Results: Mean Ki- 67 percentage for NVUC was 19,05 % (range 0–50 %) and for NVB 12 % (range 0–35 %). Seventy-five percent of VBN (9/12) had Ki- 67 $\leq$15 % and 58,33 % of NVUC (7/12) were $\geq$ 15 %. 83,33 % of NVUC cases were male with a mean age at diagnosis of 70,91 years. Six of 12 cases (50 %) died due to bladder cancer and 3 died (25 %) of other causes (urinary sepsis, respiratory failure and renal failure).

Conclusion: The low rate of Ki67 does not rule out NVUC although a tendency to biological aggressive behavior is noted in cases with higher expression.

PS-24-039

Mucinous tubular and spindle cell carcinoma of the kidney: A controversial entity

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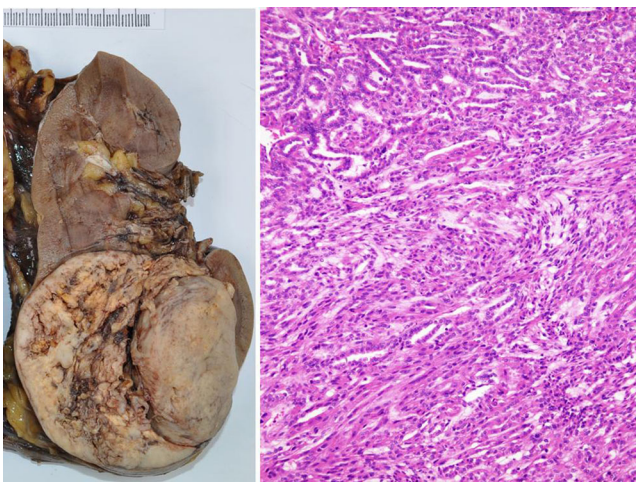
Objective: Mucinous tubular and spindle cell carcinoma of the kidney (MTSCC) is a very uncommon neoplasm recently included in the WHO classification. It has a slight middle-age female preponderance.
Method: 48-year-old smoker female with a history of HLA27+ ankylosis spondylitis under chronic NSAID, steroids and immunomodulators treatment who presented microscopic hematuria as an incidental finding and the renal ultrasound showed a well defined and hyperechoic right renal mass.
Results: Gross examination showed a partially encapsulated, yellowish and bland mass that measured 8 cm with a nodular, elastic and brownish area. Microscopically the tumour was close to the medulla, had an expansive growth patter and a polymorphic appearience. It was composed of tubules lined by cuboidal cells and were mixed with low grade spindle cells separated by a variable amount of mucinous-mixoid stroma. Some other areas showed a tubulopapillary pattern.
Conclusion: MTSCC's histogenesis has been suggested as the loop of Henle or collecting duct but it is still unclear. MSTSCC shares histological, cytogenetic and immunochemistry features with the papillary renal carcinoma and even though its low aggressiveness, low tumour metastatic potential and good prognosis are still controversial, its recognition and correct classification is necessary specially in exceptional morphologic cases such as this one presented.

Mucinous tubular and spindle cell carcinoma of the kidney:



PS-24-040

Metanephric adenoma of the kidney

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Objective: Metanephric adenoma (MA) of the kidney is an uncommon benign epithelial tumour. Less than 100 cases are reported in the literature. It occurs in female adults at any age. It's sometimes difficult to distinguish it from papillary renal cell carcinoma (PRCC). The aim of our study is to discuss the radiological and pathological features of this rare tumour.
Method: We report the case of a 22 year-old women who presented with left flank pain with fever. The scanner CT showed a superior polar cystic tumour of the left kidney. A local tumour resection was performed.
Results: Macroscopically, it was a 3.5 cm, well-circumscribed and non encapsulated tumour. Histologically, the tumour proliferation was densely cellular with slit-like spaces, acinar and glomeroid structures. Numerous psammoma bodies were noted. Immunohistochemical analysis showed that tumour cells were negative for CK7, EMA and Racemase. The immunostaining for WT1 was also negative with a positive control. The diagnosis of MA was made.The patient remains disease free 7 months after surgery. Our case is unique by the absence of expression of WT1 inspite of characteristic morphologic features.
Conclusion: Immunohistochemical staining is useful to differentiate between MA and PRCC. The treatment is based on total nephrectomy or partial resection.

PS-24-041

A case of adult granulosa cell tumour of the testis

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Objective: Adult granulosa cell tumours of the testis (AGCTT) are classified as sex cord-stromal tumours. Only 34 cases have been reported. We add this rare case.
Method: A 40-year-old male presented with complaint of mild pain in both testicles. A testicular ultrasound revealed a 4 × 3 cm hypoechoic lesion within the left testicle. A radical orchiectomy was performed.Histologicaly the lesion were composed of granulose cells in a predominantly microfollicular pattern, although trabecular and insular patterns were present. The microfollicles were filled with eosinophilic secretions characteristic of Call-Exner bodies. The surrounding granulosa cell nuclei were generally oval in shape with occasional nuclear grooves. Scattered mitotic figures were present without appreciable atypia. The lesion had a thin fibrous capsule and was non-infiltrative. The tumour cells showed strong membrane and cytoplasmic staining for inhibin and vimentine.
Results: Given the histopathologic findings, as well as the immunohistochemistry, the patient was diagnosed with AGCTT.
Conclusion: AGCTT is a rare tumour and information regarding its presentation, gross and microscopic morphology, and immunohistochemical characteristics is lacking. This report provides an update of the immunohistochemical findings and adds to the available data concerning this tumour.

PS-24-042

Histological characteristics of high grade invasive urothelial carcinoma

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Objective: Urothelial carcinomas are heterogeneous lesions which show different histological features. The recognition of the morphological variants is important because of the diagnostic, prognostic, or therapeutic implications thay have.
Method: We analyzed 77 cases of high grade invasive urothelial cancers of urinary bladder out of 106 received in our institution as endoscopically or surgically obtained material in 2 years. Transurethrally resected (TUR) material was completely embedded and standard dissection of operative material was performed. Immunostains were used in 12 cases with atypical morphology.

