Archive of Oncology was founded in 1993 and is a successor of the Onkološki Arhiv Journal.
Founder and owner: Oncology Institute of Vojvodina, Put dr Goldmana 4, 21204 Sremska Kamenica, Serbia (Zoran Radovanović, CEO).
Publisher: Oncology Institute of Vojvodina.
Co-Publisher: Faculty of Medicine, University of Novi Sad.
Archive of Oncology is published semi-annually, in electronic version only.
The Journal is indexed in Directory of Open Access Journals (DOAJ), Sherpa/Romeo, Scopus, Embase, Engineering Village, Reaxys and SCIndeks

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Layout Edition
Graphit Plus doo,
Adel Nemešanji 19, 21203 Veternik, Serbia

Layout Editor
Edvard Tel

DOI is assigned by National Library of Serbia, Skerlićeva 1, 11000 Belgrade

Archive of Oncology is financed by the Oncology Institute of Vojvodina. The journal is registered by the Bureau for Intellectual Property of Serbia

Official Journal of the Oncology Institute of Vojvodina Sremska Kamenica, Serbia

Founded in 1993

CIP – Каталогизација у публикацији
Библиотека Матице српске, Нови Сад

616-006

ARCHIVE of Oncology [Elektronski izvor]
Glavna urednica: Tatjana Ivković-Kapicl
Elektronski časopis. - 1997 - .

Način pristupa (URL):
http://www.onk.ns.ac.rs/archive/home.asp
Dva puta godišnje.
ISSN 1450-9520 = Archive of Oncology (Online)

COBISS.SR-ID 81032204

ARCHIVE OF ONCOLOGY

Volume 30 • Issue 1S • May 2024

eISSN 1450-9520 • ISSN 0354-7310 • UDC 616-006

ARCHIVE OF ONCOLOGY
Volume 30 • Issue 1S • May 2024

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ARCHIVE OF ONCOLOGY
Volume 30 • Issue 1S • May 2024

18TH NATIONAL CONGRESS OF SERBIAN PATHOLOGIST AND CYTOLOGISTS ASSOCIATION

with international participation

9-11 MAY 2024, NOVI SAD, SERBIA

Word of the Guest Editor

Dear Colleagues,

On behalf of the Serbian Pathologists and Cytologists Association, it is our great honor and pleasure to present you a brief Supplement from our 18th National Congress of the Serbian Pathologists and Cytologists Association (SPCA) with International Participation.

The Congress Scientific Committee has devoted substantial effort to provide valuable insights into current advancements in pathology, with a particular focus on the field in Serbia. We have carefully selected a series of sessions featuring distinguished speakers from both our nation and abroad. These sessions encompass symposia, short courses, special sessions, slide seminars, oral presentations, poster sessions, and, most notably, keynote lectures. This diverse program affords all of us the opportunity to convene and engage in discussions pertaining to the latest developments, challenges, and issues within our profession.

We extend a special invitation to those who are relatively new to the field of pathology, particularly our pathology residents, to partake in this significant event that takes place biennially. Participation in this congress will undoubtedly enhance their knowledge, contributing to the future advancement of pathology.

As we engage in the scientific program, exchange ideas, make new connections, and cultivate friendships, we look forward to creating cherished memories while experiencing the traditional Serbian Vojvodina hospitality in Novi Sad.

We warmly welcome you all and eagerly await your participation in the congress.

This Supplement comprises around 70 abstracts from all pathology fields, primarily contributed by younger pathologists to our Congress. Additionally, invited speakers have contributed with abstracts of their talks. Thus, the content of this Supplement provides a realistic picture of our local practices and research. The poster session will accordingly highlight those aspects, and recognize the best posters.

Warm regards,

Prof. dr Milana Panjković
President of SPCA


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News in the WHO 2022 classification of urothelial neoplasms

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Objective: While morphology remains fundamental for tumor taxonomy, emerging approaches integrating molecular insights into the classification of urothelial carcinomas and the management of neoplasms with novel therapeutic modalities like immunotherapy are gaining prominence. However, further research is warranted to translate these advances into routine pathology practice and patient care.
Introduction: The fifth edition of the World Health Organization (WHO) Classification of Tumors series for urinary and male genital tract tumors has been released after six years, coinciding with advancements in treatment strategies and the accumulation of new molecular data on urological cancers.
Material and Methods: The 2022 WHO Classification of Tumors of the Urinary System and Male Genital Organs introduces updates in the classification of urinary tract tumors, offering fresh perspectives on grading heterogeneous non-invasive urothelial neoplasms, defining inverted neoplasms, grading invasive urothelial carcinomas, delineating the diverse morphological appearances of urothelial carcinomas, characterizing precursor lesions, and elucidating tumor lineage differentiation.
Results: Aligned with these advancements, this study aims to assess grading heterogeneity in non-invasive papillary urothelial carcinomas, addressing interobserver variability and proposing standardized diagnostic criteria essential for therapeutic decisions and prognostic accuracy. Following WHO 2022 guidelines, the study evaluates grading consistency in papillary tumors, particularly regarding high-grade component presence. Analysis reveals significant grading heterogeneity, underscoring the necessity for standardized criteria adoption. The proposed categorization of tumors with ≥5% high-grade component as high-grade enhances reproducibility and clinical correlation, aligning with evolving diagnostic paradigms.
Conclusion: Standardizing grading criteria, especially for heterogeneous tumors, is crucial for enhancing interobserver reproducibility and prognostic accuracy, facilitating future diagnostic advancements supported by emerging technologies like machine learning and artificial intelligence.

Keywords: Urothelial neoplasms, grading, papillary tumors, interobserver reproducibility, diagnostic criteria.

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Bland faces of aggressive intestinal lymphomas – report of two cases

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Objective: Gastrointestinal tract (GIT) is the most frequent extranodal localization of non-Hodgkin lymphoma (NHL). However, lymphomas account for only 1-4% of all GIT malignancies. Intestinal lymphomas comprise heterogeneous group of tumors with variable histology, biological behavior, and clinical outcomes. Herein, we present two cases of intestinal lymphomas with quite different clinical and gross presentation, but similar bland, uniform morphology and clinically aggressive course.
Case report: The first case is a 61-year-old gentleman with a family history of colorectal cancer who complains of pain in the lower right abdominal quadrant, slight weight loss (4kg in 4 months), and occasional night sweats. Colonoscopy reveals numerous sessile polyps throughout the terminal ileum and right colon, as well as fungating masses

adjacent to the ileocecal valve and in ascending colon. A biopsy of ileocecal mass was performed and the pathologist subspecialized in GIT pathology delivered a diagnosis of chronic active polypoid colitis with low grade dysplasia. However, because of the compelling endoscopic finding, the gastroenterologist decided to repeat the colonoscopy with a biopsy from the same location. Pathological analysis showed polypoid fragments of colonic mucosa with diffuse monomorphic lymphoid infiltration, and with no lymphoepithelial lesions. Tumor cells were small to medium size, with only slight nuclear pleomorphism and angulation, and scant pale cytoplasm. Immunohistochemically, lymphoid cells expressed CD20, CD79a, CD5, Bcl-2, CyclinD1, and SOX11, while CD3 was negative. Proliferative Ki67 index was 35%. The patient was diagnosed with classic Mantle cell lymphoma (MCL) with a presentation in the form of multiple lymphomatous polyposis. Subsequent gastroscopy found multiple polypoid lesions in the stomach and duodenum, while computed tomography discovered multifocal nodular infiltrates in the lungs and liver, as well as mesenterial and retroperitoneal lymphadenopathy. Bone marrow was unremarkable. At the time of diagnosis, the patient was in clinical stage IV, MIPI 7, ECOG 1. He was treated with 3 cycles of CHOP followed by 3 cycles of DHAP and partial remission was achieved. The patient was not motivated for stem cell transplantation, thus Ibrutinib has been recently introduced.

The second case is a 58-year-old overweight gentleman with a medical history of arterial hypertension and diabetes who was admitted to the emergency hospital with vomiting, a 3-day absence of stool, and acute abdominal pain. The patient had no history of inflammatory bowel disease or celiac disease. Paralytic ileus was suspected, and the patient underwent surgery. Resection of a -long segment of the jejunum was performed. Intraoperatively, a small perforation of the jejunum was found surrounded by a swollen, thickened, rubbery wall. Pathology revealed diffuse monomorphic cellular lymphoid proliferation that expands lamina propria, including the villi cores, and shows transmural propagation. Neoplastic infiltration was composed of small to medium size monotonous ovoid cells, with round nuclei, inconspicuous nucleoli and dispersed chromatin, and pale cytoplasm. Epitheliotropism was also noted. Immunohistochemical stains resulted in diffuse expression of CD3, CD8, CD56, granzyme B, and Bcl-2, while B-cell markers were negative. Proliferative Ki67 index was 80%. In correlation with clinical and radiological findings, the diagnosis of Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) of the jejunum was rendered (clinical stage IV, a, IPI2, ECOG0). Bone marrow was not infiltrated with neoplastic lymphoid cells. Currently, the patient is being treated with the fourth cycle of induction chemotherapy according to CHOEP14 protocol, with a plan for consolidation of the first response with autologous stem cell transplant.

Conclusion: Due to the wide spectrum of clinical presentations, intestinal lymphomas are diagnosed on small endoscopic biopsies, as well as on surgical specimens. Different types of NHL may have similar morphologic appearance, and may imitate indolent lymphoproliferative disorders or inflammatory conditions. Diagnosis of intestinal lymphoma may be quite challenging, especially in cases with bland, uniform morphology that may be overlooked in small biopsies, and requires training and experience in hematopathology.

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Keywords: gastrointestinal tract, immunohistochemistry, intestine, lymphoma, morphology

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Lymphoproliferative pathology - pattern approach

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Objective: Lymphoproliferative neoplasms are heterogeneous group of diseases characterized by uncontrolled clonal lymphocyte proliferation with/without bone marrow (BM) infiltration. Low grade lymphoma patients even with BM infiltration can be followed without treatment, while aggressive lymphoma needs to be treated upon diagnosis.
Case report: A 68-year-old female came to a hematologist complaining of fatigue and early satiety. Splenomegalia, anemia, thrombocytopenia and elevated ESR were present. BM examination revealed hypercellularity, 80-90%, with all three lineages hematopoiesis elements presented. Centromedullary, nodular and partly paratrabecular lymphoid infiltrate was observed, consisted of small and medium lymphoid cells with scanty cytoplasm, round or easily cut nuclei, loose chromatin, small nuclei, making about 50% of the BM cell population. Immunohistochemically, tumor cells expressed CD20, PAX5, CD23, Bcl6, MUM1 and IgM and were negative for CD3, CD5, LEF1, BCL2, CyclinD1, HCL, AnexinA1, CD25, CD11c, IgG, IgD. CD10 was inconclusive. Moderate fibrosis was detected by reticulin staining method (MF2). Findings corresponded to BM infiltration by Non-Hodgkin B-cell lymphoma. Lymph node biopsy was recommended, but there was no significant lymphadenopathy. Differential was diffuse large B-cell lymphoma (DLBCL)/follicular lymphoma grade 3 leading to treatment with R-CHOP.
Conclusion: BM infiltration assessment is important for staging and predicting clinical course, but not optimal for establishing diagnosis of lymphoproliferative neoplasm. Since BM involvement in DLBCL is quite discordant and frequently characterized by small lymphoid cells infiltrate with cleaved nuclear contours admixed with only rare or no large lymphoid cells, so morphologically suggestive for a low-grade lymphoma, close cooperation between pathologist and hematologist is essential.

Keywords: lymphoma; bone marrow; DLBCL;

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Diagnosis-guided treatment of chronic lymphocytic leukemia

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Objective: To determine the profile and frequency of predictive molecular markers in a group of patients diagnosed with chronic lymphocytic leukemia using NGS methodology, with the aim of selecting target therapy.
Introduction: Chronic lymphocytic leukemia (CLL) is a malignancy of mature CD5+ B lymphocytes that is characterized by exceptional clinical and biological heterogeneity. The Rai and Binet staging systems, developed in the late 1970s to early 1980s, are used in clinical practice to stratify CLL patients into risk categories and to help guide clinical follow-up options: to treat or to watch and wait. However, in early-stage disease, these systems are unable to predict what patients will face the progression to a more aggressive disease. Over the years and along with the development of molecular methods, new markers have been recognized that significantly contributed to a better stratification of CII patients. For instance, next-generation sequencing (NGS) studies have led to the discovery of recurrently mutated genes in CLL, such as NOTCH1, SF3B1, BIRC3, XPO1, POT1, NFKBIE and EGR2, that are associated with poor clinical outcome. Nowdays, a number of molecular markers with prognostic and/or predictive impact exist and

their assessment is strongly recommended in all patients prior to treatment initiation.

Material and Methods: During the one-year period (March 2023. - March 2024.) and using NGS technology, 189 patients diagnosed with CII and before the first therapy, were analyzed. The Sophia Genetic panel for CLL, which includes 23 genes and allows identification of the single nucleotide variations (SNVs), Insertions and deletions (InDels) and copy number variations (CNVs), was used. NGS data were compared with fluorescence in situ hybridization (FISH) and cytogenetic results.

Results: Our group includes 189 patients, 47 women and 142 men. The results of NGS analysis showed the presence of variants in 95% of patients, of which 24% had one and 76% had two or more variants. Changes in the number of gene copies were detected in 66% of patients.

TP53 gene mutation was detected in 23.3% of patients, of which 58.6% had the presence of a mutation without previously detected deletion of 17p by the FISH method. When comparing the findings of NGS and FISH methods, a high concordance between single gene mutations and chromosomal aberrations was found. Moreover, Also, markers of poor prognosis (NOTCH1, NFKBIE, SF3B1, POT1, XPO1, BIRC3, EGR2, BTK and PLCG2) were detected with high frequency.

Conclusion: Each patient with CLL may have several clinical and molecular markers of prognostic significance simultaneously, making the precise prognostication challenging.

Today is of the greatest importance to apply ultrasensitive techniques to deterime molecular profile of the CII patients before the first therapy, to reveal relapse after therapy initiation and to detect minimal residual disease after patient achieve complete response.

Keywords: Chronic lymphocytic leukemia, molecular markers, next-generation technology, target therapy

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Adrenal gland pathology: revision of nomenclature and genetic basis

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Objective: The objective of this study is to provide a comprehensive overview of the latest WHO classifications pertaining to tumors originating from the adrenal medulla, extra-adrenal paraganglia, and adrenal cortical proliferations.

Introduction: The World Health Organization (WHO) has recently introduced updated classifications (2022) for various endocrine neoplasms, reflecting significant advancements in understanding and diagnosing these conditions. In this paper, we aim to elucidate the embryonic origins, genetic predispositions, histological characteristics, and diagnostic markers associated with these tumor classifications.

Material and Methods: We conducted a thorough review of the literature to compile information regarding the classifications of tumors of the adrenal medulla, extra-adrenal paraganglia, and adrenal cortical proliferations as outlined by the WHO. This included an analysis of embryonic derivation, genetic predispositions, histological features, and diagnostic biomarkers associated with these tumors.

Results: Our review revealed that paragangliomas, comprising sympathetic and parasympathetic variants, represent a distinct subset of neuroendocrine neoplasms characterized by catecholamine secretion and genetic susceptibility. Diagnostic methodologies outlined in the WHO classification include specific biomarkers such as GATA3 and enzymes involved in catecholamine synthesis. Additionally, the classification of adrenal cortical proliferations encompasses a spectrum of pathologies, with refined classifications of nodular diseases and subtyping of carcinomas based on morphological attributes. Diagnostic algorithms and biomarkers such as SF1 and paranuclear IGF2 expression aid in precise diagnosis and prognosis assessment.

Conclusion: The updated WHO classifications provide valuable insights into the diagnosis and management of tumors originating from the adrenal medulla, extra-adrenal paraganglia, and adrenal cortical proliferations. This classification facilitates a more precise approach to diagnosis and prognosis assessment. This synthesis serves as a practical

resource for multidisciplinary endocrine oncology teams, offering the latest methodologies consistent with the 2022 WHO classifications.

Keywords: Paraganglioma, Pheochromocytoma, Adrenal cortical adenoma , Adrenal cortical carcinoma, Adrenal cortical hyperplasia

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Diseases of the parathyroid glands /WHO 2022/ - understanding of the basic pathogenetic mechanism

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Objective: The 2022 updates to parathyroid disease classification reflect new insights into their genetics and pathology, aiding specialists in improving diagnosis, treatment, and research, thus enhancing patient care and understanding of these conditions.

Introduction: The World Health Organization's (WHO) latest classification acknowledges the genetic and molecular heterogeneity of parathyroid lesions, offering a more nuanced approach to their categorization.

Material and Methods: The updates distinguish between various types of parathyroid adenomas, hyperplasias, and carcinomas, emphasizing the importance of genetic profiling in the differentiation of these conditions.

Results: Parathyroid adenomas, the most common cause of primary hyperparathyroidism, are now classified based on their genetic mutations, such as those involving the MEN1, CDC73, and CASR genes. This genetic lens aids in understanding their behavior, recurrence risk, and familial patterns. Hyperplasia of the parathyroid glands, often linked to secondary or tertiary hyperparathyroidism, has been redefined with a focus on the underlying pathophysiological mechanisms, such as those related to chronic kidney disease. Parathyroid carcinoma, a rare but aggressive form, is now better defined, with criteria that distinguish it from atypical adenomas and hyperplasias. The pattern of growth/invasion and molecular markers, such as parafibromin, Ki-67, galectin-3, PGP9.5, and Rb protein, are crucial to differentiate benign from malignant parathyroid tumors.