Results: There were 46 operative materials and 31 TURs. All operated patients underwent previous TUR. Sixty-five cases were diagnosed as typical high grade papillary urothelial carcinoma with severe cell atypia and high mitotic index, showing 9–28 mitotic figures/10HPF. Using immunostains we diagnosed 2 squmaous cell cancers, 3 sarcomatoid variants, one limphoepithelioma like, one plasmacytoid, one microglandular, 2 small cells undifferentiated, 2 neuroendocrine cancers and 10 cases of papillary urothelial carcinoma with areas of clear cells. The tumour was classified as pT2 in 35 cases, pT3 in 7, pT4 in 4 and pT1 in 31 cases.
Conclusion: Immunohistochemistry is a useful tool for diagnosing urothelial cancers and the recognition of types and subtypes of urothelial cancer has important prognostic and therapeutic implications.

PS-24-043
Impact of Ki-67 and E-cadherin expression on lymphovascular invasion in upper urinary tract urothelial carcinoma
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Objective: To investigate the correlation between lymphovascular invasion (LVI) and immunohistochemical expression of two frequently routinely applied markers, Ki-67 and E-cadherin, in upper urinary tract urothelial carcinoma (UUTUC).
Method: The specimens from 106 patients with UUTUC who had undergone nephroureterectomy were analyzed for pathologic parameters and LVI, while Ki-67 and E-cadherin expression was assessed by immunohistochemistry.
Results: Ki-67 was overexpressed in 38 % of the cases, while 45 % of tumours demonstrated aberrant E-cadherin staining. The presence of LVI was associated with high grade, advanced stage, solid growth, nodular invasion pattern, high Ki-67 labeling index and altered E-cadherin expression. In logistic regression model analysis, besides the non-papillary tumour architecture and nodular invasion pattern ($p < 0.05$, respectively), only Ki-67 expression was found to improve the prediction of LVI in UUTUC ($p < 0.05$).
Conclusion: Our results suggest that Ki-67 overexpression is an independent predictor of LVI in UUTUC, indicating the progression of the disease. E-cadherin staining adds no valuable information to LVI probability assessment. Patients with Ki-67 overexpression, especially in non-papillary tumours, should be monitored more closely after surgery.

PS-24-044
Primary renal lymphoma: Presentation of two cases
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Objective: Lymphoma presenting as a renal mass can occur in two settings. Secondary renal lymphomas (SRL) in the case of systemic diffuse lymphomas, and primary renal localized lymphomas (PRL) without systemic manifestations. Less than 100 of cases of PRL have been described. It is defined as a localized lymphoma arising primarily in the renal parenchyma, with no invasion from any adjacent extrarenal mass and without evidence of systemic involvement. The pathogenesis of primary renal lymphoma is poorly understood, as the renal has not usually lymphoid tissue. We present two PRLs.
Method: We have search our database looking for renal lymphomas from 1995 until 2015 excluding those with systemic disease at presentation.
Results: First case is a 60 years old man with a renal mass that was resected with diagnosis of Diffuse Large B-cell lymphoma who disseminated rapidly. He died 8 months later of adriamicine cardiotoxicity but without evidence of active disease. The second case is an 81 years old woman with follicular lymphoma, alive 7 months later without systemic involvement.
Conclusion: PRL are extremely rare but can be found in nephrectomy specimens. Prognosis is dependent of histologic type.

PS-24-045
CD204 and CD3 inflammatory infiltration of prostate benign, premalignant and malignant lesions reflect ERG expression and rearrangement
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Objective: Prostate inflammation is associated with increased risk of prostate cancer. In the present study, we immunohistochemically examined the infiltration patterns of CD204 and CD3 positive cells in areas of benign hyperplasia, intraepithelial neoplasia and carcinoma of the prostate and correlated these variables with ERG expression and rearrangement status.
Method: Formalin-fixed, paraffin-embedded tissue samples were obtained from 100 patients with prostate cancer who had undergone radical prostatectomy and prior examination for TMPRSS2-ERG fusion. We assessed the number of infiltrating CD3+ T lymphocytes and CD204+ macrophages in benign, premalignant and malignant foci and analyzed the relationship with expression and fusion of ERG.
Results: CD204+ macrophages infiltrated malignant areas to a greater extent than those of benign glands. The same trend was also shown by CD3 lymphocytes. The response of both cellular types was dependent on ERG expression status and on the fusion gene TMPRSS2-ERG. Patients with gene fusion and genome rearrangement as well as higher expression of ERG had significantly higher infiltration of carcinoma tissue by CD3+ a CD204+ cells.
Conclusion: The greater abilitiy of inflammatory cells with CD3+ and CD204+ phenotype to infiltrate malignant and premaligant regions in the prostate may be a consequence of immune reaction against tumourous cells but according to recent data this could bes a manifestation of immune tolerance and tumour promotion.

PS-24-046
A case of giant symplastic leiomyoma of scrotum
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Objective: Smooth muscle tumours of the scrotum are very uncommon, and those with degenerative-appearing atypia, variably designated as "atypical," "symplastic," or "bizarre" leiomyomas, are extremely rare with only 20 cases in the literature. Because of their rarity, the diagnostic criteria and prognosis of symplastic leiomyomas are not well established.
Method: We describe one case of scrotal symplastic leiomyoma and compare their histopathologic characteristics to usual leiomyoma and leiomyosarcoma of the scrotum.
Results: Our patient was 68 years-old. Surgical excision was performed with the preoperative diagnosis of paratesticular tumour The tumoural size was 6 × 5,5 × 4,2 cm. Histologically showed histological features of leiomyoma with striking nuclear atypia and low mitotic activity.
Conclusion: Symplastic leiomyomas, despite the presence of nuclear atypia, share histologic features with usual leiomyomas including small size, low cellularity, lack of mitotic activity, and low Ki67 proliferation rate. Degenerative nuclear atypia, including large pleomorphic nuclei, yet with hyperchromatic smudgy chromatin, was the defining feature of symplastic leiomyomas. All tumours described are relatively small with a mean size of 1 cm but our case is notable for its size. It is important to establish the diagnostic criteria and the differential diagnosis with leiomyosarcoma.