Conclusion: These updates facilitate a more precise and personalized approach to diagnosing and treating parathyroid diseases, underscoring the shift towards molecular and genetic factors in medical taxonomy. This new classification is a testament to the evolving understanding of parathyroid pathology, promising improved patient outcomes through tailored therapeutic strategies.

Keywords: WHO 2022, parathyroid glands, adenoma, carcinoma, hyperplasia

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Do not throw away the placenta - the importance of its histopathological analysis

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Objective: "Placenta pathology provides an autopsy of the pregnancy." The true nature of this statement is obvious knowing that the placenta is a part of the foeto-placental unit during intrauterine development and that in most pregnancies with adverse outcome there is some form/degree of abnormal function and/or histomorphology of the placental tissue. Earlier studies have shown that the quality of placenta investigation and the clinical usefulness of the final report – as prerequisites of our understanding what went wrong during that particular pregnancy - are hugely variable, especially when the report is not produced by qualified experts (perinatal or paediatric pathologists). This presentation intends: 1) to analyse the number of factors (i.e., clinical, pathological and other) which have impact on the quality of the final placenta report (which is a teamwork!) and, 2) how to create an efficient pathway of placenta investigation in practice. Our recent, better understanding of the pathophysiology of placenta and function, and the identification of numerous 'patterns' of histological changes in the placental tissue often associated with some of the well-defined obstetric syndromes (like premature deliver, intrauterine growth restriction, preeclampsia, maternal diabetes, stillbirth) improved both our diagnostic skills and

the ability to put those findings into a clinical context, and to create a meaningful clinico-pathological correlation. With this end product the pathologist offers the users better understanding of the reason and mechanism by which certain pregnancies had problems or adverse outcome.

Case report: Factors contributing to the quality of the pathological investigation of placenta can be divided into two rough categories. One is the clinicians' ability: i) to select appropriate placentas for investigation (defined by maternal. foetal and placental criteria), ii) to supply relevant clinical information to the pathologist; iii) to send selected placentas to appropriate experts, in a timely manner. The other group of factors relate to the pathologists' activity and consists of their: i) full awareness of 'normal' histology in developing placenta during pregnancy; ii) insight into the basics of related clinical disciplines (i.e., obstetrics, perinatology, etc.,) iii) knowledge about both naked eye & microscopic changes in placenta; iv) awareness of the interaction, correlation and clinical significance of these lesions; v) ability to use the most recent, standardised nomenclature/terminology; vi) to produce a comprehensive report with description relevant lesions, diagnoses and putting those findings into a clinical context, creating a meaningful clinico-pathological correlation, securing high level of clinical usefulness of the report, which is the ultimate purpose of the placental investigation.

Conclusion: Attention will also be given to microscopic diagnostic features of selected placental lesions/entities of particular clinical significance, including: Ascending Infections (Maternal & Foetal Inflammatory Responses), Villitis of Unknown Etiology/VUE, Histiocytic Intervillositis, Maternal Floor Infarct/Massive Perivillous Fibrin Deposition/MPFD, Villous Maturation Disorders (both Accelerated & Delayed), Maternal & Foetal Vascular Malperfusions/MVM &FVM, etc.,

Suggestions will also be given for a design of an efficient pathway for high quality pathological investigation of placenta and clinical usefulness, with short turnaround time, supporting the users needs.

Keywords: Placenta investigation, perinatal pathology, clinico-pathological correlation

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Cytological analysis of follicular thyroid lesions - old and new bethesda classification

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Introduction: Fine needle aspiration (FNA) of thyroid nodules and cytomorphologic examination of obtained material is the essential tool in evaluation non-neoplastic and neoplastic proliferations and considered as fast, reliable and minimally risky procedure in the diagnosis and treatment of thyroid gland lesions.

The first two editions of the Bethesda system for the interpretation of cytopathological findings of changes in the thyroid gland (The Bethesda System for Reporting Thyroid Cytopathology -TBSRTC) , published in 2010 and 2017, has allowed cytopathologist to use standardized, category based reporting system for thyroid fine needle aspirations based on cytomorphological findings, provided a a guide for clinicians to treat patients and presented the risk of malignancy (ROM) for each category based on clinical follow-up and pathological findings of surgical materials that were published in papers.

The third edition of the Bethesda system, published in 2023, standardizes the new, clearly explained names for six diagnostic categories: (I) nondiagnostic; (II) benign; (III) atypia of undetermined significance, nuclear/architectural atypia; (IV) follicular neoplasm; (V) suspicious for malignancy; and (VI) malignant. In relation to the previous edition, they were eliminated alternative designation in three categories: "unsatisfactory specimen" (belonged to Bethesda I), "follicular lesion of undetermined significance - FLUS (belonged to Bethesda III) and "suspicious of follicular neoplasm" (belonged to Bethesda IV). For each of the six diagnostic categories, the "risk of malignancy" (ROM) was revised based on data from published studies, which was derived from the surgical pathology follow-up reported after the second edition TBSRTC. The new edition presents ranges for the ROM for each diagnostic category with and without non-invasive follicular thyroid neoplasm with papillary-like nuclear fea-

tures (NIFTP), as the low-risk neoplasm is a surgical diagnosis and cannot be diagnosed based on cytomorphology. Using new TBSRTC terminology and recommendation that all thyroid FNAC reports begin with the name of a diagnostic category followed by the category number, cytopathologists can effectively, concisely, unambiguously guide clinicians in the management of a patient (clinical follow-up, repeat FNA, molecular testing, surgery).

Nomenclature has been updated to align with the 2022 World health Organization Classification Of Thyroid Neoplasms. Regarding the previous term "follicular neoplasm, Hurthle cell type" recommends "follicular neoplasm-oncocytic follicular neoplasm". The term "papillary thyroid carcinoma variants is now changed to "papillary thyroid carcinoma, subtypes". The previously recognized "cribriform morular variant of papillary thyroid carcinoma" is now designated as a separate tumor entity. The older nomenclature of "poorly differentiated thyroid carcinoma" has been replaced with new term "high-grade follicular-derived thyroid carcinoma".

The latest TBSRTC introducing new separate chapters addressing clinical perspectives related to radiologic findings and molecular diagnosis, and reporting of thyroid FNA in pediatric population with estimates for ROM and recommendation for clinical management.

Conclusions: This classification, like the previous two, by introducing standardized reporting formats for thyroid FNAC specimens and ROM monitoring will allow comparisons in practice between different institutions and create the basis for a multitude of research publications focused on thyroid nodules and contribute to consider another review of the TBSRTC.

Keywords: Fine needle aspiration cytology; Thyroid gland; Bethesda system; WHO classification

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A rare mesenchymal tumor of the lung

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A solitary fibrous tumour (SFT) is a rare, slow-growing, mesenchymal neoplasms initially described in the pleura but have since been discovered in nearly every anatomic location. Klemperer and Rabin reported 5 cases of primary pleural neoplasms in 1931 and proposed that SFT was of submesothelial origin. However, in the subsequent decades, on the basis of immunohistochemical analyses and ultrastructural features, it is now recognized that SFTs arise from primitive fibroblast-like cells in connective tissue. The development of intrapulmonary SFT may be attributed to the direct continuity between the subpleural mesenchyme and interlobular septa or the presence of lung fibroblasts in the submesothelial areas of normal pulmonary parenchyma. SFTs most often occur in the pleura, but over the past 90 years, these tumors have been identified in numerous extrapleural locations. SFTs are extremely rare in the lung. To date, about 50 cases of intrapulmonary SFT have been reported in the English language literature.

Intrapulmonary SFTs are usually found incidentally and may be associated with chest pain and cough. Sometimes, patients with SFTs present with refractory hypoglycaemia, which is a paraneoplastic syndrome that secretes a prohormone form of insulin-like growth factor-II (IGF-II). Due to their atypical clinical and radiographic appearance as a common lung tumour, the diagnosis of intrapulmonary SFTs presents unique challenges. Imaging examinations, including chest X-rays, CT and MRI showed that intrapulmonary SFTs are well-defined ovoid or round pulmonary nodules.

Histologically, spindle-shaped cells, patternless and hemangiopericytic growth with variably fibrosis and collagenous deposits are characteristic, but SFTs can show many

faces, including round cells, giant-cells, myxoid areas, pleomorphic pattern, fat-forming tumors and dedifferentiated forms. Aberrant epithelial, muscular or neuroendocrine marker expression has been described which may lead to confusion with other tumors that share a similar morphology. For that reason, the diagnosis of SFTs may not be confirmed without immunohistochemical staining. The most valuable immunohistochemical marker in the diagnosis of SFTs is STAT6. However, STAT6 expression has also been reported in dedifferentiated liposarcoma and GLI1-amplified tumors, hence, in cases with overlapping morphology and STAT6 immunoreactivity, additional molecular studies are needed to establish a definitive diagnosis. On a molecular level, SFTs have been shown to be pathogenetically linked to a gene fusion secondary to a paracentric inversion on chromosome 12q13 and involves NAB2 and STAT6, which are highly sensitive and specific markers for SFT.

According to the WHO classification, the prediction of metastatic risk in SFTs are follows: (1) patient age in years (≥ 55); (2) mitoses per 10 high-power fields; (3) tumor size in cm, and (4) tumor necrosis. Although multiple factors, such as age and tumor size, have been associated with survival, higher histologic grade has been considered to have the strongest correlation with prognosis.

Complete resection with free margins is considered the treatment for intrapulmonary SFT. Adequate wedge resection, anatomic segmentectomy, and lobectomy, depending on the location of the mass, are the common procedures for surgical resection of intrapulmonary tumors. Careful follow-up of the postoperative course is important, even in cases hisologically diagnosed as low metastatic risk.

Keywords: intrapulmonary solitary fibrous tumor; STAT6; risk stratification systems

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Diagnostics of differentiated high-grade thyroid carcinoma

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Background & Objective: In the 5th edition of the World Health Organization (WHO), the histologic classification of thyroid tumors originating from follicular cells divides them into benign, low-risk, and malignant neoplasms (1,2). Several changes were introduced regarding terminological issues that reflect the molecular basis of lesions. For example, the term "follicular nodular disease" is introduced to account for multifocal hyperplastic/neoplastic lesions, and morphologically different papillary thyroid carcinomas (PTC) were designed as „subtypes" irrespective of tumor size instead of „variants". The term variant is reserved to describe lesions with distinctive genetic alterations such as invasive encapsulated follicular variant PTC. These changes do not reflect modifications in the diagnostic criteria, and they are not expected to have clinical significance (1-3). The main changes introduced by the latest WHO edition are related to the introduction of a grading scheme for the characterization of differentiated carcinomas. Accordingly, the presence of tumor necrosis and high mitotic count in the PTCs, follicular thyroid carcinomas and oncocytic carcinomas defined them as differentiated high-grade thyroid carcinomas (DHGTC). DHGTC together with poorly differentiated thyroid carcinoma (PDTC) determined according to Turine consensus, comprises a group of follicular-derived carcinomas with high-grade features, aggressive biological behavior and intermediated risk between well-differentiated

thyroid carcinomas and anaplastic carcinoma (1-4). The work aims to present the main clinicopathological characteristics of DHGTC with a literary review, as well as to present a diagnostics approach and results from our Institute.

General Features: DHGTCs account for less than 5% of primary thyroid malignancies, reported together with PDTC in the range between <1% to 6%. They occur in older age, usually over age 50 with a slight female predominance. Tumors are often larger than 4 cm and develop as rapidly growing masses with widely invasive growth, angioinvasion, gross extrathyroid extension and early development of lymph node metastases (2,4). Five-year disease-specific survival and 5-year overall survival, of DHGTC are similar to PDTC and are approximately 66% and 60%, respectively (2,4-6). The treatment includes a total thyroidectomy with central and possible lateral neck dissection and additional radioactive iodine therapy (4).

Pathology: Grossly, DHGTCs disclose invasive borders, or rarely tumors are circumscribed, partially or completely encapsulated. On cross-sections, tumors are often firm, solid, and white-tan or pink-tan. Necrosis and hemorrhage could be seen. To confirm the invasiveness of circumscribed and/or encapsulated tumors, extensive or total tumor capsule sampling should be done. For grossly invasive lesions at least one section per 1 cm of tumor tissue is required. Necrosis, hemorrhage, or areas of unusual appearance must be processed. For accurate diagnosis in microscopically insufficient cases, additional sections may be required. Staging of disease sometimes warrants correlation with clinical/surgical findings (2,4).

Histologically, the diagnostic criteria of PDTC have not been modified. According to the Turin criteria, adopted also by the last two WHO classifications, PDTC has a solid, trabecular and/or insular growth pattern, absence of the conventional nuclear features of PTC, and at least one of the following characteristics: convoluted nuclei, ≥3 mitosis per 10 high-power fields/~2 mm2, and tumor necrosis (1, 7). In cases when the morphological dedifferentiation is absent and tumors retain an architectural and/or cytological pattern of PTC, follicular or oncocytic carcinoma with the presence of necrosis and/or ≥5 mitoses per 2 mm2, the tumor should be diagnosed as DHGTC (1-4). Tumor necrosis is coagulative or comedotype and contains identifiable nuclear debris. Individual cell necrosis scattered throughout the tumor is a feature of PDTC/ DHGTC (2,4). Pathologic high-grade features may also be identified in subcentimeter tumors as well as in non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). In addition, poorly differentiated areas can be present as a minor component of DHGTC. In all these instances, the proportion of these components needs to be reported. In the pathological report, all the tumor components and their pathological characteristics should be described (2,3). Progression of well-differentiated tumors to poorly differentiated/high-grade morphology may be found in local or distant metastasis. Both DHGTC and PDTC should not have more than moderate nuclear pleomorphism, a useful feature for distinguishing them from anaplastic thyroid carcinoma. In the differential diagnosis, DHGTC needs to be separated from PDTC, well-differentiated carcinomas of follicular cell-derivation, most commonly solid subtype of PTC or carcinomas with necrosis induced by fine needle aspiration biopsy. Differentiation from medullary thyroid carcinomas with mitotic activity and tumor necrosis could be the most difficult and additional immunostaining must be done (2-4,8). DHGTC are positive for TTF1, PAX8, cytokeratin 7, and thyroglobulin. Thyroglobulin tends to be weak and focal with a dot-like appearance. Neuroendocrine markers and calcitonin are negative. The Ki67 proliferation index is elevated, usually in the range of 10 to 30% (2,4). Regarding molecular basis, the vast majority of DHGTC are enriched with V600EBRAF mutations, most display the cytoarchitectural features of PTC and have a propensity for cervical lymph node metastases. In contrast, PDTC have a higher prevalence of RAS mutations and are more prone to spread distantly. Additionally, DHGTC and PDTC commonly carry secondary mutations related to their aggressiveness, most frequently mutation of the TERT promoter or mutation of PIK3CA and TP53 (2-4,8).

Conclusion: The 5th WHO edition defined DHGTC, as a new entity that includes any differentiated thyroid carcinoma showing ≥5 mitoses per 2mm2 and/or tumor necrosis. New classification required more accurate histological characterization of differentiated carcinoma, specifically regarding the presence of mitosis and microscopic foci of necrosis. This approach shows a need for more extensive tissue sampling. The true incidence and clinical impact of DHGTC are yet to be established.

Keywords: WHO classification, Thyroid cancer, High-grade differentiated, Nomenclature

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What is new in the "Blue Book" of Urinary and Male Genital Tumors

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The classifications of benign pathological conditions and tumors represent a unique language that facilitates communication, both among pathologists and with clinicians. The fifth, revised classification of tumors of the urogenital system of the World Health Organization was issued in 2022. The current classification has many more chapters, since next are separated as new: tumors of the seminal vesicles, testicular adnexa, neuroendocrine neoplasms, metastatic, hematological, soft tissue tumors, melanocytic lesions and genetic tumor syndromes. Introductory chapters have been added: topographical and morphological coding of tumors, as well as TNM staging of tumors, which in the previous edition were at the beginning of each organ chapter. Nomenclature changes are noticeable: instead of „variant", the name "subtypes" is used, and the tumor names have been renamed to the following: "clear cell renal cell carcinoma" to "clear cell renal cell tumor", "TCEB1-mutated renal cell carcinoma (RCC)" to "ELOC"-mutated RCC", hereditary leiomyomatosis and renal cell carcinoma" in "fumarate hydratase-deficient RCC", "RCC Unclassified" in "RCC-Not Other Specified". In the group of kidney tumors, the division into type 1 and 2 papillary RCC was eliminated, the entity oncocytoma/chromophobe RCC-like features was also added, and "Eosinophilic solid and cystic RCC" was highlighted as a separate entity. It is recommended that the WHO/ISUP grade be applied to all RCCs. The current classification emphasizes the important connection of molecular tests in the framework of the pathological diagnosis of kidney tumors, and the chapter "Molecularly defined renal carcinomas" is highlighted. In the group of urothelial tumors, each tumor type is presented chronologically from benign to malignant development. The possible application of a classification based on the molecular characteristics of tumors in the near future is suggested. Grading for non-invasive urothelial carcinoma is high grade if the high-grade component is present in ≥5%, the application of The Paris System for cytological diagnosis of urine is also recommended, and special attention is also paid to inverted tumors. In the chapter on prostate cancer, the nomenclature has been changed from "basal cell carcinoma of the prostate" to "adenoid-cystic (basal-cell) carcinoma of the prostate" and the need to note intraductal carcinoma of the prostate IDC-P is emphasized, and it is emphasized that Prostatic intraepithelial neoplasia (PIN)-like carcinoma is not the same as ductal carcinoma. Special attention is paid to the grading of acinar adenocarcinoma and the prognostic significance of cribriform cancer growth. In the group of testicular tumors, new entities stand out: Signet ring stromal tumor and Myoid gonadal stromal tumor, with a change in the nomenclature "Well-differentiated neuroendocrine tumor (monodermal teratoma)" to "Testicular neuroendocrine tumor, prepubertal type", as well as "carcinoid" to "neuroendocrine tumor". The criteria for the diagnosis of "Teratoma with somatic transformation" have been changed, while in the group of sex-cord stromal tumors, mitoses are counted per mm2, instead of the high-power field. For Well-differentiated papillary mesothelial tumor, it was pointed out that the prognosis is good. In the penile tumor group, the nomenclature was changed from "subtypes" to "patterns". When a second component is observed in addition to the Usual type of invasive squamous cell carcinoma, the tumor is marked as mixed, while the term hybrid is omitted, with a note that it is useful to state the % of individual components. For the first time, a separate classification of scrotal tumors is present-

ed. Each classification highlights new entities that enable more precise pathohistological diagnosis and, in the spirit of modern medicine, along with molecular tests, they often represent a prerequisite for personalized therapy, which is a step forward in the fight against disease.

Keywords: WHO tumor classification; kidney; urinary bladder; prostate; testicle; penis; molecular analyses;

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Renal carcinoma with unusual morphological characteristics

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Renal cell carcinoma (RCC) is the most common kidney tumor, which despite the development of new diagnostic procedures and new therapeutic modalities is still the most lethal urologic malignancy. RCC subtypes show different genetic abnormalities, phenotypic characteristics, different biological behavior, which has significant implications on prognosis and therapeutic approach. The main morphologic feature of the RCC may be the presence of clear cytoplasm, papillary architecture or eosinophilic cytoplasm, which may be helpful in routine practice during diagnostics RCC with unusual morphologic features. RCC with clear cytoplasm include clear cell RCC (ccRCC) which may have a poor prognosis, while multilocular cystic renal neoplasm of low malignant potential and clear cell papillary RCC are tumors with indolent clinical course. Translocational RCC may exhibit different molecular changes compared to ccRCC and therefore sometimes do not respond to conventional targeted therapy used in ccRCC. Papillary architecture in RCC is not only a characteristic of papillary RCC (pRCC), but this growth pattern is present in different entities with different morphology, molecular alterations and clinical outcome. Mucinous tubular and spindle cell carcinoma is a rare subtype of RCC, which can show significant morphologic and immunophenotypic overlap with type 1 pRCC, with a typically indolent clinical course. On the other hand, hereditary leiomyomatosis and RCC (HLRCC) has morphological and immunophenotypic overlap with pRCC type 2. Also RCC arising in kidneys with acquired cystic disease and end stage renal disease can show papillary architecture with eosinophilic/clear cells, and it has an indolent course. Collecting duct carcinoma is aggressive tumor, which in some cases shows papillary and micropapillary growth. Although RCC with eosinophilic cytoplasm is a characteristic of chromophobe RCC, it can also be seen in succinate dehydrogenase deficient RCC, tubulocystic RCC, thyroid-like follicular carcinoma of the kidney, and RCC associated with neuroblastoma. Several subtypes of RCC can show morphological overlaps and the key in the diagnostic procedure is the recognition of the conventional component in the tumor, the application of immunohistochemical staining and, if necessary, the analysis of the entire tumor tissue and/or clinicopathological correlation.

Keywords: Morphology, Renal carcinoma, Prognosis, Subtypes

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Acknowledgements: This work is financed by the Science Fund of the Republic of Serbia (IDEAS), project number: 7750154 (NPATPETTMP-CB).

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Morphological parameters of aggressiveness in prostate cancer

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Prostate cancer, the most common cancer in Western men, is an illness with a diverse clinlcal presentation, histopathological tumor growth patterns and survival. Recent statistics for 2023. year estimates prostate cancer as number one for new cases and second for mortality in USA. Most tumors do not cause significant clinical symptoms, but there is a certain number of patients where prostate cancer takes an aggressive course. So, individual assessment of a tumor's aggressiveness is critical for clinical decision-making in therapy of prostate cancer. In every day practice, age, elevated serum PSA levels, suspicious digital rectal examination or trans-rectal ultrasonography are reasons enough for performing a needle biopsy of a prostate. Precise histopathological report must include Gleason score, presence of Gleason grade 4 and 5, perineural invasion, specific variants of prostate cancer (intraductal carcinoma, ductal adenocarcinoma, signet cell-like carcinoma, pleomorphic giant cell carcinoma, sarcomatoid carcinoma) and tumor volume both on needle biopsy and radical prostatectomy. By reporting needle biopsy and radical prostatectomy specimen in this way we help clinicians to choose the best therapeutic approach for each patient.This lecture serves as a comprehensive review and reiteration of morphological indicators pertaining to the aggressiveness of prostate cancer, alongside an elucidation of actual protocol advancements. Implementation of novel histopathological markers is required for individual assement of a tumor's aggressive potential and by that helping to reduce prostate cancer specific mortality and avoiding overtreatment.

Keywords: Gleason grade system, Morphology, Prostate cancer, Perinural invasion

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Kidney tumors with granular-oncocytic cytoplasm

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Kidney tumors with granular-oncocytic, eosinophilic cytoplasmic cells include a wide range of kidney lesions with different and very specific morphological, immunohistochemical and molecular genetic characteristics.. Regardless of all the above, they can have morphological overlaps and represent a real diagnostic challenge in the daily work of pathologists, regardless of whether whether it is a pathohistological analysis of material after partial and total nephrectomy or/ and a kidney tumor biopsy. In its latest classification of tumors of the kidney and male genital organs from 2022, the WHO even singles out a special subgroup of epithelial renal tumors, the so-called oncocytic and chromophobe renal tumors, which includes already well-known neoplasms, such as renal oncocytoma, chromophobe kidney carcinoma and tumors associated with "Birt-Hogg-Dube" syndrome (hybrid oncocytic tumors/HOT), but also completely new entities, such as "eosinophilic vacuolated tumor (EVT)" and "low-grade oncocytic tumor" (LOT). Of course, depending on the histological picture of the kidney tumor, one should think about other neoplasms of granulated-oncocytic cytoplasm, which are not part of this subgroup of renal epithelial tumors: "oncocytic papillary renal neoplasm with reverse polarity, succinate dehydrogenase deficient renal cell carcinoma, translocation-associated renal cell carcinoma, eosinophilic solid and cystic renal cell carcinoma, high grade clear cell renal cell carcinoma, acquired cystic disease-associated renal cell carcinoma, epithelioid angiomyolipoma (E-AML)/ epithelioid PEComa of the kidney (E-PEComa)" etc. Precise pathohistological typing of these tumors is necessary considering the differences in biological behavior from benign to malignant with indolent but also very aggressive.

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Role of oncogene-induced cellular senescence in malignant transformation and progression of breast tumors

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Despite the importance of certain prognostic factors, their accuracy in assessing outcomes and determining treatment strategies for breast cancer patients is limited. Therefore, the definition of new molecular biomarkers could provide a more reliable approach for prediction of the prognosis of this disease.

The aim of this study was to examine the expression of markers p16, p53, p21, pRb and GLB1 in benign and malignant breast changes, as well as their participation in malignant transformation.

The research included the analysis of tissue material of benign and malignant changes in patients operated at the University Clinical Center Kragujevac. All macro and micromorphological prognostic factors (histological type and grade of tumor, size, nodal status, desmoplasia, necrosis, mononuclear reaction, etc.) were defined on H&E stained preparations. Immunohistochemically, using antibodies (p16, p53, p21, pRb, GLB1) tissue expression of markers were determined by a semiquantitative reading of a positive reaction. By defining cut-off values, cancers were classified into positive and negative groups for each analyzed marker. The expression of all markers increased with the progression of cytological changes in the epithelium. Their ex-

pression positively correlated with various changes in the breast, with the proliferative index and HER2+ tumors. The expression of p16, pRb, p21, GLB1 is the highest in HER2+ breast cancers, while the expression of p53 is the highest in TNBC. A significant correlation was found between the expression of p16 and p53, p21 and pRb, p21 and GLB1, as well as between pRb and GLB1 in invasive cancer.
The analyzed markers play an important role in proliferation, malignant transformation, as well as in the progression of breast cancer, which recommends them for further research and possible use for diagnostic, prognostic and predictive purposes.

Keywords: breast cancer; cellular senescence; cyclin-dependent kinase inhibitor p16; tumor suppressor protein p53; cyclin-dependent kinase inhibitor p21; retinoblastoma protein.

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Depression and anxiety association with neurokinin receptor expression in women with breast cancer

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Breast cancer (BC) remains a pressing global problem, both in terms of incidence and mortality. In recent years, efforts have been made to define new molecular and signaling pathways involved in the pathogenesis of BC, in order to obtain a more complete and clearer picture in terms of predicting the prognosis and the effectiveness of the applied therapy.The aim of this research is to examine the relationship between anxiety and depression with the expression of neurokinin receptors (NKR) in breast cancer, as well as their possible relationship with clinical, pathohistological, and immunophenotypic characteristics of the tumor.
The research involved filling out questionnaires for self-assessment of depression/anxiety of the affected women, as well as a complete pathohistological analysis of the patient's tissue material. All significant morphological parameters of BC were defined on the standard stained preparations. Immunohistochemically, tissue expression of relevant markers was determined using antibodies (NKR, VEGF, CD105, Ki67, and caspase-3). Two groups of women were defined, with and without a present depressive/anxiety disorder, as well as existing differences in terms of clinical and histopathological characteristics.
Among the examined women, a significant number of those with a certain degree of depression/anxiety were found. The expression of NKR was positively correlated with a significant degree of depression and with the expression of significant predictors of cancer behavior such as the proliferative index marker Ki67, tumor angiogenesis markers VEGF and CD105, as well as the apoptosis marker caspase-3.
It has been unequivocally shown that the comorbidity of BC and depression is significant from a clinical point of view, that there are interwoven molecular mechanisms, the more detailed understanding of which would help in the field of discovering new therapeutic procedures that would act in a targeted manner in preventing tumor growth and invasion.

Keywords: breast cancer; depression; anxiety; carcinogenesis; angiogenesis; metastasis; neurokinin receptor NKR.

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Molecular markers of prostate cancer aggressiveness

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Prostate adenocarcinoma is the most common malignancy of the prostate gland that originates from prostatic secretory epithelium. The pathological diagnosis of prostatic adenocarcinoma is primarily based on histological features. The fifth WHO edition classifies prostatic glandular neoplasms as prostatic cystadenoma, high-grade prostatic intraepithelial neoplasia, intraductal carcinoma of the prostate, acinar adenocarcinoma, ductal adenocarcinoma and treatment-related neuroendocrine prostatic carcinoma. Subtypes of prostate adenocarcinoma are acinar, ductal, atrophic, pseudohyperplastic, microcystic, foamy gland, mucinous, signet ring subtype, pleomorphic giant cell ad-

enocarcinoma and sarcomatoid adenocarcinoma. More important for assessing tumor aggressiveness is morphological pattern presented through Gleason score. Regardless the subtype and Gleason pattern, the vast majority of prostatic adenocarcinomas express prostate specific antigen (PSA). It should be emphasized that up to 15% cancers with high grade features are completely negative for PSA by immunohistochemistry (IHC).

Tissue-based molecular biomarkers for prostate cancer diagnosis include PTEN IHC for intraductal carcinoma of the prostate, PIN-4 cocktail and ERG IHC for atypical small acinar proliferation (ASAP), RB1 and cyclin D1 IHC for neuroendocrine prostate cancer. Tissue-based diagnostic biomarker (Confirm MDx) is a DNA methylation assay that is prostate tissue biopsy based, and evaluates the methylation status of several genes known to be frequently found in prostate cancer. These markers have been demonstrated to have a "field effect", meaning that the test should be performed for management of men with elevated PSA and a cancer-negative prostate biopsy. It is included in the European Association of Urology (EAU) and NCCN 2020 guidelines for repeat biopsy decision making, for PIRADS 4 and 5 lesions on MRI (1). Molecular biomarkers for aggressive prostate cancer–targeted therapy include AR-V7 transcripts (androgen receptor signaling), somatic mutations, PTEN alterations, and gene fusions (recurrent molecular alterations), DNA repair mutations (PARP1 inhibition), and PDL1 IHC (immunotherapy). Loss of PTEN function can be detected via FISH or IHC and is associated with Gleason score upgrading, locally advanced disease, decreased recurrence-free survival and poor clinical outcome (2). The latest data reveals that germline or somatic alterations in DNA repair genes are present in as many as 20% of aggressive primary and metastatic prostatic carcinomas. BRCA1/2 mutations increase risk by 5-fold, BRCA1/2 associated cancers occur at a lower age, have worse survival outcomes, and are likely to respond to PARP1 inhibition, whereas patients with DNA mismatch repair-deficient cancers are offered immune checkpoint inhibitors. The presence of intraductal carcinoma and/or cribriform architecture (Gleason pattern 4) has been shown by some to be associated with a higher incidence of inherited germline alterations in DNA repair genes. There is a recommendation to do germline genetic testing in all patients with Gleason pattern 4 (3). It remains to be seen whether such an expensive approach will enter clinical practice.

Molecular regulator proteins of cell cycle, such as p53, Bcl-2, Ki-67, EZH2, CXCL12/CXCR4, allow the assessment of tumor growth, local invasion, distant metastases, and provide additional knowledge of aggressivity compared to standard markers. HIF-1 overexpression correlates with tumor aggressiveness and chemoresistance. HIF-targeting agents in combination with androgen receptor targeting, synergistically inhibits castration-resistant prostate cancer cells (4). Hypoxia, via HIF signaling can activate angiogenesis, enhance invasiveness and metastatic potential, and induce cancer stem cells (CSC) features. Recent studies have indicated that CSC have a key role in cancer development and progression by stimulating proliferation of metastatic clones resistant to apoptosis. Already established, prostate CSC (CD117, CD133, CD44, NF-kB) play key role in tumor initiation and development, disease progression, recurrence and metastasis, can modify the effect of chemotherapy and are important markers in assessment of prostate cancer aggressivity (5). Hypoxia leads to membranous NOTCH3 expression, which in turn, sustains proliferation of cancer cells. NOTCH3 pathway represents a promising target for adjuvant therapy in patients with radio/chemo resistant prostate cancer (6).

Everything summarized in this short review is recently discovered and leads to molecular approach in prostate cancer treatment.

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Prenatally diagnosed congenital malformations and fetal autopsy – a series of case reports

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Objectiv: To emphasize the importance of adhering to the fetal autopsy protocol in the evaluation of prenatally diagnosed congenital malformations through the presentation of several autopsy analyses.
Introduction: In modern fetal and perinatal pathology, it is essential to adhere to the modern protocol of autopsy analysis of the fetal phenotype and to use molecular diagnostic analyses as often as possible in accordance with the capacities of the health care system in developing countries.
Methods: Presentation of several fetal autopsy analyses in cases of prenatally suspected congenital malformations.
Results: Three fetal autopsies that followed prenatally diagnosed suspected congenital malformations are presented: Pierre-Robin sequence, Otopalatodigital syndrome type I, Megacystis microcolon intestinal hypoperistalsis syndrome.
Conclusion: Even in the circumstances of limited financial possibilities of the health care system and limited opportunities for education in specific areas of medicine, it is possible to perform analyses based on principles close to the requirements of modern medicine. Adherence to the fetal autopsy protocol with the special importance of photo-documentation and the increasingly frequent use of modern genomic analysis is of great importance in family planning.

Keywords: fetal autopsy, molecular diagnosis, congenital malformation, prenatal diagnosis

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Fetal growth restriction in stillbirths devoid of structural or genetic abnormalities

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Objective: This study aims to provide practical guidelines for detecting and estimating fetal growth restriction (FGR), as well as identifying its underlying causes, during routine perinatal post-mortem examinations.
Introduction: FGR is a pregnancy complication that represents a substantial cause of stillbirth, neonatal morbidity, and mortality. It is the result of one or more maternal, placental and fetal disorders.
Material and Methods: A retrospective review was conducted on all perinatal autopsies performed at the University Clinical Centre of Serbia, spanning from January 1, 2020, to December 31, 2023. This study analyzed a total of 331 stillbirths and neonates whose deaths occurred after 20 completed weeks of gestation but before the first 7 completed days of life. Assessment of fetal growth restriction (FGR) was limited to singleton pregnancies.
Results: By utilizing birth weight for gestational age below the 10th percentile and a brain to liver weight ratio greater than 4, we identified 68 cases (20.5%) at or beyond 20 weeks of gestation as fetal growth restriction (FGR), while 43 cases (12.9%) at or beyond 24 weeks of gestation were classified as FGR. The cause of FGR remained unclear in 4 out of 68 cases (5.8%).
Conclusion: Fetal and neonatal autopsy provides invaluable insights into the cause of death and underlying disease processes, offering crucial guidance for subsequent pregnancies to physicians. Consequently, pathologists must meticulously investigate the causes of stillbirth and fetal growth restriction, taking into account factors related to the placenta, fetus/neonate, and maternal health.