PS-24-047

Clinicopathological features of renal cell carcinoma subsets diagnosed according to the ISUP Vancouver Classification

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Objective: To determine the distribution of renal cell carcinoma (RCC) subsets in Hungary, and to establish which pathological factors predict cancer-specific survival independently in clear cell carcinoma.
Method: 805 RCCs were reevaluated; the diagnosis was supported by panels of immunostainings. Pathological predictors of outcome were tested with Kaplan-Meier curves and Cox models.
Results: 84 % were diagnosed as clear cell, 6.7 % papillary, 4.6 % chromophobic, 2.1 % unclassified, 1.2 % Xp11 translocation, 0.9 % clear cell tubulopapillary, and 0.3 % collecting duct carcinomas. The 5-year survival rates were as follows: chromophobic 100 %, clear cell tubulopapillary 100 %, clear cell low-grade 95 %, papillary type 1 91 %, clear cell high-grade 63 %, papillary type 2 61 %, unclassified 58 %, Xp11 translocation 14 %, and collecting duct 0 %. In clear cell carcinoma, only the grade, stage and positive surgical margin were independent prognostic factors.
Conclusion: This series was characterized by a strikingly high incidence of clear cell carcinoma and low incidences of non-clear cell entities. Low-grade clear cell carcinomas and type 1 papillary carcinomas displayed good, high-grade clear cell carcinomas and type 2 papillary carcinomas moderate, and Xp11 translocation and collecting duct carcinomas poor outcomes. Microscopic tumour necrosis in clear cell carcinoma did not predict the outcome independently of the tumour grading.

PS-24-048

ERb expression in the hyperplastic and neoplastic prostate lesion

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Objective: Prostate adenocarcinoma is the most common cancer in men. Acini in BPH have continuous basal cell layer. HGPIN lesions precede invasive cancer. PCa implies a complete absence of basal cells and stromal invasion by malignant acini. ERb is located in nuclei of acinar basal and secretory cells and partially in stromal cells. Demonstration and localization of ERb in BPH and in PCa. Expression of ERb in most moderately-differentiated PCa, and that the observed receptor expression is lost with increasing of the Gleason score.
Method: Five groups were formed: control with BPH, PIN and three groups of PCa with different Gleason scores. Sextant prostate byopsies are observed for ERb (Novocastra).
Results: ERb expression in acinar epithelial cells was the weakest in well-differentiated adenocarcinoma. A decline of ERb expression was noticed in malignant lesions of the prostate vs benign ones. Less-differentiated adenocarcinomas showed a decrease of ERb expression in basal and in the secretory cells. PIN lesions have mild decrese of ERb expresssion in secretory cells and stronger in basal ones. The ERb expression in the basal cells was stronger than in the secretory ones in BPH and well-differentiated adenocarcinoma.
Conclusion: ERb enables the protection role of estrogen on prostate epithelium from proliferation, neoplastic transformation and oxydative damage. Losing of ERb leads to uncontroled cell prolifferation. ERb localisation in secretory cell indicate that differentiated section is target for estrogen action in prostate.

PS-24-050

Evaluation of apoptosis and matrix metalloproteinase activity at the spermatic vein wall in patients with varicocele

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Objective: Studies from lower limb varicose veins suggest that a reduction of apoptosis and increased metalloproteinase activity may lead to the morphological alterations of varicose veins. Hence we tested whether similar changes occur in patients with varicocele presenting with infertility.
Method: Specimens of internal spermatic veins (ISV) from 45 patients operated for varicocele were compared with normal veins (controls). We immunohistochemically evaluated the expression of regulators of instrinsic (Bcl-2 and Caspase-9) and extrinsic (Caspase-8) apoptotic pathways and the matrix metalloproteinases MMP-1, MMP-9 and the inhibitor TIMP-1. Morphological alterations of varicose veins were demonstrated by anti-Actin immunostaining.
Results: Varicose ISV demonstrated a media wall thickening with alternating segments of atrophy and hyperplasia. Nuclear immunostaining for Caspase 9 was significantly higher in the tunica media of ISV compared to controls ($p < 0.0001$) Few cases exhibited higher expression for Caspase 8 while Bcl-2 was not detected in any specimen. MMP-1 and TIMP-1 cytoplasmic immunostaining was significantly higher in ISV ($p < 0.0001$). MMP-9 expression was limited to ISV smooth muscle cells only.
Conclusion: Increased MMP/TIMP activity is a common finding in varicose veins; however our findings on dysregulation of apoptosis differ from those reported in limb varicose veins, suggesting that in varicocele other mechanisms are probably involved.

PS-24-051

Langerhans cell histiocytosis of the kidney concurrent with clear cell renal cell carcinoma: Report of a case

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Objective: Langerhans cell histiocytosis (LCH) is a proliferative histiocytic disorder characterized by a proliferation of S-100 and CD1a immunopositive cells resembling the normal Langerhan cell of the immune system. Simultaneous occurrence of LCH and a solid tumour is rarely detected. We describe a case of kidney's LCH concurrent with clear cell renal cell carcinoma (ccRCC). To our knowledge, only two, similar, cases have been reported so far.
Method: A 50-year-old male patient underwent left partial nephrectomy due to a tumour of 2 cm greatest diameter. Morphological and immunohistochemical study of the surgical specimen was performed.
Results: The tumour showed histopathological features of ccRCC of Fuhrman grade 2. In the perimeter of the tumour, two foci (0,2 and 0, 35 cm of greatest diameter) were detected in which mononuclear cells [Pankeratin, EMA: -, Vimentin: +, S-100, CD1a: +] with convoluted nuclei and nuclear grooves were intermingled with eosinophils leucocytes. The morphological and immunohistochemical features of these foci were consistent with foci of LCH.
Conclusion: LCH may be associated with malignant neoplasms (especially lymphoma, leukemia, lung carcinoma). However, the detection of LCH within the area of a renal cell carcinoma is extremely rare. Although the phemomenon is still unresolved, it seems likely that the deregulation of the immune system due to the carcinoma promotes the development of LCH. Further laboratory examination (especially imaging studies) is necessary in order to rule out systemic LCH.

PS-24-052

Mucinous tubular and spindle cell renal cell carcinoma: Report of a case

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Objective: Mucinous tubular and spindle cell renal cell carcinoma (MTSCRCC) is an uncommon variant of renal carcinoma associated with good prognosis, presenting mainly in adult women. We report a case of MTSCRCC.
Method: A 60-year-old male patient underwent left partial nephrectomy due to a tumour of the lower pole measuring 2,5 × 2,2 × 2 cm. Morphological and immunohistochemical study of the surgical specimen was performed.
Results: A circumscribed neoplasm, composed of cuboidal or elongated-spindle cells [Pankeratin, CK7, CK34BE12, EMA, Vimentin, AMACR: +, CD10, TTF-1, Chromogranin, SMA:-] with moderate nuclear atypia, arranged mainly with a trabecular, cord-like or tubular pattern, was identified. Within the tumour stroma aggregates of mucinous material (mucicarmine:+) were detected. The findings were consistent with a diagnosis of MTSCRCC.
Conclusion: MTSCRCC represents an unusual type of renal carcinoma which histogenesis has been debated. The specific morphological and immunohistochemical features of the neoplasm allow its differential diagnosis from other primary and secondary tumours (such as: papillary renal cell carcinoma, collecting duct carcinoma, neuroendocrine or mesenchymal tumours).

PS-24-053
Sarcomatoid carcinoma of the urinary bladder: Histopathological characteristics of nine cases
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Objective: Sarcomatoid carcinoma is a rare variant of bladder tumour showing both epithelial and sarcomatous components. In this study, the histopathological findings of nine cases are described.
Method: Nine cases diagnosed as sarcomatoid carcinoma of the bladder between 2004 and 2014 were reviewed for histopathological characteristics of the epithelial and sarcomatous components.
Results: All of the patients were male with a mean age of 71 years old (range 52–79 years). Sarcomatous components of the tumours were characterized by poorly differentiated spindle or pleomorphic tumour cells. One case showed focal heterologous chondroid elements. Carcinomatous components were urothelial carcinoma ($n = 4$), squamous cell carcinoma ($n = 2$), urothelial carcinoma combined with squamous cell carcinoma ($n = 1$), and urothelial carcinoma in situ ($n = 1$). In one case sarcomatoid carcinoma diagnosis was made depending on CK7 positivity. Lymphovascular invasion and perineural invasion were seen in 5 and 2 cases respectively. All of the cases were invasive, including stages of pT1 ($n = 1$), pT2 ($n = 3$), pT3 ($n = 3$), pT4 ($n = 2$).
Conclusion: Sarcomatoid carcinoma of the bladder is an aggressive disease which majority of the cases are presented at an advanced stage. The sarcomatous component is most commonly characterized by high grade spindle and pleomorphic cells. The epithelial component is predominantly composed of urothelial carcinoma followed by squamous cell carcinoma.

PS-24-054
Secondary tumours of the urinary bladder: A retrospective study of 18 years in Cantabria (Spain)
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Objective: Secondary tumours of the urinary bladder are rare, less than 2 % of all bladder neoplasms. The urinary bladder is secondarily involved by a wide spectrum of malignancies. Colon, prostate, rectum and cervix are the most common primary tumours, involving the bladder by direct extension. Stomach, skin, lung and breast are the most common primary sites in distant metastases. As it is an uncommon finding, we reviewed our hospital's cases in order to better characterize this entity.
Method: We reviewed, in our autopsy and biopsy series, all cases of tumours involving the bladder from 1996 to 2014.
Results: We found 41 cases, 6 autopsies (14.63 %) and 35 biopsies (85.37 %). Colon was the primary site most frequently involved (48.78 %), followed by rectum (12.20 %), prostate (14.63 %), endometrium (7.32 %), skin (7.32 %), stomach (2.44 %), uterine cervix (2.44 %), Fallopian tube (2.44 %) and esophagus (2.44 %).
Conclusion: Bladder metastases are a rare finding. Differential diagnosis between these tumours and bladder carcinomas can be difficult. A proper clinical history and histological correlation can help in the correct interpretation of bladder metastasis, as immunohistoquemistry plays a limited role. Our findings are in agreement with the literature, except for a higher rate of Fallopian tube and esophagus metastases.

PS-24-055
The relationship of p16, ki-67, bcl-2, p53 and ck20 immune expressions with recurrence in superficial bladder tumours
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Objective: Superficial urothelial carcinoma of the urinary bladder account for 70–80 % of all newly diagnosed bladder cancer cases. We investigated the relationship between the recurrence rate and the expressions of various genes via immunohistochemical analysis in order to assess their applicability as prognostic factors for clinical behavior and differential diagnosis.
Method: We used P53, bcl-2, Ki-67, CK20 and P16 for 58 cases diagnosed with primary superficial bladder cancer.
Results: Recurrence was detected in 62.1 % of the cases. Progression to a higher grade tumour was detected in 38.9 % of the 36 cases that showed recurrence. A marked statistically significant relationship was found between recurrence and diffuse or no staining with CK20, more than 50 % heterogeneous expression with P16, and more than 1 % expression with bcl-2. A significant relationship was found between the pathological stage and histological grade of the cases and the CK 20 and Ki 67 expressions.
Conclusion: In conclusion, determining CK20, bcl-2, and p16 expressions with immunohistochemical methods can provide guidance in predicting the recurrence of superficial bladder tumours. Abnormal CK20 staining and Ki-67 expression is related to tumour grade and can be used to support the diagnosis in controversial cases.

PS-24-056
Epithelial and stromal androgen receptor expression in prostatic carcinoma and benign prostatic hyperplasia
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Objective: The aim of this study is to determine the differences in androgen receptor expression in the nuclei of epithelial and stromal cells in both prostatic carcinoma and benign prostatic hyperplasia.
Method: Archive paraffin blocks from radical prostatectomy specimens from 30 cases of prostatic carcinoma were used for this study. Samples were selected in which both prostatic carcinoma and benign prostatic hyperplasia were present. Immunohistochemical analysis was performed using androgen receptor antibody. The signal was evaluated using the histological score system (HSCORE) that combined percentage of positive cells (P) and intensity of the signal (i): no signal 0, weak signal 1, moderate signal 2 and strong signal 3, using the formula Pi(i+1).

Results: The most intense signal was found in epithelial cells of benign prostatic hyperplasia with HSCORE 86 followed by malignant epithelial cells with HSCORE 83, benign stromal cells with HSCORE 51 and stromal cells in prostatic carcinoma with HSCORE 37. While the difference between epithelial malignant and benign cells was small the difference between malignant and benign stromal cells was much bigger.
Conclusion: Loss of androgen receptor expression in stromal cells of prostatic carcinoma may partly be responsible for prostatic carcinoma development and progression.