Keywords: fetal growth restriction, stillbirth,

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Mucoepidermoid carcinoma of the hard palate in a 9-year-old boy: Case report

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Introduction: Tumors of the salivary glands in children are rare, and when they appear, there is a high probability that they are malignant. Mucoepidermoid carcinoma (MEC) is the most common malignant tumor of the salivary glands diagnosed in children and young adults, with a peak incidence in the second decade of life. It is made up of solid and cystically arranged mucinous, intermediate (bright cells), and squamoid tumor cells, and the most common localization is on the palate.

Aim: We present the case of a nine-year-old boy diagnosed with primary MEC of the hard palate. We would like to highlight the importance of timely diagnosis of MEC in the pediatric population and the criteria for differentiation from other neoplastic and non-neoplastic changes.

Case report: In the case of a nine-year-old boy, the parents noticed a change in the palate a month before coming to the examination. The examination revealed a change located on the border between the hard and soft palate, shaped like a hemisphere, 2x1.6cm in size. The change was vaguely bounded from the surrounding tissue, fixed, painful on pressure and fluctuating. The mucous membrane above the change was smooth, and partly bluish. The change was surgically removed (excision).

Macroscopically, the change was 1.7x1.4x1.3cm in size. On cross-section, it was partly cystic, with a softer consistency. Cystic spaces were filled with liquid, dark content. Histologically, the change was made up predominantly of cystic, and to a lesser extent, solid areas. Mucinous, intermediate and epidermoid cells were seen in the change. Cystic spaces were lined with mucinous cells and filled with mucus mixed with blood. The cells have a uniform appearance, low mitotic activity (0 - 1/10HPF), no invasion of lymphatic, blood and nerve structures and no necrosis. Between the cystic structures, there are partitions (septa) that make up the stroma. An inflammatory infiltrate, composed of lymphocytes, plasma cells and histiocytes, was focally present in the stroma. Based on the morphological characteristics, the diagnosis of MUC - low grade - was established. The patient tolerated the treatment well and is currently disease-free during the follow-up period (3 months).

Discussion: Malignant epithelial tumors in children are rare and represent a diagnostic challenge. In the differentiation of MUC of low grade of malignancy, non-tumorous cystic lesions of salivary glands, and other benign and malignant tumors of low grade of malignancy come into consideration. Differential diagnosis includes abscess, necrotizing sialometaplasia, mucocele, sclerosing polycystic adenosis, sclerosing sialoadenitis, pleomorphic adenoma with squamous metaplasia, Warthino's tumor, schwannoma, and neurofibroma. Most often, low-grade MUC localized intraorally is clinically understood as a mucocele. Morphologically, it can be misinterpreted as a mucinous retention cyst. MUC is categorized into tumors of low-, intermediate-, and high-grade malignancy based on nuclear polymorphism, necrosis, cell type (mucinous, intermediate, and epidermoid), the grade of mitotic activity, and predominant mode of growth (solid or cystic). Tumors of a low grade of malignancy grow slowly, are generally treated only surgically by excision with negative resection margins, and have a good prognosis.

Conclusion: Low-grade MEC needs to be differentiated from other tumor and non-tumor lesions. Complete surgical resection is the primary treatment for low-grade MEC.

Keywords: Mucoepidermoid carcinoma; Hard palate; Child.

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Rare tumors of the larynx – report of two cases of adenoid cystic carcinoma

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Objective: Although laryngeal tumors are the second most common malignancy in the head and neck region, adenoid cystic carcinoma is one of the rarest types, composing less than 1% of laryngeal tumors. We present two cases with a literature review.
Case reports: **Case 1**: 73-year-old man presented with cough and difficulty swallowing. CT verified right-sided subglottic tumor mass without regional lymphadenopathy. On biopsy, tumor was diagnosed as adenoid cystic carcinoma. Patient underwent total laryngectomy with bilateral neck dissection. Tumor penetrated the thyroid cartilage, showed lymphovascular but not perineural invasion and was present on resection borders. Lymph nodes showed reactive changes. Patient was staged as pT4aN0R1. Fourteen months post surgery, there is no sign of recurrence.
Case 2: 79-year-old man presented with hoarseness lasting several months. CT scan showed a hyperdense alteration adjacent to the glottis exerting pressure on right vallecula. Biopsy revealed adenoid cystic carcinoma. Patient underwent total laryngectomy with right sided neck dissection. Tumor penetrated the thyroid cartilage and showed both vascular and perineural invasion, while resection borders were clear. Lymph nodes showed reactive changes. Patient was staged as pT4aN0R0. Seven months post surgery, patient is still disease free.
Conclusion: Laryngeal adenoid cystic carcinoma is a rare malignancy, not associated with typical risk factors for laryngeal carcinoma, often diagnosed at advanced stage. It should be considered in cases of advanced laryngeal tumors in patients lacking usual risk factors, but final diagnosis needs to be pathohistological.

Keywords: adenoid cystic carcinoma, larynx, head and neck, surgery

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Malignant melanotic nerve sheath tumour of mediastinum - rare tumor on the rare localisation

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Objective: Malignant melanotic nerve sheath tumour (MMNST), formerly known as melanotic schwannoma, is a rare tumour of nerve crest derivation, typically characterised by PRKAR1A lost. Initially MMNST was classified as benign, it has been defined as a malignant tumour in the 2020 WHO classification due to its aggressive behaviour. We report a rare case of MMNST of the mediastinum.
Case report: A female patient, aged 72, was diagnosed with a mediastinal tumour close to the left atrium, ventricle, and left coronary artery. A surgical procedure involving a left-lateral thoracotomy, partial pericardiectomy and lymph node extirpation. The pathohistological analysis revealed the presence of a hypercellular tumour composed of spindle cells that had a generally consistent morphology, lacking defined boundaries. Tumour cells were organized into short fascicles with palisading arrangement around blood vessels, without signs of necrosis or bleeding. Certain cells exhibited a cytoplasmic pigment that varied from fine-grained brown to dark brown, which is proved to be a melanin pigment by Masson Fontana staining. The pericar-

dium had been infiltrated by the tumour, while there were no nodal metastases. The tumour expressed Vimentin, S-100, S0X-10, MiTF, H3K27ME, and p53, but not HMB-45, PRAME, CD10, or Melan A. The Ki-67 proliferation index was 5%, and the mitotic rate was < 2/mm2. Lost expression of the PRKAR1A was the basic diagnostic criterion for distinguishing from malignant melanoma.

Conclusion: MMNSTs are rare and diagnostically challenging tumours that may be associated with the Carney complex, especially when there is a loss in PRKAR1A expression.

Keywords: MMNST, PRKAR1A lost, rare tumour

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Hodgkin Lymphoma Associated with Peripheral T-cell Lymphoma, NOS: a Case Report

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Objective: In diagnostic setting, the co-occurrence of a classical Hodgkin lymphoma (cHL) and peripheral T-cell lymphoma (PTCL), NOS, each with appropriate morphology and immunophenotype, either in the same tissue or separate tissues, defines a composite lymphoma.

Case report: We present the case of 68-year-old patient who underwent an examination for cervical lymphadenopathy, which was associated with weight loss, night sweats, and chronic skin itching. A right cervical lymph node excisional biopsy was performed. Morphologic analysis revealed effacement of lymph node architecture by diffuse lymphoid infiltration. An atypical medium and large lymphoid cells were positive for LCA, CD2, CD3, CD4, CD5, CD7, CD30, CD43, LEF1, c-myc, MUM1, ICOS, and GATA3 and negative for TdT, PAX5, CD20, CD10, bcl-6, PD1, Granzyme B, perforin, TIA-1, CD8, TBX21, ALK-1, EBV-LMP, CD57, EMA, CD25. A Ki-67 proliferation index was 70%.
In the same tissue there were Hodgin-Reed-Strenberg cells negative for LCA and positive for PAX5, CD20, CD30, fascin, MUM1, EBV-LMP, EBER and focally positive for CD15.
Those morphologic and immunophenotypic features were consistent with diagnosis of composite synchronous lymphoma with co-occurrence of a cHL and a PTCL, NOS, GATA3 subtype.
The patient was scheduled for admission to the Hematology Department for staging procedure and further analyses to be reviewed by the hematology team for the therapeutic approach. However, the patient has still failed to appear six months after diagnosis.

Conclusion: Composite lymphomas are extremely rare. They pose a particular diagnostic challenge. In this case, morphologic and immunophenotypic features may simulate angioimmunoblastic T-cell lymphoma, cHL and ALK-anaplastic large cell lymphoma.

Keywords: Peripheral T-cell lymphoma, NOS, classic Hodgkin lymphoma, composite lymphomas.

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Aortic dissection in a young patient with clinically unrecognized sarcoidosis - an autopsy case

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Objective: Case report of undiagnosed sarcoidosis in a young man who died due to aortic dissection.

Case report: A 39-year-old man was urgently hospitalized due to suspected acute myocardial infarction. The patient had been treated for chronic obstructive pulmonary disease. The patient died shortly after admission to the hospital, prompting a clinical autopsy. Autopsy revealed dissection of thoracic aorta with propagation down the anterior descending branch of the left coronary artery and the abdominal aorta. The myocardium showed discoloration. The kidneys appeared in a state of shock. No specific substrate was found in other organs. Representative samples were

taken from all organs, and routinely processed. Sections were stained using various histochemical methods. The myocardium showed mild perivascular fibrosis, cytoplasmic vacuolization of subendocardial cardiomyocytes, and small foci of contraction band necrosis. Atherosclerotic lesions with luminal narrowing of approximately 50% were found in the initial part of the left coronary artery. Lung, liver, kidney, spleen, and mediastinal lymph nodes, showed well-defined, non-necrotizing epithelioid cell granulomas with multinucleated giant cells with rare asteroid and conchoid intracytoplasmic inclusions within. Histochemical staining excluded the presence of pathogenic microorganisms. This chronic granulomatous inflammation consistent with sarcoidosis. Granulomatous inflammation was not detected in sections from the aorta.

Conclusion: The significance of autopsies in sudden deaths cannot be overstated, even when clinical symptoms appear clear. It is crucial to systematically conduct autopsies in such cases. Histopathological analysis plays a crucial role, especially in cases that may initially seem clear, as it can provide valuable insights that may not be apparent macroscopically.

Keywords: aortic dissection, sarcoidosis, autopsy

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Epidermoid Cyst of the Kidney - Tumor Mimicry and Diagnostic Challenges

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Objective: This is a case report and discussion of benign lesion mimickers of malignant renal neoplasia.

Case report: Here we present a 76-year-old female admitted to the hospital due to pain in the lumbar area. An ultrasound revealed a kidney tumor, which was verified on computer tomography. Radical nephrectomy was performed, and the specimen was sent for pathological analysis. On gross examination of the kidney, a cystic nodule was observed on the upper pole, partially filled with a soft, compact material, with a maximal diameter of 50 mm. Underneath the cystic nodule, a calculus with a maximal diameter of 12 mm was detected. The ureter was also filled with the same material as seen in the nodule. Histologically, the tumor was composed of cysts lined with squamous epithelium, filled with abundant lamellar keratin. Immunohistochemical analysis including CK5/6,CKAE1/AE3, p40, showed diffuse positivity of the squamous epithelium as well as lamellar keratin. The preformed immunohistochemical analysis confirmed the diagnosis of an epidermoid cyst of the kidney. The material in the ureter was also keratin, verified by immunohistochemistry.

Conclusion: Renal epidermal cyst is a rare and benign lesion. The etiology of epidermoid cysts has not yet been explored, but the presence of the renal calculus can be an etiological factor due to mechanical irritation. Its preoperative diagnosis is a real challenge due to its rarity, low clinical, and especially radiological specificity, which can lead to mistaken diagnosis as a malignant tumor. The macroscopic appearance of the cyst can also mimic an echinococcal cys

Keywords: kidney, epidermoid cyst, immunohistochemistry

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Significance of histomorphological damage of saphenous vein grafts in coronary bypass surgery

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Objective: The aim of this study was to deterimine the degree of histomorphological damage on saphenous veins harvested by using three different surgical techniques and their significance in coronary artery bypass grafting (CABG).
Introduction: The great saphenous vein is mostly used conduit for coronary revascularisation. Early and late vein graft occlusion still represents insufficiently pathogenetically elucidated problem in patients with coronary artery disease (CAD).
Material and Methods: The study included 83 saphenous vein samples obtained from patients who underwent one of three different surgical techniques: conventional (CVH), endoscopic (EVH) and „no-touch“ (NT) vein harvesting on the Dedinje Cardiovascular Institute, Cardiac Surgery Department, Belgrade, Serbia between June 2019. and December 2020. Collected saphenous vein samples were stained by hematoxylin-eosin (H&E) and immunohistochemically analyzed by using CD31, factor VIII, Caveolin and eNOS antibodies.
Results: Histomorphological evaluation of H&E vein sections showed significantlly lower microstructural damage in NT harvested veins compared to CVH and EVH group of patients ($p<0.001$). Immunohistochemical examination revealed strong positive staining in the NT group compared to CVH and EVH group (CD31: $p=0.02$; FVIII: $p<0.001$; Caveolin: $p=0.001$; eNOS: $p=0.003$) which was confirmed a lower degree of structural damage and mostly intact wall integrity in NT group.
Conclusion: The preservation of structural integrity and vein patency represent essential factors for long-term functionality of saphenous vein grafts. NT vein harvesting showed the best morphological preservation of the vein wall, while leg wound complications were the least in EVH group of patients. Consequently, the development and implementation of the endoscopic no-touch technique would significantly advance coronary artery bypass grafting.

Keywords: coronary artery bypass grafting, conventional vein harvesting, endoscopic vein harvesting, no-touch vein harvesting, saphenous vein, vascular damage

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Pediatric ileal intussusception caused by myoepithelial hamartoma - a case report

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Objective: Myoepithelial hamartoma (MEH) is a benign tumor-like lesion composed of dilated glandular formations lined by single-layered columnar epithelium surrounded by bundles of smooth muscle cells. MEH is most commonly localized in the stomach and duodenum, while distal localization in the small intestine is very rare.
Case report: A male infant was urgently admitted to the University Children’s Hospital, Belgrade. Upon detailed examination, ileal intussusception was diagnosed. Fol-

lowing surgical intervention, a segment of the ileum with a tumor-like lesion was excised. Excised ileal segment revealed a submucosal tumor-like lesion, with multicystic appearance upon cross sectioning. Histopathological analysis revealed a well-demarcated lesion localized within the submucosa and muscularis propria, comprised of dilated tubular structures. These structures were lined by a single-layered columnar epithelium positive for CK7, as well as for CD10 (apical positivity). Focally, dilated structures were lined by stratified epithelium positive for CK 5/6 and p63 (basal cells). All epithelial cells demonstrate immunohistochemical positivity for PDX1, CDX2, CA19.9, MUC1, with some showing positivity for MUC5AC and focal positivity for MUC6. However, staining for SATB2, MUC2, CK20, and OCT4 is negative. Bundles of smooth muscle cells (□-SMA positive) were observed around each tubular structure.

Conclusion: Although the pathogenesis of this lesion remains incompletely understood, there are opinions suggesting that the lesion is an heterotopic pancreatic tissue. The positivity of certain immunohistochemical markers such as PDX1, CA19.9, CDX2 supports this theory. Despite its rarity, our case adds to the growing body of evidence in the literature, providing further insights into the diagnosis of this rare entity.

Keywords: myoepithelial hamartoma, intussusception, pediatric pathology

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Cytological and histological features of lung adenocarcinoma with positive predictive biomarkers

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Objective: Examination of differences in the frequency of morphological features between ALK, EGFR, PDL1, and TN group of patients with lung adenocarcinoma (LA).

Introduction: There is a limited data describing the cytomorphological features that could suggest mutation status or PD-L1 expression in LA.

Material and Methods: The retrospective study included 132 patients diagnosed with LA. Based on molecular findings, patients were categorized into four groups: PDL1 group, ALK group, EGFR group, and triple negative (TN) group. Examined morphological features encompassed: cell cluster size, arrangement of tumor cells, size of nuclei, nuclear atypia, visibility of nucleoli, presence of necrosis, intracytoplasmic vacuoles, signet ring cells, stromal characteristics, and inflammatory infiltrate presence.

Results: Solid arrangement, large nuclei, presence of intracytoplasmatic vacuoles, signet ring cells, and abundant stroma were statistically significantly more frequently present in PDL1 group compared to TN group ($p<0.05$). The predictive model composed of these features was statistically significant for high PD-L1 expression as criterion ($x^2=40.626;p<0.001$). Accuracy, sensitivity and specificity for this model were 83.61%, 86.67%, 80.65%. Statistically significant differences were observed in size of the nuclei, histological arrangement of cells, visibili-

ty of the nucleoli, and presence of intracytoplasmic vacuoles, and signet ring cells between ALK, EGFR, and TN group. The predictive model composed of these features was statistically significant for mutation status as criterion ($x^2=67.541;p<0.001$). The predictive model achieved classification success rate for ALK, EGFR, and |TN group of 72.4%, 69%, and 71%, respectively.

Conclusion: Our results confirm that certain cytological and histological features of LA are associated with the mutational status and PD-L1 expression in LA.