PS-24-058
Is tumour budding an independent prognostic factor for bladder cancer?
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Objective: Presence of tumour budding has been correlated with lymph node and distant metastasis, recurrance and decreased survival in several cancers. The present study aims to evaluate the prognostic significance of tumour budding in urothelial carcinoma of bladder (UCB).
Method: A total of 60 patients who underwent radical cystectomy for muscle-invasive UCB were included in the study. Tumour budding was defined as positive in the presence of small clusters (< 5 cells and >1 cells) of tumour cells identified at the invasive margin.
Results: The mean age of patients was 65.6, of whom 52 were males and 8 were females. Twenty-seven patients were alive, 33 were dead. The histologic type was pure urothelial carcinoma. Of the tumours 11 were stage II, 18 were stage III, 31 were stage IV. The number of cases with absent, mild, moderate and marked scores of budding were 8, 18, 13, 21, respectively. Overall survival for budding scores absent, mild, moderate and marked were 40, 29, 30 and 19 months, respectively. No statistically significant relationship was found between tumour budding and overall survey ($p = 0.14$).
Conclusion: Although there was no statistical significant correlation of budding with survival, presence and intense of budding had a trend to an adverse impact on survival.

PS-24-059
Proteomics and morphometry in embryonic testicular carcinoma diagnosis
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Objective: The incidence of testicular germ-tumours presents a remarkable geographical range. The highest level of incidence (8–10/100000 young-age population) was met in industrialized countries. Researches regarding the causes of appearance of testicular tumours were guided by their beginning assumptions since intrauterine life and consist differentiate abnormal fetal-primordial germ-cell populations.
Method: It distinguish that embryonic carcinoma metastases can differentiate to other testicular tumours in over 8 % cases. Embryonal carcinomas cells express PLAP in 85–95 % cases, focal expression and less marked than seminomas. Retrospective study (patients were diagnosed in Constanta ECC-Hospital) examines the techniques of immunohistochemistry and morphometry in histopathological diagnosis of certainity in ambiguous cases.
Results: Embryonal carcinoma is the most undifferentiated testicular malignant tumour, composed of large cells, with different architectural aspects. It can occur in pure form or as a frequent component of mixed germ tumours. Embryonic carcinoma is a risk factor for relapse malignant germinal testicular tumours.
Conclusion: These findings demonstrate the usefulness of research proposed by achieving the objectiv: protocol for a complex histopathological diagnosis of testicular embryonic carcinoma. This work benefited from financial support through the project "CERO-CAREER PROFILE: Romanian researchers", contract no. POSDRU/159/1.5./S/135760, a project co-financed by European Social Fund through the Sectorial Operational Program Human Resources Development 2007–2013.

PS-24-060
NKX3.1 and Cadherin-17 are the useful markers to distinguish prostate from colorectal cancer
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Objective: Malignant epithelial tumours located in the male pelvis as prostate (PC) and colorectal (CRC) cancer are one of the most common neoplasms in the western countries. These tumours have similar histological appearance, especially in advanced cases and may be difficult to distinguish without the aid of immunohistochemistry. The aim of this study was to establish the diagnostic value of NKX3.1 and Cadherin-17 in high grade prostate and colorectal adenocarcinomas.
Method: Two tissue microarrays were constructed from paraffin blocks-donors: 23 cases of PC and CRC were included. Each tissue microarray consists of 72 cores: 3 cores from each case included in the study and 3 controls.
Results: Among 23of PC cases 15 (65 %) showed positive and 8 (35 %) negative NKX3.1 nuclear staining in the tumour glands, while the positive expression in CRC was only in 3 cases (13 %). Cadherin-17 staining was positive in 21 of 23 cases (91 %) of CRC (CRC) and 2 of 23 (8,6 %) in PC.
Conclusion: The results give us a reason to include NKX3.1 and Cadherin-17 separately and in combination with routinely used markers for the correct diagnosis in a number of unclear and advanced undifferentiated cases of PC and CRC. Acknowledgements: Grant HO14/2014 by Medical University - Plovdiv.

PS-24-061
Testicular metastasis from a bladder carcinoma presenting with a palpable testicular mass
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Objective: We present a very rare example of a testicular metastasis from a bladder carcinoma.
Results: A 71-year-old male underwent transurethral resection of the bladder and prostate which were diagnosed as high grade urothelial carcinoma (pT4; prostatic invasion). No lymph node involvement or metastatic tumour was detected. Because he rejected surgery, he was treated with chemoradiotherapy. One year later, he presented with a palpable right testicular mass. No other recurrent tumour was present in the bladder at that time. A right orchiectomy was performed. Gross and microscopic examination revealed pleomorphic tumoural infiltration with entrapped seminifer tubules within the tumour and widespread lymphovascular invasion. Immunohistochemical findings (positive for HMWCK and CK 7; negative for PLAP and CD30) and morphological features were consistent with urothelial carcinoma metastasis.
Conclusion: Metastases from bladder urothelial carcinoma to the testis are very rare and usually found on autopsy of patients with advanced disease. Our case is a rare example of metastatic urothelial carcinoma of the bladder to the testis presented with a clinically palpable testicular mass. Metastatic testicular tumours may mimic primary germ cell tumours. Patients' age and medical history are helpful features that should be sought after.

PS-24-062

E-cadherin expression in clear cell renal cell carcinoma

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Objective: Our study aimed to investigate the E-cadherin profile in clear cell renal cell carcinoma (CC-RCC) and to correlate its expression with the classical clinicopathological prognostic factors.
Method: The study was conducted on 44 cases of CC-RCC. The tissue fragments underwent standard processing procedures for immunohistochemical examination, using anti- E-cadherin antibody. The E-cadherin expression was assessed by using a combined score, based on percentage of positive tumoural cells and intensity of immunoreaction.
Results: Tumoural areas were characterized by a low expression of E cadherin, reflecting the loss of cell polarity. From the study group, 16 cases (36.36 %) were evaluated with a score value of 2, 18 cases (40.9 %) with score 3, 6 cases (13.64 %) with score 4 and 4 cases (9.10 %) with score 5. E-cadherin expression was significantly correlated with tumour stage and histologic grade of tumour. We also noted the presence of E-cadherin in distal and collecting tubules in normal kidney adjacent to the tumoural areas.
Conclusion: The role of adhesion molecules in CC-RCC is still controversial, few studies being published in the literature on this topic. Our results sustain the involvement of E-cadherin in the progression of carcinogenesis process and its potential role as prognostic factor.

PS-24-064

Small Cell Carcinoma (SCC) of the penile urethra with negative cytokeratin staining: A case report

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Objective: The urogenital tract is one of the most infrequent locations of primary small cell carcinomas (SCC). Rarely, they may be negative for cytokeratin markers posing a diagnostic problem. PAX5 is a B-cell lymphocytic marker, whose expression has been described in SCC. We report a rare case of a SCC of the penile urethra that was negative for a variety of cytokeratin cocktails and positive for PAX5.
Method: A 73 year-old man presented with a painful mass protruding through the urethral meatus. Preoperative studies revealed the presence of inguinal lymph nodes metastases, but no other evidence of disease. The patient underwent a total penectomy.
Results: The tumour originated from the penile urethra and infiltrated the corpus cavernosum and was composed of a diffuse proliferation of intermediate sized cells with scant cytoplasm, hyperchromatic nuclei and inconspicuous nucleoli. Mitotic rate was 15/HPF. NE markers and PAX5 were expressed. Various cytokeratin cocktails and B and T lymphocytic markers were negative. Ki-67 expression was at 95 %. The diagnosis of SCC of the penile urethra was rendered.
Conclusion: SCC should be considered in the differential diagnosis of a urethral mass and may be negative for cytokeratins. PAX5 expression may help in diagnostically challenging cases.

PS-24-065

Small cell carcinoma of urinary bladder: A clinico-pathologic case series from a tertiary care oncology centre

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Objective: Small cell bladder cancer is an uncommon malignancy with biological behavior different from urothelial carcinoma.
Method: Cases of small cell carcinoma of bladder were retrospectively analyzed from 2005 to 2013.
Results: Ten patients of small cell carcinoma of bladder were identified. All patients were of male gender. The median age of presentation was 62 years. All patients presented with locally advanced disease and 3 had metastatic disease at presentation. Six patients had pure small cell morphology on histology and four patients had admixture of high grade urothelial carcinoma areas. Combined immunohistochemical positivity for synaptophysin and chromogranin (7 patients), CD56 and CK7 (2 patients) and synaptophysin and CD56 (1 patient) helped in confirming the diagnosis. Seven patients with localized, resectable disease underwent a radical cystectomy following initial transurethral resection of bladder tumour. Post operative chemotherapy was administered in three patients. Median follow up was 13.5 months (range 4–39 months). The 2 year overall survival was 42 % with a median overall survival of 23 months.
Conclusion: Small cell carcinoma of bladder can be correctly diagnosed by high index of morphological suspicion and ancillary immunohistochemistry. Outcome is poor owing to aggressive biologic behavior.

PS-24-067

ERG oncoprotein evaluation and its correlation with other molecular biomarkers in prostate cancer

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Objective: The aim of this study was to assess the frequency of expression of the ERG oncoprotein, a product of the chimeric gene TMPRSS2:ERG, in cancer containing prostate biopsy material, to evaluate its prognostic significance and correlation with other molecular biomarkers.
Method: Expression of the markers such as ERG oncoprotein, Ki-67, cycline D1 (CycD1), topoisomerase IIα (TopoIIα), chromogranin A (ChrA), androgen receptors (AR) and estrogens α and β receptors in epithelium (ERα, ERβ) and stroma (SRα, SRβ), p53, BCL2, BAX, VEGF, TGFβ, EGFR was assessed immunohistochemically in the biopsy material from 238 cases of prostate cancer.
Results: ERG expression was found in 47 % of the patients. It was demonstrated that ERG-positive cancer if compared to ERG-negative type is characterized by enhanced ($p < 0.05$) expression of Ki-67, CycD1, TopoIIα, AR, ERα, p53, TGFβ and EGFR and decreased expression of BAX, ERβ, SRα and SRβ, whereas no difference in expression of ChrA, BCL2 and VEGF was revealed. It was shown that marked ERG expression in biopsy samples is associated with poor prognosis: higher risk of biochemical recurrence and clinically significant disease progression after radical prostatectomy.
Conclusion: ERG-positive cancer was found in biopsy material from 47 % of patients and is characterized by enhanced proliferative activity, increased expression of AR, ERα, p53, TGFβ and EGFR, and decreased expression of BAX, ERβ, SRα and SRβ; it is associated with higher risk of unfavorable outcome.

PS-24-068

Eosinophilic variant of chromophobe renal cell carcinoma: Clinical, macroscopic, histologic, and immunohistochemical data on five cases

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Objective: Analyze clinicopathological features.
Method: 706 patients were diagnosed with renal cell carcinoma (RCC) from 1998 to 2014. 65 were chromophobe RCC and only five were eosinophilic variant. Data were obtained from medical and pathological records.
Results: The mean age was 62.2 years (range, 39–76). Sixty percent were male. All patients underwent partial nephrectomy, and one of them underwent radical nephrectomy after positive surgical margins. Mean tumour size was 4.8 cm (range, 3.5–7.5). All cases had well-defined

borders and brown color. Only one case was encapsulated. Architecture was tubular or tubulocystic (60 %), nested (60 %), and solid sheets (20 %). No sarcomatoid features or necrosis were identified, presenting haemorrhagic foci four cases. The cytoplasms were granular, eosinophilic, with poorly defined borders. All cases presented "raisin-like" nuclei (range, 5–20 %). Only one case had eccentric nuclei, others were centrally located. Perinuclear halo, binucleations and nucleoli were infrequent. All cases were positive for CK7 and EMA, and were negative for CK-20, vimentin and racemase. Eighty percent were pT1. One case was pT2. All cases are currently free of disease. A second primary tumour was found in one case that is now being studied because of the onset of hematuria.
Conclusion: These data are helpful for a correct differential diagnosis between eosinophilic renal tumours.