Keywords: Cytology; Histopathology; Lung Adenocarcinoma; Epidermal Growth Factor Receptor; Anaplastic Lymphoma Kinase; Programmed Cell Death Ligand 1

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Clinical-pathologycal characteristic of hormone-independent lobular breast carcinoma

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Objective: The eyelid can be the site of various tumors but primary non-epithelial tumors are rare. Solitary circumscribed neuroma is a benign neural tumour composed of Schwann cells, frequent on the head and neck, but it is rarely described on the eyelid. We aim to present a rare case of solitary circumscribed neuroma of the eyelid diagnosed at Clinic for Ophthalmology of University Clinical Centre of Serbia.

Case report: A 69-year-old female patient presented with solitary, slightly raised, painless nodule on the lower eyelid skin, 3.5 mm in the greatest diameter. Histopathological evaluation showed a well circumscribed, partially encapsulated intradermal nodular tumor. It was composed of elongated spindle cells arranged in irregular fascicles, with hyperchromatic nuclei without prominent atypia and no nuclear palisading. Mitoses were not noticed. The tumor cells expressed SOX10, S-100, and CD34 but not GFAP. Neurofilament was positive in entrapped small nerves. GLUT-1 was expressed in remnants of perineurium in the tumor periphery. There was no recurrence noted in this case.

Conclusion: Primary non-epithelial eyelid tumors are uncommon and may be a diagnostic challenge for ophthalmic pathologists. Other spindle cell tumors must be considered when encountered with solitary circumscribed neuroma, especially those that may be associated with systemic syndromes. Morphological features are usually enough for the diagnosis but immunohistochemical analysis can be helpful.

Keywords: solitary circumscribed neuroma, eyelid, peripheral nerve tumor

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Non-epithelial tumors of eyelid: a case of solitary circumscribed neuroma as an uncommon tumor

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Objective: The eyelid can be the site of various tumors but primary non-epithelial tumors are rare. Solitary circumscribed neuroma is a benign neural tumour composed of Schwann cells, frequent on the head and neck, but it is rarely described on the eyelid. We aim to present a rare case of solitary circumscribed neuroma of the eyelid diagnosed at Clinic for Ophthalmology of University Clinical Centre of Serbia.
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Conclusion: Primary non-epithelial eyelid tumors are uncommon and may be a diagnostic challenge for ophthalmic pathologists. Other spindle cell tumors must be considered when encountered with solitary circumscribed neuroma, especially those that may be associated with systemic syndromes. Morphological features are usually enough for the diagnosis but immunohistochemical analysis can be helpful.

Keywords: solitary circumscribed neuroma, eyelid, peripheral nerve tumor

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Primary intraosseous myxoid liposarcoma: a case report

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Objective: Liposarcoma is the most common type of sarcoma in adults which mostly arises in deep soft tissues of the extremities, especially the thigh. Primary intraosseous liposarcoma is an extremely rare tumor and accounts for less than 0.1% of all malignant bone tumors. Tumor is accompanied by non specific symptoms such as pain, swelling and decreased range of motion.
Case report: We present a 66 years old female patient with a one year history of pain and swelling in the left knee area. The X-ray showed a distal femoral osteolytic lesion. MRI revealed intramedullary lesion mass measuring in the greatest diameter 12.5 cm, destroying the cortex. Initially open biopsy revealed intraosseous malignant mesenchymal tumor - high grade myxoid liposarcoma, composed of uniform, small ovoid cells without significant atypia neither brisk mitotic activity embaded in abundant, lightly basophilic myxoid stroma with delicately arborizing capillary network. Approximately 15% of tumor contained hypercellular areas composed of small round cells which classified it in high grade neoplasm. Immunohistochemically, the tumor cells showed strong diffuse positivity for vimentin and focal positivity for p53 and desmin. Nuclear Ki67 positivity

was found in approximately 10% tumor cells. Diagnosis of myxoid liposarcoma confirmed by DDIT3 FISH analysis. Surgical procedure has been chosen as initially treatment modality followed by adjuvant chemotherapy.

Conclusion: Primary intraosseous myxoid liposarcoma has no specific symptoms neither radiography imaging, thus pathohistological finding is esencial in diagnosis. Considering myxoid liposarcoma could be mistaken with other tumors that have myxoid appereances, we emphasise importance of immunohistochemical and DDIT3 FISH analysis.

Keywords: bone, myxoid liposarcoma, primary tumor

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PD-L1 expression in metastatic colorectal carcinoma

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Objective: Programmed cell death ligand-1 (PD-L1) expression in colorectal cancer and its prognostic role in metastatic colorectal carcinoma (mCRC) is not well established. In our study we aim to evaluate the expression of PD-L1 in mCRC and its correlation with the clinicopathological characteristics in these patients.

Introduction: The treatment of metastatic colorectal carcinoma (mCRC) has been improved over the recent years mostly due to molecular classification and new technologies for personalized therapy. PD-L1 is the key inhibitor of the cytotoxic immune response and causes rapid tumor progression with poor prognosis.

Material and Methods: Diagnosed 75 cases of mCRC at Clinical Hospital Acibadem – Sistina were evaluated for PD-L1 expression using clone SP263 in tissue microarray. The expression was evaluated by different cut-offs of >1%, >10%, >50% of tumor cells.

Results: PD-L1 was evaluated positive in 17 cases of mCRC (26,6%). More than a half of positive cases (11) showed cut off >1%. Seventeen percent of positive cases showed cut off >10% and all of them were located in rectosigmoid colon with stage IIIB and IIIC. Three cases were evaluated with a cut off >50% all of them G3 mCRC, stage IIIC and IVA, of which 2 cases were in right colon associated with BRAF mutations.

Conclusion: Expression of PD-L1 was found in almost one third of the cases. A higher cut off was correlated with higher grade, high pathological stage and BRAF mutation. This suggests that mCRC with high PD-L1 expression may show a survival advantage with immune checkpoint inhibitors therapy.

Keywords: Colorectal carcinoma, PD-L1, immune checkpoint inhibitors

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Hepatic Echinococcosis – presentation of case reports

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Objective: To present the differences between cystic and alveolar echinococcosis with the first two cases of multilocular echinococcosis in Serbia.

Case report: The first case was a 67-year-old female from a small village in Srem municipality who was admitted to our hospital due to liver pain, which progressed over time. Differential diagnoses included haemangioma, cystic echi-

nococcosis and abscess formed in the cystic echinococcal lesion. Pathological examination clearly showed multilocular echinococcosis with numerous small and empty vesicle spaces with chitin membrane without protoscolices, surrounded by massive fibrosis and infiltrative type of growing into the liver parenchyma. The second case was a 57-year-old man who was admitted to our hospital due to 10-day lasting symptoms of jaundice, nausea, and stomach pain. Differential diagnoses included malignant tumor. The lesion of the liver underwent radical resection. It was confirmed as alveolar echinococcosis by pathological examination, which showed multiple multilocular cysts covered with chitinous membranes, accompanied by numerous foreign body granulomas and broad areas of necrosis. Perineural propagation of echinococcis and one hilar lymph node with wide necrotizing granulomas with chitinous membranes were also present. Both of the patients had no surgical complications after the operation and were discharged with an 800 mg daily dosage of Albendazole.

Conclusion: These are the two first recorded human cases of multilocular echinococcosis in Serbia. Infections with these parasites are considered extremely serious, contributing to significant morbidity and mortality. Therefore, we must improve prophylactic and diagnostic procedures and surgical techniques to cure this zoonotic disease.

Keywords: echinococcosis, cystic, multilocular, liver

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Metastatic synovial sarcoma of the uterus - Is it possible to diagnose it without FISH analysis?

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Objective: Synovial sarcoma is classified as a malignant mesenchymal tumor of unclear histogenesis, typical for the locomotor system. Its visceral localization has been rarely described. We present the significance of molecular FISH analysis in verifying a rare metastatic synovial sarcoma of the uterus with divergent smooth muscle and osteoblastic differentiation.

Case report: A lung tumor biopsy was performed on a 63-year-old patient. The scant biopsy sample showed tumor composed of pleomorphic epithelioid cells surrounded by an eosinophilic matrix. Immunophenotypically, the cells exhibited mesenchymal differentiation (positive Vimentin, CD99, SMA, SATB2, p16, TLE, WT1, Desmin). FISH analysis detected SS18 gene rearrangement in 40% of the nuclei typical for synovial sarcoma. Additionally, a heterozygous deletion of the CDKN1A gene was confirmed in 57% of the nuclei.

It was later discovered that the patient had undergone a hysterectomy three years prior, when the diagnosis of uterine leiomyoma was made. Reevaluation of the uterine biopsy demonstrated a tumor composed of pleomorphic spindle cells with mesenchymal differentiation (positive SMA, p16, Desmin, TLE, SATB2, negative for ER). FISH analysis

detected SS18 gene rearrangement in 28% of the nuclei, that led to a diagnosis of primary synovial sarcoma of the uterus.

Conclusion: A comparative analysis of both tumors showed immunohistochemical and FISH overlaps, indicating that both biopsies correspond to a rare form of malignant mesenchymal tumor- synovial sarcoma displaying divergent smooth muscle and osteoblastic differentiation. We concluded that the tumor in the uterus was the primary neoplasm, while the lung tumor should be considered a secondary deposit.

Keywords: Synovial sarcoma, SS18, smooth muscle and osteoblastic differentiation.

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Detection of EGFR mutations in cytology samples - liquid biopsy opens a new chapter in molecular diagnostics

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Objective: Activating mutations of the epidermal growth factor receptor (EGFR) are found in 10-15% of lung adenocarcinomas in the Caucasian population. The presence of these mutations is associated with sensitivity to EGFR tyrosine kinase inhibitors (TKIs). The secondary T790M mutation in exon 20 of the EGFR gene is the most common mechanism of acquired resistance to first- and second-generation TKIs, occurring in 50-60% of resistant cases with progressive disease. Although tissue is considered the gold standard for molecular biomarker testing, numerous studies and guidelines recommend the use of cytological specimens (smears and cell blocks) for EGFR testing, including detection of the EGFR T790M mutation. Considering tumor heterogeneity, a single sample is often insufficient to gain insight into the molecular profile of a malignancy. Liquid biopsies are promising minimally invasive procedures based primarily on the molecular analysis of circulating tumor cells or cell-free tumor DNA (ctDNA) isolated from blood and other body fluids. However, ctDNA is limited in the bloodstream and still represents a hurdle on the way to promising precision medicine. Therefore, pleural and pericardial effusions can be used as a source of biomarkers, such as ctDNA, in liquid biopsy to investigate tumor mutations.

Case report: In August 2022, a 69-year-old woman, a former smoker, came to the Institute for Pulmonary Diseases of Vojvodina in Sremska Kamenica due to dyspnea and weight loss. Computed tomography (CT) of the chest showed a tumorous lesion in the right upper lobe of the lung, with a diameter of 4 cm, mediastinal lymphadenomegaly, and a pericardial effusion. A pericardiocentesis was performed because of an impending cardiac tamponade. Numerous erythrocytes and individual reactive mesothelial cells were found in the cytological smear of the obtained pericardial effusion. A bronchoscopy was performed and the pathohistological examination confirmed lung adenocarcinoma at stage T3N3M0. EGFR testing was performed using the extracted genomic DNA from the cytological smear - brush from the right upper lobe. The real time PCR Cobas® EGFR Mutation Test V2 detected the presence of L858R mutation in exon 21. The patient received first-line therapy with afatinib (second-generation TKI), at a dose of 40 mg/day. The overall treatment with afatinib was carried out over a period of 15 months. A partial radiological response according to RECIST (Response Evaluation Criteria in Solid Tumours) v.1.1 was achieved. In December 2023, a CT scan of the chest showed a recurrence of the pericardial effusion. The patient underwent a pericardiocentesis. No malignant cells were found in the cytological smear of the pericardial effusion. A liquid biopsy was performed. The ctDNA was isolated from blood plasma and the molecular test was negative for EGFR mutations. The multidisciplinary tumor board decided to repeat a liquid biopsy from the supernatant isolated from the pericardial efussion. The Cobas® EGFR Mutation Test V2 revealed coexisting L858R mutation with T790M mutation in the ctDNA isolated from the pericardial effusion. In January 2024, the patient was administered second-line therapy with osimertinib (third-generation TKI) at a dose of 80 mg/day. The patient is currently on the proposed therapy without side effects. The first follow-up CT scan is expected shortly.

Conclusion: Malignant effusions can serve as alternative samples if no tumor tissue is available. The cell pellet obtained by centrifugation can be used for the preparation of smears or cell blocks and for genotyping if it contains a

sufficient number of tumor cells. The separated supernatant can be explored as an alternative source for liquid biopsy in lung cancer patients to diagnose early disease progression even if no malignant cells were seen in the effusion. Liquid biopsy using the supernatant of pleural/pericardial effusions could be more effective than blood plasma samples because the effusions are richer in tumor products released by the cancer cells. It is playing an increasing role as a complementary molecular testing strategy even when tissue tests are available so that more patients can receive targeted therapy.

Keywords: Cell-Free Nucleic Acids, Cytology, Lung Neoplasms

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Unraveling Adult Renal Cell Tumors: Exploring the Role of Lipocalin-2

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Objective: This study aims to scrutinize LCN2 expression in different types of adult kidney tumors and ascertain its potential significance as a diagnostic and prognostic marker.

Introduction: Renal cell carcinoma (RCC) poses a growing health concern with its escalating incidence and diagnostic complexities. Lipocalin-2 (LCN2) is a multifaceted protein expressed across various tissues, engaging in diverse biological functions. However, its involvement in modulating the proliferation, invasion, and metastasis of RCC remains inadequately explored.

Material and Methods: A cohort of 206 patients undergoing nephrectomy at the Urology Clinic, Clinical Center of Serbia, constituted the study population. Patient demographics, tumor dimensions, and survival data were extracted from medical records. Tissue microarrays were constructed following established protocols and immunohistochemically stained for LCN2. Subsequent staining evaluation and statistical analyses, encompassing descriptive statistics, chi-square tests, and Kaplan-Meier curves, were conducted.

Results: Moderate cytoplasmic expression of LCN2 was discerned in healthy tubular cells. Notably, a statistically significant correlation between histological tumor type and LCN2 expression was identified, with elevated expression in renal oncocytoma (RO) and heterogeneous expression in clear cell RCC (ccRCC). While LCN2 did not exhibit prognostic utility in this study, its ubiquitous presence across RCC types intimates a plausible involvement in tumor progression.

Conclusion: Our findings underscore the substantial expression of LCN2 in diverse kidney tumors, particularly RO, with notable heterogeneity observed in ccRCC. Despite its non-identification as a prognostic marker, the pervasive occurrence of LCN2 across RCC variants hints at its involvement in tumorigenesis. Further investigations are imperative to elucidate LCN2's precise role in kidney cancer pathogenesis and its potential as a diagnostic and prognostic biomarker.

Keywords: lipocalin-2; renal cell carcinoma; oncocytoma; ccRCC

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Spectrum of microscopic changes in testicular specimens during physical adaptation of male to female

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Objective: To provide a clinicopathological review of features identified in testicular tissue specimens after bilateral sex-affirming orchiectomies were performed.

Introduction: Hormonal therapy use of antiandrogens in combination with estrogen before sex reassignment surgery is the basis of preparation for people with gender dysphoria. The Endocrine Society guidelines recommend gender confirmation surgery after at least 1 year of continuous and coordinated hormonal preparation.

Material and Methods: We analyzed and statistically processed data on age, length of hormone therapy and testicular histopathological changes in patients who underwent bilateral orchiectomies from January 2019 to January 2023 for gender reassignment.

Results: A total of 117 persons were analysed aged from 18 to 66 years (average, 31.71±11.74). The mean length of hormone therapy was 28,78±31.23 months (range, 12 to 240 months). Mean testicular mass was 13,97±4,50g (right) and 13,79±5,32g (left). There were no germ cell

tumors, sex cord-stromal tumors, or germ cell neoplasia in situ. Thickening of the basement membranes of the seminiferous tubules and edema were found in all testicular samples. Sertoly cells occurred in 114 (97,4%), hypospermatogenesis in 44 (37,6%), normal spermatogenesis in 4 (3,4%), and 30 (25,6%) testes showed fibrosis/obliteration. All results were statistically significant ($p<0,0001$). There was no statistical significance between the length of hormone therapy and the pathological changes in testicular tissue.

Conclusion: Our results represent a rare institutional experience of physical adaptation of male to female persons. The spectrum of pathohistological findings corresponds to changes in testicular tissue after the preoperative application of hormone therapy.

Keywords: Orchiectomy; Testes histopathology; Transgender

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Clinicopathological features of Renal Collecting Duct Carcinoma - Institutional experience

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Objective: We aim to analyze the frequency and clinicopathological features of Renal Collecting Duct Carcinoma (CDC) diagnosed at our Institute over twelve years.

Introduction: CDC represents a rare primary renal cell adenocarcinoma that arises from the principal cells of the distal nephron and accounts for less than 1% of primary renal malignancies. CDC is an aggressive tumor with 67% of patients dying within the first 2 years. Due to diverse morphology and unspecific immunophenotype pathohistological diagnosis of CDC is challenging.

Material and Methods: A surgical pathology archive from 2012 to 2024 has been searched for cases of CDC in the final diagnosis. Patients' age, gender, tumor size, stage group (SG), morphologic patterns, mucin presence, and tumor immunophenotype were analyzed.