PS-24-069
Pleomorphic giant cell carcinoma of the prostate: A case report
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Objective: Pleomorphic giant cell carcinoma is extremely rare and aggressive variant of prostate cancer with large bizarre anaplastic giant cells. These lesions must be differentiated from sarcomatoid carcinoma of the prostate, giant cell carcinoma of bladder, metastatic giant cell carcinoma. Case presentation: A 65 year old man was admitted to our Urology Surgery out-patient clinic with hematuria and his prostate-specific antigen (PSA) level was 12.1 ng/mL. A transrectal ultrasonography-guided biopsy was performed. Prostatic biopsy revealed a undifferentiated acinar prostatic adenocarcinoma with Gleason score 10 (5 + 5) in 10 of 10 specimens. There he underwent transurethral resection (TUR) for recurrent hematuria. At microscopy, poorly differentiated adenocarcinoma was seen, which was characterized by markedly pleomorphic, giant, bizarre, anaplastic cells immunohistochemical panel was done for the primary prostatic tumour and the metastase, revealing to be positive for PSAP and negative for PSA, P63, CDX2, chromogranin A, synaptophysin.
Conclusion: Pleomorphic giant cell carcinoma is a rare aggressive variant of prostatic adenocarcinoma with a poor prognosis. This tumour must be differentiated from metastatic malignancy to the prostat including pleomorphic giant cell carcinoma of the bladder.

PS-24-070
Beta-catenin expression as a prognostic factor in bladder superficial urothelial carcinoma
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Objective: Prognosis of non muscle invasive urothelial bladder carcinoma (NMIBC) remains unpredictable for both recurrence and progression. Standard endoscopic and histopathological prognostic parameters are insufficient. Some molecular parameters such as Beta-catenin, an adhesion protein, are recently described contributing to a more precise assessment of tumour's behavior. We aim to evaluate Beta-catenin immunostaining as a prognostic factor for recurrence and progression in NMIBC.
Method: Series of 40 patients with NMIBC was recorded between 2008 and 2013. Immunohistological staining for Beta-catenin was evaluated. Chi-squared test was used to evaluate the association between Beta-Catenin expression and recurrence/progression. Kaplan-Meier analysis was used to evaluate recurrence-free (RFS) and progression-free survival (PFS).
Results: 35 % cases recurred. 7.14 % of them expressed Beta-catenin. 42.3 % of tumours without recurrence were Beta-catenin positive. Beta-catenin had negative correlation with recurrence (p = 0.02, Pearson index = -0,366). Beta-catenin expression was not correlated to RFS (p = 0.009). 12 % cases progressed and all of them had negative immunostaining. 34.28 % of tumours without progression expressed Beta-catenin. Beta-catenin was neither correlated to progression (p = 0.08) nor to PFS (p = 0.17).
Conclusion: There is an association between Beta-catenin immunoexpression and NMIBC recurrence. Beta-catenin can be used to stratify patients for therapeutic strategies.

PS-24-071
E-cadherin and tissue progenitor/transit amplifying cells in superficial bladder carcinoma
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Objective: Recently, interest has been focused on the significance of e-cadherin adhesion molecule, in the process of neoplastic transformation and invasiveness in non muscle invasive bladder carcinomas (NMIBC). We aim to study E-Cadherin expression pattern in NMIBC in correlation with grade and stage.
Method: Series of 40 cases of NMIBC was recorded (2008–2013). Immunohistochemical staining was scored including type of positivity and topographic distribution within different layers.
Results: E-Cadherin was positive in 64.2 % of pTa tumours and in 8.33 % of pT1 tumours, correlating to stage (p = 0.001, Pearson = −0.513). E-Cadherin was positive in 73.08 % of Low grade tumours (LGT) and negative in all high grade tumours (HGT) correlating to grade (p = 0.0000000, Pearson = −0.698). Grade was correlated with staining topographic distribution. Staining was negative or superficial in HGT. It was basal, epibasal or interesting all layers in LGT.
Conclusion: Epithelial cells resting on basal membrane and cells adjacent to this basal layer display properties of tissue progenitor/transit amplifying cells (TPTAC), showing more primitive phenotype and E-Cadherin highest level expression. In HGT, there is a loss of E-Cadherin expression. In LGT, positive staining extends towards surface, suggesting prolonged survival of cells displaying properties of TPTAC.

PS-24-072
Pseudotumoural eosinophilic cystitis: A Tunisian case report
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Objective: Eosinophilic cystitis (EC) is a rare inflammatory pathology of the bladder wall which physiopathology remains controversial. It occurs most often in women and children with allergic condition and hyper-eosinophilia. Less commonly, this pathology is found in cases of non- allergic patients particularly in elderly men with urological past history. Our aim is to study the clinico-pathological features of a pseudotumoral EC case.
Method: We report the case of a 60-years old Tunisian man, presenting with dysuria since few months. Cystoscopy showed a bladder tumour measuring 1 cm in diameter. Histopathological examination showed a dense inflammatory infiltrate of the bladder wall made of eosinophils. No tumour proliferation was found.
Results: The final diagnosis was pseudotumoral EC.
Conclusion: EC is a rare disease having variable clinical and endoscopic manifestations. Pseudotumoral form is very rare and is misleading at endoscopic examination. Histology is mandatory to rectify the diagnosis.

PS-24-076
Immunohistochemical features in prostate atrophy
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Objective: Prostatic atrophy is a benign lesion that mimics well differentiated adenocarcinoma from histologically point of view and on transrectal ultrasound exam. Among all microscopical forms, partial atrophy require most discussion of differential diagnosis.
Method: Have been studied 30 cases of prostatic atrophy diagnosed by transurethral resection the excised material of the prostate in men aged between 55 and 89 years, with a mean serum PSA of 10.85 ng / ml. Monoclonal Mouse Anti-Human High Molecular Weight Cytokeratin (HMWCK), Clone 34βE12, p63 - clone p63-DAK and anti-Human Monoclonal Alpha Methyl Acyl Coenzyme A racemate (AMACR) - clone 13H4 were applied. The control group was composed of 30 prostatic adenocarcinomas with small glands.
Results: Immunohistochemical techniques highlighted the presence of continuous or discontinuous basal cell in benign lesion while cases of adenocarcinoma were negative for basal cell markers ($p < 0,05$). The AMACR immunostaining was focal positive in 13 cases of atrophy, negative in 17 cases of atrophy and positive in adenocarcinoma.
Conclusion: Immunohistochemical assessment of basal cell was useful in proving the benign nature of atrophic lesions and AMACR immunostaining alone was not sufficiently discriminatory in the differential diagnosis of prostate atrophy with adenocarcinoma. This work benefited from financial support through the project,, CERO-CAREER PROFILE: Romanian researchers, contract no. POSDRU/159/1.5/S/135760, a project co-financed by European Social Fund through the Sectoral Operational Program Human Resources Development 2007–2013.

PS-24-077
Androgen deprivation dynamically modulates the expression of genes involved in prostate cancer progression
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Objective: To analyze the dynamic modulation of the expression of genes involved in prostate cancer progression by androgen-deprivation therapy (ADT).
Method: ERG: TMPRSS2, WNT-11, SPINK-1, CgA, AR and PDEF gene expression was analyzed by means of real-time PCR in a series of 78 surgical samples of prostate carcinomas, including 47 cases preoperatively treated with androgen deprivation (ADT+) and 31 untreated cases (ADT-), and in 43 corresponding biopsies. The same genes were analyzed in androgen-deprived and control LNCaP cells.
Results: Three genes were significantly up-modulated (WNT-11 and AR) or down-modulated (PDEF) in ADT+ vs ADT- cases, as well as in androgen deprived LNCaP cells. The effect of ADT on CgA gene up-modulation was almost exclusively detected in cases positive for the TMPRSS2: ERG fusion. The correlation between bioptic and surgical samples was poor for all genes tested. Gene expression analysis of separate tumour areas from the same patient showed an extremely heterogeneous profile in all 6 untreated cases tested.
Conclusion: Our results demonstrate that ADT induces relevant transcriptional modifications, potentially associated to the onset of a more aggressive phenotype. However, intra-tumoral heterogeneity limits the use of this gene as potential prognostic or predictive biomarkers in patients treated with ADT.

PS-24-078
Primary sclerosing epithelioid fibrosarcoma of kidney
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Objective: Sclerosing epithelioid fibrosarcoma (SEF) is a rare aggressive malignant mesenchymal tumour of soft tissues. Here, we present two cases of SEF with primary renal origin. To our knowledge, these are the third and fourth reported cases of SEF involving kidney.
Method: Case#1 was that a 16 year-old female presented with flank pain. A 6 cm mass at upper-pole of left kidney was identified. Case#2 was a 57 year-old female with incidentally encountered 7.5 × 5.5 × 4 cm left renal tumour during ultrasonography.
Results: Both tumours were located clearly within kidney parenchyma microscopically. They were characterized by nests, cords, and strands of epithelioid cells within dense hyalinized-collagenized stroma. The renal tubules entrapped within the tumour exhibited focal papillary hyperplasia, mimicking malignant mixed epithelial stromal tumour (MEST) of kidney. EMA, bcl2, CD99 and TLE1 (weak) positivity in one case suggested possible diagnosis of synovial sarcoma. Both tumours strongly expressed MUC4 and showed EWSR1-CERB3L1 translocation by FISH, consistent with the diagnosis of SEF.
Conclusion: Herein we report 2 cases of primary renal SEF, showing features identical to those in conventional locations. Renal SEF should be distinguished from malignant MEST and synovial sarcoma. Improved recognition of this rare clinical presentation should allow for better understanding of its unique features.

PS-24-080
Extragastrointestinal stromal tumour of prostate
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Objective: Extragastrointestinal stromal tumours (EGISTs) are rare soft tissue neoplasms arising from extra gastrointestinal tract.
Method: We present a 56-year-old male who has symptoms of urologic problems since 2010. His previous prostatic biopsy was misdiagnosed as leiomyoma in 2010. On December 2014 a new prostatic biopsy was performed.
Results: Histopathologic study of the specimen showed spindle cell proliferation arranged in fascicles. The results of immunohistochemical staining showed positive immunoreactivity for CD117 (c-kit), CD34. He was diagnosed "EGIST of the prostate".
Conclusion: EGIST is extremely rare and confirmation of the diagnosis should be based on immunohistochemistry. The differential diagnosis should be made carefully and mutation analysis can be performed to the difficult cases.

PS-24-082
A rare case of renal angiomyoadenomatous tumour/clear cell (tubulo) papillary carcinoma associated to secondary amyloidosis
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Objective: To present a unique case report of a renal angiomyoadenomatous tumour/clear cell (tubulo) papillary carcinoma (AMA/CCPC) associated to kidney amyloidosis AA.
Method: We reviewed the clinical history of the patient and histological and immunohistochemical analyses were performed.
Results: A 66-year-old man with a history of chronic renal failure of unknown etiology, ankylosing spondylitis, rheumatic fever and Reiter syndrome had an abdominal ultrasound in 2013 where a renal mass was identified. Abdominal CT confirmed a right kidney tumour. The patient had CT follow ups for 2 years, and in 2015 a radical nephrectomy was performed. The specimen weighed 433 grs and had a brown solid tumour that measured 3 × 2,5 cm with a white capsule. Histologically the tumour showed tubules of clear epithelial cell with a low cytological atypia intermingled with fascicles of smooth muscle. The tumour cells were positive for cytokeratin 7, AE1/AE3, vimentin, carbonic anhydrase 9, and very focally for CD10, but negative for racemase, CD117, MelanA

and HMB-45. The non tumoural kidney had glomerular, intersticial and vascular deposits of amorphous eosinophilic material, Red Congo positive, Amyloid A positive.
Conclusion: As far as we know, we present the first case of renal AMA/CCPC associated to secondary amyloidosis.

PS-24-084
Plasmacytoid urothelial carcinoma of urinary bladder: A case report and review of literature
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Objective: Plasmacytoid urothelial carcinoma (PUC) of the urinary bladder is a rare and very aggressive variant of urothelial carcinoma. Because of its late presentation and poor prognosis, there is need for increased awereness of this under-recognized variant of bladder carcinoma. A correct histological diagnosis is critical for optimal therapeutic approaches.
Method: An 75-year-old male presented with gross hematuria, due to bladder tumour. A TURBT was performed. Formalin-fixed paraffin embedded tissue was examined with histology and immunohistochemistry.
Results: Microscopically, a high-grade urothelial carcinoma, characterized by discohesive cells with plasmacytoid appearance was revealed. In situ carcinoma and muscle invasion were also observed. Immunohistochemically, neoplastic cells were CK7(+), CK20(+), p63(+), CD138(+), E-cadherin (loss of membranous expression), CD20(-), Ki-67 (20 %).
Conclusion: The majority of PUC show markedly reduced membranous staining for E-cadherin, which mediates cell-to-cell adhesion. It has been suggested that the loss of E-cadherin as a sign of an epithelial-to-mesenchymal transition and the upregulation of transcriptional repressors of E-cadherin may contribute to a reduced sensitivity to chemotherapeutic agents. The optimal therary for PUC remains to be proposed.