Results: From a total of 1693 patients with performed nephrectomy for the surgical treatment of renal tumors, CDC was diagnosed in 11 cases (0.65%). Ten patients were males and one was female. The average age was 58.45 ± 12.59. The mean tumor size was 103.73 ± 45.52mm. Seven patients were in SG III and four patients were in SG IV. Papillary and tubulopapillary patterns predominate in seven cases. Tubular and microcystic patterns predominate in four cases. Stromal desmoplasia, mixed inflammatory infiltrate, and the focal presence of mucin were detected in all cases. Immunophenotype was unspecific with the most commonly positive reaction for HMWCK.

Conclusion: CDC is a rare high-grade adenocarcinoma in an advanced stage at the time of diagnosis with the most common papillary pattern and mucin presence. The final diagnosis implies the exclusion of other primary and secondary kidney malignancies.

Keywords: Collecting Duct Carcinoma; CDC; High-grade.

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Pathohistological characteristics of bone marrow in patients with multiple myeloma

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Objective: To find out proportion of pathologically verified MM in the total number of clinically suspected cases, as well as correlation with the patients gender and age and pathohistological characteristics of the bone marrow.

Introduction: Multiple myeloma (MM) is a hematological neoplasm characterized by clonal expansion of B-lymphocytes, specifically plasma cells in the bone marrow. The diagnosis of this malignancy requires bone marrow biopsy with pathohistological analysis.

Material and Methods: A-6-year retrospective study (2018-2023) involved 438 patients with a referral diagnosis of MM. Monitored variables were age, gender, bone marrow cellularity, atypical plasma cells infiltration percentage an clonality, the reticulin grade (G0-G3) and all were compared between the group with a pathohistological confirmed MM and the group that remained clinically suspected.
Results: Within the observed sample, the proportion of clinically suspected (30.6%) and confirmed diagnoses (69.4%) didn't significantly change over the years. The average patient's age was 65 with slightly male predominance (54%). The largest number of pathohistologically confirmed cases was in year 2023. Cellularity and reticulin fibers were increased in group of proved MM with average plasmacytic infiltration of 50%. Kappa monoclonality was registered in 58% of all cases and in all years separately except during 2019 when lambda was slightly more expressed.
Conclusion: MM is a disease of the older population with heterogeneity in general demographic characteristics as well as in the bone marrow pathohistological findings, therefore the key of care and survival of patients is early diagnosis, adequate therapy and timely treatment of complications.

Keywords: multiple myeloma; kappa; lambda; bone marrow

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MALT lymphoma and Helicobacter pylori infection, 10 years, single institution

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Objective: To find out the association between Helicobacter pylori infection and gastric MALT lymphomas in a 10 years material in our hospital.
Introduction: MALT lymphomas make about 9% of all lymphomas and about 50% of gastric lymphomas. There is a well-known association of Helicobacter pylori, Borellia Burgdorferi, Chlamydia, Campylobacter jejuni and Achromobacter xylosoxidans infection with gastric, cutaneous, ocular, intestinal and pulmonary MALT lymphoma respectively.
Material and Methods: All biopsies of gastric MALT lymphomas diagnosed at the Oncology Institute of Vojvodina from January 2010 to March 2020. Demographic and medical data were taken from the hospital information system. HE and HP Giemsa staining and immunohistochemistry were performed according to standard procedures. Microsoft Excel and IBM SPSS Statistics were used for data analyses.
Results: There were 79 patients, which makes 6,5% of all lymphomas during this period. There were 32 men (29 to 81 years old) and 47 women (30 to 82 years old). Patients were on average about 60 years old and median 63 for both sexes. Helicobacter pylori infection was present in 52,63% of all cases, equally in both sexes.
Conclusion: Patients were mostly elderly, without any statistically significant differences between sexes. The incidence of disease is similar to neighboring countries and the USA but lower than in western Europe. The incidence of Helicobacter pylori infection in our patients is higher than in western Europe and similar to European data from a few decades ago, probably due to insufficient diagnosis of gastric problems and consequently insufficient eradication therapy for Helicobacter pylori.

Keywords: B-cell lymphoma, Helicobacter pylori, MALT lymphoma

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JAK2 mutations and endogenous erythroid colony formation in patients with polycythemia vera

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Objective: The aim of this study was to determine the frequency of JAK2V617F and JAK 2 exon 12 gene mutations and to compare the results with the presence of endogenous erythroid colony (EEC) formation.

Introduction: Polycythemia vera (PV) is a chronic myeloproliferative neoplasm characterized by increased red blood cells. The most frequent genetic abnormality is the somatic mutation of Janus kinase 2 gene (JAK2V617F) and it occurs in more than 95% of patients. In 2-5% V617F negative PV patients were detected JAK2 exon 12 mutations.
Material and Methods: Peripheral blood and bone marrow samples of 116 patients with PV were analyzed. The diagnosis of PV was established according to the bone marrow criteria of the World Health Organization (WHO). Mutation of JAK2V617F was determined by allele-specific PCR (AS-PCR) analysis. A group of exon 12 mutations (I540-E543Del, R541-E543Del, F537-K539Del, H538-K539Del, K539L,N542-E543Del) were determined by RQ-PCR mutations screening based methodology. Assay for human clonal heamatopoietic progenitor cells with agar-leukocyte conditioned medium (Agar-LCM), without recombinant human erythropoietin (EPO), was used for detection of EEC.
Results: Mutation of JAK2V617F was found in the samples of the peripheral blood in 108/116 (93%) PV patients. EEC formations were obtained in the sample of bone marrow in 109/116 (94%) PV patients. In 106/116 (91%) patients we detected presence of EEC formation and mutation of JAK2V617F at the same time. One JAK2V617F unmutated patient, with EEC, has mutation in JAK2 exon 12 gene.
Conclusion: Presence of JAK2 mutation and EEC are essential characteristics of PV. Considering these results, it is clear that the EEC formation observed in PV, are the part of the JAK2-dependent activation signaling pathway.

Keywords: EEC, JAK 2

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Detection of JAK2 (V617F), CALR and MPL mutations in patients with thrombocytosis

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Objective: Detection of most frequent gene mutations, involved in pathogenesis of myeloproliferative disorders.
Introduction: Mutations in JAK2, CALR and MPL genes, were introduced as diagnostic parameters. The aim of detecting those mutations, in the patients with persistent thrombocythosis, is to establish diferentialy diagnose of myeloproliferative neoplasia (MPN). JAK2 encodes for a non-receptor tyrosine kinase. CALR gene is coding multifunctional protein, named calreticulin, which is involved in control of gene activity, cell growth, proliferation, migration, adhesion and apoptosis. MPL is oncogene, which encodes for thrombopoietin receptor.
Material and Methods: We analysed 708 pts with persistant thrombocythosis, by the ARMS-PCR method for JAK2 V617F mutation detection. We selected 20 JAK2 negative pts, for further analysis of MPL W515K/L and CALR mutations, by the RQ-PCR muation detection kit. DNA was extracted from peripheral blood, according to standard procedures.
Results: JAK2 V617F mutation was positive in 372 pts. (52.5 %). CALR mutations were detected in 10 out of 20 pts. (50%), predominantly Type I (6 pts, 60%) and Del I (6pts, 60%) , Type II (3pt, 30%), Del II (0%), Del III (3 pt, 30%) . Eight of ten (80%) had more than one mutation. The Del II mutations were not detected. MPL W515L/K mutations were not detected too, in this group of pts.
Conclusion: We provided a diagnostic parameters which differentiate a group of MPN pts. with thrombocytosis. Further investigations of new diagnostic mutations, in the genes involved in pathogenesis of MPNs, are important for defining new potentional targets for molecularly targeted therapy, in treating malignant diseases.

Keywords: CALR, JAK2V617F, MPLW515K/L, MPN

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Immunosuppressive features in epithelial ovarian tumors

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Objective: We analyzed differences in PD-L1 expression in epithelial ovarian tumors.
Introduction: Ovarian tumors can suppress the host's immune responses by activating the PD-1/PD-L1 mechanism. PD-L1 immunosuppressive function can make tumor cells resistant to effector lymphocytes, which leads to aggressive clinical behavior.
Material and Methods: PD-L1 expression was analyzed in 328 subjects, 122 with epithelial ovarian carcinoma (OC), 42 with atypical proliferative tumor (APT), and 164 with benign epithelial ovarian tumor (BOT). Immunohistochemical analysis was performed using the tissue microarray and correlated with a set of histopathology parameters.
Results: The higher PD-L1 expression was found in OC than in APT/BOT. The intensity of PD-L1 expression was higher in serous (79.6%) than in mucinous or endometrioid OCs ($p < 0.001$). PD-L1 expression was higher in high-grade serous carcinoma (HGSC) than in low-grade serous carcinoma (LGSC) ($p = 0.007$). The high level of PD-L1 expression was more frequent in OCs with stage FIGO III /IV than in those with lower stages ($p < 0.001$). PD-L1 high expression level was significantly more frequent in OCs with tumor necrosis, lymphovascular invasion, and lymphocytic infiltration.
Conclusion: We showed a significantly higher level of PD-L1 expression in OCs than in APT/BOT, most frequently in the HGSC histology type. These findings underline the possibility of the usage of PD-L1 inhibitors in patients with more aggressive ovarian cancers, such as HGSC.

Keywords: immunosuppressive; epithelial ovarian tumor; PD-L1

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Prognostic value of separate extramural vascular invasion reporting in rectal cancer

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Objective: The aim of this study was to examine the prognostic significance of pathohistologically detected EMVI in untreated rectal cancer and its implications in separate reporting.
Introduction: Vascular invasion, especially extramural vascular invasion (EMVI) has emerged as prognostic parameter for rectal cancer (RC) in recent years. Prediction of reccurence and metastases development poses a significant challenge for oncologists, needing markers for prediction of adverse outcome.
Material and Methods: We examined 100 untreated RC patients who underwent curative resection from January 2016 to June 2018 with follow up of 5 years. Patients were divided in equal EMVI- and EMVI+ groups based on histological examination of H&E stained postoperative surgical samples. Exclusion criteria were neoadjuvant treatment and distant metastases. Overall and disease-free survival distributions were estimated by the Kaplan-Meier method.
Results: Out of the total RC patients, 66% were still alive during the follow-up period (median 56, range 12-76 months), while 30% had verified recurrence of the disease. The median survival without recurrence of the disease was 52 (range 4-76) months. EMVI+ patients had significantly shorter average OS (56.230±3.350 months) compared to EMVI- patients (64.640±2.845 months) (p=0.040). Among EMVI+ cases, significantly shorter DFS was recorded than within EMVI- cases (52.162±4.319 vs. 61.338±3.041 months, p=0.028). Concerning LVI, differences in OS between LVI+ and LVI- patients were not statistically significant (p=0.068), while LVI+ patients had significantly shorter DFS (p=0.024).
Conclusion: Obtained results strongly suggest significance of separate reporting of EMVI from lympho-vascular invasion, as it is potentially a surogate marker for adverse prognosis and outcome.

Keywords: rectal cancer, extramural venous vascular invasion

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EGFR mutation analysis in cytological specimens: An institutional experience

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Objective: To evaluate EGFR mutation testing in cytological lung adenocarcinoma (LUAD) specimens.
Introduction: Epidermal growth factor receptor (EGFR) is a predictor for tyrosine kinase inhibitor (TKI), which is efficient in LUAD treatment. Activating EGFR mutations are usually found in never smokers, females, and Asian population. The most of LUAD patients are diagnosed at advanced stages of the disease when surgical resection is not possible, so cytological specimens is alternative for EGFR mutation detection.
Material and Methods: This prospective study included 101 cytology samples (bronchial brushing, fine needle aspiration, transbronchial needle aspiration or pleural effusion) who underwent EGFR mutation analysis during a 6-months period at the Institute for Pulmonary Diseases of Vojvodina. DNA was isolated using the Cobas®DNA Sample Preparation Kit. The target DNA was detected using real time PCR Cobas®EGFR Mutation Test v2.
Results: There was 69 (61.4%) men and 32 (38.6%)

women included in the study. Median age was 65.4 (62.8 women and 67.1 men). Majority of patients were active or former smokers (54.5% and 32.7%). EGFR mutation rate was 9.9%. The most common mutation type was deletion in exon 19 (5/10 specimens), L858R mutation in exon 21 (4/10 specimens). In one specimen G719 point mutation in exon 18 was detected. There was no significant correlation between the number of tumor cells and the DNA concentration. One mutation positive specimen had extremely low DNA yields (0.71ng/μl).

Conclusion: Our results confirmed the effectiveness of a sensitive real-time method in EGFR gene mutation detection in cytology specimens.

Keywords: Keywords: adenocarcinoma, cytology , EGFR, mutation test

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Cytological evaluation of breast lesions with histopathological correlation

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Objective: To find out cytological and histopathological correlation in patients with surgical resection of breast lesions.
Introduction: Cytology is a fast and non-invasive diagnostic procedure and part of tumor board for evaluation of breast lumps.

Material and Methods: Retrospective study of 198 patients included 90.4% (179/198) women and 9.6% (19/198) men, age between 15 and 93, average 57.80±18,78.
Cytological material was sampled using ultrasound-guided fine-needle aspiration (FNA) in 39.9% (79/198) patients, FNA in 33.33% (66/198), core biopsy in 18.69% (37/198) and breast secretion smear in 8.08% (16/198) patients. Surgical treatment was indicated after cytological evaluation in 52.02% (103/198) patients.

Results: In 50.50% (100/198) of patients sample was obtained from left breast, and in 28.4% (56/198) from upper lateral quadrant. Cytological samples were divided into 5 categories: 19.2% (38/198) non-diagnostic, 42.4% (84/198) benign, 8.6% (17/198) atypical, 9.6% (19/198) suspicious for malignancy and 20.2% (40/198) malignant. The most frequent cytological diagnosis in 27.78% (55/198) patients was adenocarcinoma, following fibrocystic breast changes in 18.18% (36/198).
There were statistically significant more women ($p<0.001$), adenocarcinoma diagnosed by cytology ($p<0.001$) and ductal carcinoma as histopathological diagnosis ($p<0.001$). There was no statistically significant difference in lump localization ($p=0.829$). Cytological and histopathological correlation was high ($r=0.163$).

Conclusion: Cytology has important role in breast lump diagnosis. Event there are more core biopsies instead of FNA due to majority of possibilities of additional studies on samples, we can still use cytology for fast evaluation.

Keywords: cytology, breast, ductal carcinoma, FNA

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A Case of Unexpected Autopsy Diagnose

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Objective: Sarcoidosis is a chronic granulomatous disease of uncertain etiology involving various organs. Pathologically, it is characterized by the presence of noncaseating granulomas in affected tissues, usually lungs. The age of presentation is between 30 and 50, commonly women. Cardiac involvement is seen in 2-5% of patients with systemic sarcoidosis and is often clinically undetected.
We present a case of unexpected diagnosis of systemic sarcoidosis involving the heart, lungs, liver and spleen.

Case report: A 74-year-old female with atherosclerosis,

diabetes mellitus, ischemic cardiomyopathy and hypertension who died under respiratory insufficiency clinical picture was autopsied at the Center for Pathology and Histology at the University Clinical Center of Vojvodina, using standard autopsy procedures. Routine hematoxylin and eosin–stained slides were prepared, as well as special staines Grocott methenamine silver stain for fungi and Ziehl–Neelsen stain for acid–fast bacilli, in addition. Single and confluent non-necrotizing granulomas were found in the heart, lungs, liver and spleen, composed of epithelioid histiocytes with abundant eosinophilic cytoplasm and a variable number of Langhans and other giant cells and lymphocytes. We also found intracytoplasmic inclusion bodies, Schaumann bodies. Stains for fungi and acid-fast bacilli were negative. Additionally, we noticed a post–myocardial infarction scar of the anterior wall and massive cardiac lipomatosis.

Conclusion: Since there is no targeted therapy for sarcoidosis, early diagnosis and treatment of the disease remain an important priority, especially when it involves vital organs such as the heart.

Keywords: autopsy; granulomas; sarcoidosis.

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Polyarteritis nodosa manifested as hypovolemic shock: an autopsy case

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Objective: Vasculitis involves fibrinoid necrosis and inflammation of blood vessels.

Case report: A 63-year old male presented with nausea, progressive weight loss (15 kg for 6 months), night fever, myalgia, and arthralgia. Blood count showed hypochromic, microcytic anemia without known underlying cause. Polyneuropathy of lower extremities was noted. Colonoscopy, esophagogastroduodenoscopy, and computed tomography (CT) of the abdomen and pelvis were unremarkable. PET CT showed a cystic lesion in the tail of the pancreas. Markers of inflammation were significantly elevated (CRP, SE, ferritin). Antinuclear antibodies (ANA) were present (1:160), whereas other markers, namely antimitochondrial, anti-MPO ANCA, anti-smooth muscle, anti-transglutaminase, and anti-LKM antibodies were negative. Testing for HBsAg, anti-HCV, anti-HIV, quantiferron and PPD test, tumor markers CEA, CA 19-9, CA 72-4, AFP, PSA, CYFRA 21-1, and NSE, was negative. Electrophoresis of urine showed protein in urine. The patient was still losing weight. After thorough workup, the patient deceased. At the autopsy, cachexia was prominent. Retroperitoneal hematoma along with hematoperitoneum and hypovolemic shock was noted due to ruptured dilated blood vessels in the kidneys. Histopathological examination of the kidney and pancreas showed fibrinoid necrosis with transmural inflammation (neutrophils, mononuclear cells) in middle-sized blood vessels. Some walls of blood vessels were nodulary and fibrotically changed with narrowing of the lumen. Diagnosis of polyarteritis nodosa was made.

Conclusion: Clinical presentation of polyarteritis nodosa can be a diagnostic challenge since there is no marker specific for this disease, and it should be considered in differential diagnosis, particularly in cases of progresive cachexia and loss of blood in the body.

Keywords: polyarteritis nodosa, vasculitis, cachexia, shock

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Triploid syndrome – A Case Report

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Objective: Triploidy is a numerical chromosomal aberration with the presence of an extrachromosomal haploid set that can be maternal or paternal in origin. In the first trimester of pregnancy, triploidy is one of the most common reasons of spontaneous abortions.
Case report: A 28-year-old patient, first time pregnant, without previous births and spontaneous or artificial abortions. In the first trimester, routine screening was performed, during which reduced values of pregnancy markers (Free beta hCG 0.047 MoM, PAPP-A 0.230 MoM, NT 1.0 mm). Because of slower growth and development, reduced quantity of amniotic fluid in the 18th week of pregnancy (on ultrasound gestational age was estimated as 16th week), an early amniocentesis was performed. Based on the results of the amniocentesis, it was established that the karyotype of the fetus is 69,XXX. Ultrasound examination revealed that the lateral cerebral ventricles were dilated, and that the transcerebral diameter was reduced with hypoplasia of the cerebellum and agenesia of the vermis.
Conclusion: Based on the results of the amniocentesis and ultrasound examination, triploidy of the fetus was confirmed with hypoplasia of the cerebellum and agenesia cerebellar vermis as well as reduced quantity of amniotic fluid with stagnation in growth and development. Keeping in mind the above data, abortus was indicated, and with the consent of the ethics committee of the Clinic for Gynecology and Obstetrics, the pregnancy was terminated.
In the autopsy report multiple syndactyly on both hands and feet, hypertelorism, micrognathia and agenesia of cerebellar vermis were observed.

Keywords: Triploid syndrome

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Goblet cell adenocarcinoma of appendix, presented with local peritonitis, diagnosed by autopsy

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Objective: Goblet cell adenocarcinomas (GCC) are rare, distinct tumors primarily arising in the appendix, characterized by their unique mix of neuroendocrine and mucinous features, presenting primarily as goblet or signet ring-like cells. Unlike typical neuroendocrine tumors, GCCs manifest a peculiar cellular composition which sets them apart.
Case report: A 72-year-old female presented with acute lower right abdominal pain, nausea, dyspnea, and atrial fibrillation and died on the day of admission. An autopsy revealed an appendix perforation leading to a periappendicular abscess adhering to the parietal peritoneum, with accumulation of pus in the peritoneal cavity, severe pulmonary edema, and bilateral hydrothorax. The histopathological examination showed diffuse alveolar damage indicative of respiratory distress syndrome. The appendix tissue showed large eosinophilic cells with intracellularly localized mucin and peripheral nuclear position. Tumor infiltration extended through the mucosa, submucosa, muscular layer, and subserosa, alongside neutrophilic infiltration across all layers and an abscess within the subserosa. Peritoneal surfaces exhibited extensive inflammation which extended to deeper structures of the abdominal wall, including skeletal muscle. Immunohistochemical staining for Mucicarmine, MUC2, SATB2, CDX2, and Ki67 was positive within the tumor cells, whereas neuroendocrine markers (Synaptophysin, Chromogranin A, and INSM1) were negative.
Conclusion: This case underscores the insidious nature of GCC, which remained asymptomatic until resulting in a fatal outcome through respiratory distress syndrome, propelled by appendicitis and peritonitis. The tumor can be clearly identified under light microscopy as GCC, confirmed by positive staining for MUC2 and Mucicarmine, with the absence of neuroendocrine immunopositivity as reported in

the literature.

Keywords: autopsy, goblet cell adenocarcinoma, appendix

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Mixed Epithelial and Stromal Tumor of the Kidney with Myopericytoma/ Myofibroma as Stromal Component

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Objective: This case report emphasizes the differentiation of the stromal component of Mixed Epithelial and Stromal Tumor of the Kidney.
Case report: A 75-year-old male was admitted to the hospital for surgery due to incidental finding of a kidney tumor during an ultrasound examination of the abdominal cavity. Partial nephrectomy was performed, and the tumor was histopathologically examined. Gross examination revealed a partially cystic tumor with a solid appearance, measuring 26 mm in maximum diameter. Histomorphological analysis showed cysts lined with a layer of cuboidal cells, surrounded by ovarian-like stroma. The solid component of the tumor consisted of bundles of elongated cells with eosinophilic cytoplasm, oval nuclei without atypia, and exhibited angiocentric growth. Nuclear atypia and mitoses were not observed. Focally, a ribbon-like hyalinized matrix was present between the cells. Blood vessels were increased, small, with a split like lumina. Immunohistochemically, the epithelial component showed positivity for CK7, CK20, Pax-8, Pax-2, Gata-3, ER, and PR, while the stromal component was positive for SMA, HHF-35, h-Caldesmon, ER (focally), PR (diffuse), Glut, Reticulin, and Collagen IV. Immunohistochemical stain on CD34, CD31, and CD99 were negative. The diagnosis of mixed epithelial and stroll tutor of the kidney (MEST) with myopericytoma/myofibroma as the stromal component was made.
Conclusion: MEST is a benign kidney tumor, predominantly observed in perimenopausal women, with leiomyoma being the most frequently diagnosed stromal component. Rare cases of malignant transformation have been reported. The prognosis of this tumor is favorable in nearly all cases published so far.

Keywords: Kidney tumors, MEST, myopericytoma/myofibroma, immunohistochemistry

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Unusual site of metastatic clear cell renal cell carcinoma in pyriform sinus - Case report

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Objective: This is a case report of an unusual site for metastatic disease.
Case report: Here we present a 56-year-old female admitted to the hospital due to the presence of granulations in the left pyriform sinus, accompanied with pain in the left half of larynx and hoarseness. A biopsy was performed, and the specimen was sent for pathohistological examination. Histological examination revealed fragments of mucosa lined with squamous stratified epithelium, without atypia, infiltrated by tumor tissue. The tumor was composed of cells with clear cytoplasm and moderate nuclear pleomorphism, forming solid fields and alveolar structures. The stroma was scanty but rich in arborized blood vessels with thin walls. Immunohistochemical analysis revealed positivity for CKAE1/AE3, CAM5.2, Pax-8, Pax-2, Vimentin, and CD10, and negativity for RCC, TTF1, and Thyroglobulin. The morphological findings, in accordance with immunohistochemical analysis, corresponded to a metastasis of clear cell renal cell carcinoma (ccRCC). According the medical documentation, the patient had a left radical nephrectomy four

years ago with the diagnosis of ccRCC; therefore, our diagnosis correlates with the diagnosis of the primary tumor.
Conclusion: ccRCC is the most common type of kidney cancer in adults, accounting for approximately 70-80% of all RCC cases. It is distinguished by the presence of clear cells due to the accumulation of lipids and glycogen within the cells. The most common sites for ccRCC metastasis include the lungs, lymph nodes, bones, liver, brain, and adrenal glands. The pyriform sinus is an extraordinary site for metastatic RCC. According to our knowledge, only one case has been reported so far, highlighting the rarity of this metastasis location.

Keywords: pyriform sinus, ccRCC, metastasis

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A Series of Two Cases and the Role of Immunohistochemistry in Differential Diagnosis

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Objective: The case report is on two distinct instances of urachal carcinoma, and emphasizes the clinical presentation, diagnostic process, and histopathological findings. The cases underline the importance of considering urachal carcinoma in the differential diagnosis of bladder tumors and highlight the distinguishing features from more common malignancies such as colorectal carcinoma infiltrating the urinary bladder.
Case report: Here we present two cases of urachal carcinoma in patients aged 47 and 69. Both individuals, identified as male, were admitted to the hospital presenting extensive hematuria and a confirmed tumor mass in the urinary bladder as evidenced by magnetic resonance imaging. The 47-year-old patient underwent total, while the 69-year-old patient partial cystectomy. Pathohistological examination was conducted on the specimens. Histologically, both tumors were identified as adenocarcinomas, characterized by mucin-producing cells originating from urachal remnants. Immunohistochemical analysis demonstrated focal positivity for CK7, CK20, CDX-2, and diffuse membrane positivity for beta-catenin, establishing the diagnosis of urachal carcinoma of the urinary bladder and ruling out metastatic colorectal carcinoma.
Conclusion: Urachal carcinoma is an uncommon and aggressive malignancy originating from the urachus, a fetal remnant connecting the urinary bladder to the umbilicus. It is crucial to differentiate it from colorectal carcinoma infiltrating the urinary bladder, which is more commonly diagnosed. These cases contribute to the broader understanding of urachal carcinoma's clinical and pathological characteristics, aiding in timely and accurate diagnosis and management.

Keywords: pyriform sinus, ccRCC, metastasis

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Testicular epidermoid cyst of an adult patient: A case report

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Objective: We present a case of testicular epidermoid cyst-a type of prepubertal teratoma that arose in the testis of an adult (postpubertal) patient.
Case report: A 30-year-old man admitted to the University Clinical Center of Vojvodina, urology clinic for surgical treatment of a right testicle tumor, which is manifested by local pain. A scrotal ultrasound was performed, which

revealed a 12x12 mm, well-circumscribed, heterogeneous intratesticular mass in the upper pole of testis. Laboratory evaluation included elevated level of lactate dehydrogenase (LDH-290 IU/l) , alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (beta-HCG) were normal. The patient underwent enuleation of the tumor through a right inguinal incision with intraoperative frozen section which was confirmed benign lesion. The surgical treatment went well and the testicle was preserved. Macroscopic examination revealed a well-circumscribed, whitish, oval mass. It contained yellow-white keratinous material with a hint of concentric of lamellar arrangement. Microscopic analysis on standard HE staining, showed a cyst that is lined with flattened squamous epithelium and contained keratinized debris. The surrounding testis tissue appears normal and did not show any atypia or germ cell neoplasia in situ (GCNIS) which was confirmed by immunohistochemical analysis-PLAP + and SALL4 +.

Based on morphological and immunohistochemical findings, the diagnosis was made: Testicular epidermoid cyst/ Teratoma testis-prepubertal type. The patient was examinated two weeks after surgery and recovered well.

Conclusion: The importance of preoperative suspicion and intraoperative frozen section conformation of benign testicular tumor, especially in postpubertal patient in reproductive age is crucial for prevention of radical orchectomy.

Keywords: teratoma testis, epidermoid cyst, GCNIS

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Spleen metastasis as the first sign of urothelial carcinoma

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Objective: Urothelial carcinoma is carcinoma derived from the urothelial cells lining the urinary tract. The most common sites of bladder cancer metastasis are lymph nodes, bones, lung, liver and peritoneum.

Case report: A-70-year old male came to abdominal surgeon due to spleen haematoma that had been diagnosed in other hospital. The patient complained of abdominal pain. After routine preoperative preparation, splenectomy was performed and intraoperatively subcapsular haematoma was registered with capsular rupture and haematoperitoneum. The specimen was sent to pathology. Macroscopically, the spleen was with ruptured capsule and with haemorrhage areas, but serial cuts showed focal nodular change in the parenchima measured 35x35x20 mm, solid, round shape and greyish-whitish colour. Standard hematoxylin-eosin stanings showed tumor tissue made up of atypical cells with an increased mitotic index and visible pathological mitoses arranged in nests and solid areas with focal necrosis. Immunohistochemically, expression of markers CK7, GATA3, p63 and Uroplakin was registered, CK20 was focally observed and PAX8 negative so the first differential was urothelial carcinoma. The surrounding splenic parenchyma has the usual histomorphological features with areas of hemorrhage.

Conclusion: Malignancies metastasizing to the spleen are very rare, isolated metastases especially. Spleen exhibit many immune functions, including the development of immunogenesis and tolerance, so it can be possibly the key in inhibiting the development of spleen metastases. In order to understand those inhibiting mechanisms that prevent metastatic deposits in the spleen, further research are required.

Keywords: urothelial carcinoma; metastasis; spleen;

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Neuroendocrine carcinoma of the cervix: a case report

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Objective: Neuroendocrine neoplasms of the gynecological tract comprise less than 2% of all gynecological cancers.
Case report: A 72-year-old woman presented with profuse postmenopausal vaginal bleeding. She reported dull pain in lower abdomen that started 2 years ago. More than a month ago, she presented with nausea and vomiting and pain in her lower back. She lost 10 kg in past 3 months. Multidetector computed tomography showed multiple deposits in the liver, presumably metastatic deposits. In the pelvis, a tumor mass of 98×74×71 mm infiltrated the cervix, the uterus along with adnexal structures, and parietal wall structures. Biopsy of the cervix showed tumor cells infiltrating the cervix in a diffuse arrangement with hyperchromatic nuclei, scarce cytoplasm, overlapping of the nuclei, and "crash artefact" with extensive areas of tumor necrosis. Tumor cells were positive for CKAE1/3 (scattered, dot-like in the cytoplasm), EMA, INSM1, synaptophysin, CD56, p16 (diffusely and strongly), and p53 (weakly), and negative for CK5/6, CD45 (LCA), p63, p40, CK7, CK20, CDX-2, chromogranin, TTF-1, PAX8, mCEA, ER, and PR. Ki-67 was positive in more than 90% of tumor cells. Mitotic activity was 21/10 hpf. Diagnosis of high-grade neuroendocrine carcinoma of the cervix was made. The patient passed away a day after diagnosis.
Conclusion: Neuroendocrine carcinomas of the cervix are very aggressive tumors with poor prognosis. Due to their rarity, those neoplasms can present a diagnostic challenge, especially in the context of limited pathologist's experience.

Keywords: cervix, neuroendocrine carcinoma, immunohistochemistry

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Echinococcal cyst of the uterus: a rare site of presentation

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Objective: Echinococcus granulosus is an anthroponosis most commonly involving the liver and lungs. The female genital tract is an extremely rare site of development. We aimed to report a case of an echinococcal cyst (EC) discovered in the uterus.
Case report: A 64-year-old postmenopausal woman presented with a three-month history of persistent lower abdominal discomfort and previous liver EC in 2022. Transvaginal ultrasound showed a thickened endometrium measuring 12mm and an unilocular cystic formation arising from the anterior wall of the lower uterine segment, approximately 50x40mm in greatest dimension. Magnetic resonance imaging (MRI) of the pelvis strongly indicated EC of the uterus. Serum tumor markers were unremarkable. The patient underwent explorative curettage due to endometrial thickening and microscopy revealed an endometrial polyp. Serological results with the enzyme-linked immunosorbent assay (ELISA) and confirmatory testing by Western blot were positive for Echinococcus granulosus. The surgical approach was a classical abdominal hysterectomy with bilateral adnexectomy after three cycles of albendazole therapy. The pathological assessment showed scoleces with a row of hooklets, and periodic acid-Schiff (PAS) staining accentuated the laminated layer. The patient is currently receiving a fourth cycle of albendazole therapy.
Conclusion: Awareness of extrahepatic manifestations of EC is very important since unusual sites of involvement are possible. The correct diagnosis demands a detailed clinical examination of pelvic masses, especially in endemic areas supported by serological tests and histopathological examination.

Keywords: uterus; Echinococcus granulosus; echinococcal cyst; diagnosis.

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Histomorphology pattern specific for certain molecular alterations in uterine leiomyoma

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Objective: Leiomyoma with (fumarate hydratase) FH deficiency manifests certain histological characteristics which should arouse suspicion for further immunohistochemical analysis and diagnosis confirmation. Patients with such leiomyomas have a five to six times increased risk for the development of aggressive forms of renal cell carcinomas. Detection of FH-deficient tumors is very important because of their hereditary association.
Case report: We represent two uterine leiomyomas with rare histomorphological characteristics, significant for prognosis and further treatment of such patients. Patients were 25 and 28 years old and both were treated at the gynecological clinic for an incidental finding of uterine leiomyoma. They have similar benign clinical and imaging presentations. Microscopic examination showed marked nuclear atypia, intracellular eosinophilic globules, and abnormal intratumoral vessels making a doubt for specific leiomyoma subtypes, which have predictive significance for additional hereditary cancer syndromes. Considering specific histomorphological characteristics we did FH and Succinat dehydrogenase, subunit B (SDHB) immunohistochemical analysis which confirmed metabolic deficiency in their tumor cells. Based on the combined histomorphological and immunohistochemistry results we suggested a diagnosis of uterine leiomyoma with FH deficiency.
Conclusion: Uterine leiomyomas with such characteristics are rare and easily unrecognized. They have predictive significance because their specific mutation point to additional hereditary cancer syndromes and the need for further examinations.

Keywords: leyomoma; fumarate/succinat deficiency

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Uterine adenomatoid tumor: a case report of an incidental finding

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Objective: Adenomatoid tumors are uncommon benign tumors most frequently seen in the genital tract of both sexes. There are usually incidental findings in the female genital tract, most often located in the fallopian tube and uterine serosa, but these are not so common in the myometrium.
Case report: A 50-year-old female attended the gynecology clinic with lower abdominal pain, malaise, anemia, and, for the past two years, menorrhagia. Since 2005, she has known about the existence of fibroids. Now, ultrasound confirms an enlarged uterus with multiple fibroids. The patient underwent a hysterectomy, and the specimen was sent for histopathological analysis. At the gross examination, the uterus measured 17x9x11 cm. In the myometrium, multiple circumscribed masses were found, with a gray to white cut surface and the largest diameter of 7 cm. Histological examination showed interspersed smooth muscle fascicles with inconspicuous nuclei (Dx: Leiomyomas). One histological specimen contained, beetween the muscle cells, a focus with tubular, pseudovascular and gland-like structures lined by flat to cuboidal cells. There is no nuclear atypia, mitotic activity, or necrosis. Lining cells expressed immunoreactivity for CK AE1/ AE3, Calretinin, and D2-40 and were negative for PAX8 and CD34. Based on the histopathological and immunohistochemical findings, the diagnosis of adenomatoid tumor of the uterus was established.
Conclusion: The true incidence of uterine adenomatoid tumors may be significantly higher. Pathologists should be aware of these tumors and advised to interpret morphologic

findings together with the results of a concise immunohistochemistry panel to avoid misdiagnosing.

Keywords: adenomatoid tumor, leiomyoma, uterine neoplasma, mesothelium

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Cervical Squamocellular Carcinoma with unusual presentation

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Objective: Tumor growth in cervical tissue was mostly locoregional in the stroma as a destructive, infiltrative pattern. In some cases, a growth pattern can be superficial with intraepithelial progression. A very uncommon and rare pattern is the proximal spreading of squamocellular carcinoma (SCC) with endometrial and adnexal colonization.
Case report: We represent microinvasive SCC with secondary endometrial and adnexal involvement, whereas the most invasive cancer behavior was in tubal segments. The patient had severe recidivate cervical epithelial dysplasia which after two years progressed to microinvasive cervical SCC. After radical hysterectomy micro-invasive cancer was confirmed with deep of invasion less than 1mm. Preoperative imaging did not detect neoplastic features in the endometrium or adnexal structures. Histomorphology examination showed unexpected SCC in the proximal uterine and adnexal structure. The mostly whole upper endometrium was colonized. We noticed micro-invasive focuses in the myometrium very similar to those in cervical tissue. Ovaries were without malignant features. In the right tubal epithelium, we found segments with remarkable neoplastic intraepithelial in situ lesions. In the extended sections, we noticed micro-invasive SCC focuses in the tubal wall. However, unlike SCC, in the cervix, here we additionally observed an invasion of lymphatic and vascular vessels.
Conclusion: Such unusual presentation of cervical SCC should be highlighted because it could be easily mistaken with primary adnexal tumors. This pattern of tumor growth should be especially considered for patients who are proposed for sparing surgical procedures. A detailed and multidisciplinary approach for every patient is very important because unpredictable cases are present.

Keywords: cervical cancer; superfitial spreading

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Adenosarcoma cervicis uteri- case report

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Objective: Adenosarcoma is a relatively rare tumor (about 10% of all gynecological tumors), composed of a malignant mesenchymal and a benign glandular component. During the routine histopathological examination, cervical curettage with endocervical polyps occurs very often, but is every polypoid structure always really only a polyp? In this case, we emphasize the significance of adequate histopathology analysis of material obtained by exploratory curettage considering sarcoma features in differential diagnosis.
Case report: We present a 38-year-old female with metrorrhagia and a clinically determined usual endocervical polyp. Histomorphological analysis showed tubular, slightly elongated endocervical glands, lined with uniform endocervical epithelium without signs of atypia. In some parts glands were discreetly compressed lumens. Endocervical stroma was mostly uniform and focal with remarkable fibrovascular spaces. Detailed analysis of stromal parts

around the glands showed a discreet increase of cellularity, without remarkable cytonuclear pleomorphism and without conspicuous increased number of mitotic figures. Such stromal features and slightly distorted glands indicate suspicious malignant lesions. Immunohistochemical analysis confirmed our doubts. The patient underwent a radical hysterectomy with bilateral adnexectomy and bilateral pelvic lymphadenectomy. Examination of the operative material confirms the definitive diagnosis of adenosarcoma of the cervix.

Conclusion: Adenosarcomas arising from the cervix can be clinically and pathologically very often confused with a benign cervical polyp. The described endocervical stromal pattern should raise doubt for neoplastic stromal features, which is crucial for further treatment.

Keywords: adenosarcoma; polypus; cervix

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Cotyledonoid dissecting leiomyoma of the uterus with intravascular growth: a case report

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Objective: Uterine leiomyomas have numerous morphologies, among which cotyledonoid dissecting leiomyoma, also known as Sternberg tumor , is a very unusual benign form of leiomyoma with an uncommon macroscopic appearance, often confused with malignant or non-uterine lesions.

Case report: A 50- year old woman presented with abdominal pain and irregular menstrual cycles. Physical examination detected an abdominal mass. A CT scan was performed, and revealed inhomogeneous, well-vascularized formation in the pelvis, 14 cm in diameter, in contact with both sides of the uterine body without clear demarcation. The patient underwent radical hysterectomy with bilateral adnexectomy. Grossly, uterus was enlarged due to presence of intramural solid-cystic nodule measuring 6cm which dissects the myometrium to the serosal surface and descends in a form of paracervical multicystic formation downward towards the vagina. Histologically, tumor presented as a bundles of oval and spindle-shaped smooth muscle cells without elements of citologic atypia. Atypical mitotic figures and fields of necrosis were not observed. Tumor tissue dissected myometrial fibers, with elements of stromal edema, hydrops changes, cystic degeneration and hyalinization. The described cells in a circular arrangement surround blood vessels with thickened walls with foci of intravascular propagation. Tumor cells showed SMA, Desmin, Caldesmon, Estrogen receptor positivity and CD10, AE1/AE3, HMB45, Melan-A negativitiy. Ki-67 proliferative index was less than 5%.

Conclusion: It is important to be aware of this entity to prevent overly aggressive treatment of this benign smooth-muscle neoplasm.

Keywords: cotyledonoid dissecting leiomyoma; leiomyoma; leiomyoma variant; sternberg tumor.

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Agressive angiomyxoma of uterus – A Case Report

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Objective: Objective was to show case of a rare uterine tumor, agressive angiomyxoma.

Case report: A 42 year-old female with the symptoms of lower abdominal and back pain was admitted to CGO. She

stated that the symptoms had started two weeks before admission. Preoperative ultrasound showed a tumor in the lower part of uterine body, initialy described as leiomyoma. From personal history we found out that the patient was nulliparous, with regular menstrual cycles and without any known family history of gynaecologic diseases. Surgery was indicated and tumor mass was partlialy excised. On frozen sections it was decided that it is necessary to postpone final diagnosis until standard HE staining would be done. Grossly tumor was described as multiple, soft, yellowish fragments, measuring 13,5cm in total diameter. On standard HE staining tumor was described as myxoid, with oval cells that had elongated eosinophilic cytoplasm and with middle to large blood vessels with thick muscular, partly hyalinized walls. Immunohistochemicaly tumor cells were: Desmin+; SMA+; CD34-; Caldesmon-; ER+; PR-/+; S100-. Following these findings a final diagnosis of deep aggressive angyomixoma was made. Two month after the initial surgery hysterectomy with bilateral salpingectomy, partial omentectomy and peritoneal biopsy was permormed and tumor tissue was identified in the cervix.

Conclusion: Aggressive angiomyxoma is a rare type of mesenchymal tumor with uncertain behavior, usually located in vulva and/or pelvic cavity and occuring mostly in reproductive age women. Tumor has a high tendency for recurence but usually very small metastatic potential.

Keywords: Aggressive angiomyoxoma, uterus

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Disseminated peritoneal leiomyomatosis: A case report

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Objective: To show a case of disseminated peritoneal leiomyomatosis (DPL).

Case report: 38-year-old female, gravida 5 para 2 (two cesarean deliveries), with a history of primary hypertension, was admitted for cesarean delivery due to oligohydramnios and intrauterine growth restriction at 34 5/7 weeks. Following relaparatomy multiple small nodules up to 5 mm in diameter were noted upon anterior uterine wall and adjacent peritoneum. Biopsy of the nodules on standard HE staining showed well-circumscribed masses consisting of intersecting fascicles of monotonous spindle cells with eosinophilic cytoplasm, cigar-shaped nuclei, and fibrous stroma with foci of hyalinization. Spindle cells were immunohistochemically positive for SMA, Vimentin, WT1, Desmin, and Estrogen, while the Ki67 proliferative index was extremely low. Microscopic and immunohistochemical analyses together with clinical presentation confirmed diagnosis of disseminated peritoneal leiomyomatosis.

Conclusion: Disseminated peritoneal leiomyomatosis is a rare benign disease characterized by the presence of multiple smooth muscle nodules scattered throughout the peritoneal cavity thus mimicking malignancy. It predominantly affects women during their reproductive age. The development of DPL is affected by genetic factors, steroid hormones, metaplasia of mesenchymal stem cells, and iatrogenic factors. Latter one, such as the frequent use of laparoscopic power morcellation nowadays has increased the incidence of DPL. It is usually asymptomatic or presented with non-specific symptoms such as abdominal pain and distension, therefore in most cases is being discovered incidentally. The risk of malignant transformation is low, but as no spontaneous regression has been reported treatment is required with surgical resection being the main choice.

Keywords: Estrogen, disseminated peritoneal leiomyomatosis, DPL, morcellation

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Malignant Brenner tumor – Two cases of rare ovarian neoplasm

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Objective: Objective was to show two cases of rare malignant Brenner tumor (MBT).
Case report: A 62 year-old with symptoms of lower back and abdominal pain was admitted to CGO. On MRI and ultrasound complex left adnexal mass was seen. Left adnexectomy with partial omentectomy was performed and on frozen sections Brenner tumor was suspected. Tumor was mostly solid white-yellowish with smaller cystic formations and calcifications, measuring 13cm. Pathohistologicaly tumor was composed of highly atypical cells resembling transitional epitelium arranged in solid sheets, nests, cystic and papillary formations with atypical mitoses. Tumor cells were GATA3+, p63+, ER-, PR-, p53- with extremely low Ki67. Pathohistological and immunohistochemical analysis confirmed MBT (FIGO stage IA). Two months after initial surgery, hysterectomy with right adnexectomy, omentectomy and left inguinal lymph node extraction was performed with no evidence of disease disemination.
A 78 year-old with symptoms of uterine prolapse and reccurent bleeding was admmited to CGO. Following complex right adnexal mass on ultrasound, adnexectomy was performed and malignant tumour was confirmed on frozen sections. Additional hysterectomy, left adnexectomy and omentectomy were performed. Tumor was described as multilocular cystic formation measuring 6cm with papillary proliferations. Pathohistologicaly tumor was composed of highly atypical cells resembling transitional epitelium, arranged in cystic formations, solid nests and papillary proliferations with atypical mitoses and foci of mucinous and squamous differentiation. These findings confirmed diagnosis of MBT with no evidence of disease disemination (FIGO stage IA).
Conclusion: Malignant Brenner tumor is a rare ovarian neoplasm with unclear origin cell and favourable prognosis in early stages.

Keywords: Malignant Brenner tumor

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Tubular adenoma of the breast: a case report

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Objective: Tubular adenoma of the breast is a rare fibroepithelial tumor accounting for 0.13-2.8% of all benign breast lesions, most commonly discovered in young women. It typically presents as a solitary, palpable, well-circumscribed mass, but clinical and radiological features are often nonspecific. Microscopically, it is characterized by densely arranged round to oval glandular structures lined by inner epithelial cells and an outer myoepithelial layer surrounded by a thick stroma. These lesions are not associated with increased malignancy risk and surgical excision is the treatment of choice.
Case report: A 43-year-old woman presented with a firm, mobile, palpable mass in the lower outer quadrant of the left breast which was surgically excised. Gross examination of the specimen showed a grayish, well-circumscribed, lobulated tumor measuring 10 x 9 x 5 mm. Histopathologically, it consisted of a well-defined proliferation of round and uniform tubular structures with a basal myoepithelial layer, lined by an inner layer of regular epithelial cells, with a surrounding scant fibrovascular stroma. The luminal cells exhibited immunoreactivity for AE1/AE3, while the myoepithelial layer demonstrated positive expression for p63, Calponin, CD10, and SMA, confirming the diagnosis of tubular adenoma.
Conclusion: Tubular adenomas of the breast are rare, benign lesions that might be challenging to distinguish from other benign or malignant breast masses without histopathological confirmation. Acquiring a comprehensive understanding of the pathological and immunohistochemical features of this uncommon neoplasm is essential for accurately determining the appropriate diagnosis.

Keywords: breast, myoepithelial cells, tubular adenoma

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Myofibroblastoma of the breast in a male patient – a case report and literature review

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Objective: Myofibroblastoma, a rare benign stromal breast tumor, is primarily diagnosed in elderly men and postmenopausal women. Clinically, it presents as a palpable, firm, mobile mass, but may also be discovered incidentally. Mammography shows myofibroblastomas as oval or lobulated, well-defined masses, while sonography shows variable echogenicity. Myofibroblastomas have various histopathological variants: collagenous, cellular, infiltrative, myxoid, lipomatous, epithelioid, and deciduoid types. The classic histopathological appearance involves bundles of spindle cells separated by broad bands of hyalinized collagen stroma. Immunohistochemically, most myofibroblastomas are positive for vimentin, desmin, actin, CD34, CD10, estrogen, progesterone, and androgen, and negative for cytokeratins, EMA, S100, HMB-45, and CD117. The treatment of choice is wide surgical excision, and the prognosis is excellent, with no malignant potential nor risk of recurrence.
Case report: A 62-year-old male presented for a clinical examination due to a palpable, mobile tumor mass measuring approximately 4 cm at the junction of the upper quadrants of the left breast. Mammography revealed a lobulated tumor shadow measuring 42 x 29 mm at the indicated location. The lesion was surgically excised. The histopathological examination revealed a stromal tumor that was positive for CD34, caldesmon, Bcl-2, desmin, actin, estrogen, progesterone, and androgen, but negative for CKAE1/AE3, S100, and p63, leading to the diagnosis of cellular myofibroblastoma.
Conclusion: Since the clinical and radiological features of myofibroblastoma are nonspecific and differential diagnoses encompass a wide spectrum of breast conditions, histopathological and immunohistochemical verification after core biopsy and/or excision is crucial for establishing the diagnosis of this rare entity.

Keywords: male breast tumors, mesenchymal tumors, myofibroblastoma

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Ductal carcinoma in situ within fibroadenoma - case report

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Objective: Fibroadenoma (FA) is a common, benign, biphasic tumour composed of stromal and epithelial elements. This report aims to present a rare case of ductal carcinoma in situ (DCIS) within a fibroadenoma.
Case report: A 37-year-old woman presented with a tumour in both breasts that was classified as BI-RADS 4A on mammography. A core needle biopsy of the tumour in the right breast revealed that it is a cellular complex fibroadenoma. A tumorectomy was performed, and a gross examination showed a well-encapsulated tumour measuring 18 mm in diameter with a grey-white, slightly firm, and lobulated cut surface. The histological diagnosis was low-grade DCIS within a FA. The stromal component was benign, however the epithelium consisted of ductal cell proliferation with cribriform and solid growth patterns. Immunohistochemical examination revealed that myoepithelial cells were positive for p63 and calponin. Tumour cells had an immunoprofile of estrogen receptor (ER) 8 and progesterone receptor (PR) 7. Because of the positive surgical margin, a subcutaneous mastectomy was performed, followed by ex tempore examination of two sentinel lymph nodes, both of which were without metastases.
Conclusion: Although FAs are a common subtype of benign tumours, they can be associated with DCIS. This case report, along with others like it, should increase awareness and encourage physicians and pathologists to consider this entity.

Keywords: DCIS, fibroadenoma, breast tumour

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Breast lumps during pregnancy – differential diagnosis: a case report

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Objective: Pregnancy is a special condition in which an organism undergoes various changes. Breast lumps occurring during pregnancy are usually small in size about 3cm, painless, solid, well-circumscribed, and mobile nodule masses that tend to grow slowly. Generally, they represent a diagnostic challenge given the reduced sensitivity of both clinical examination and radiological findings, due to the high density of the breast tissue. Elevated hormone levels during pregnancy stimulate the proliferation of blood vessels and glandular tissue while reducing stromal tissue. This case aimed to report a lactating adenoma and distinguish this entity from other lesions during pregnancy.
Case report: We present a case report of a 34-year-old female with lactating adenoma. Her clinical presentation included a change in the breast in the third trimester of pregnancy. A circumscribed, painless, and mobile mass was discovered with no additional findings. Pathohistological examination of specimens revealed hyperplastic lobules with glandular formations showing more or less abundant hobnailing phenomena with intraluminal eosinophilic secretions and inconspicuous myoepithelial cell layer separated by delicate fibrovascular stroma. The immune profile of the preparations showed a positive reaction of CK14 and p40 markers, which proved the presence of myoepithelial cells and distinguished this case from other breast lesions.
Conclusion: Although, only 3% of solid breast masses are represented as breast carcinomas, surgical extirpation along with the following pathohistological and immunohistochemical analysis must be conducted to avoid overdiagnosing and distinguishing the benign lesions, such as lactating adenomas or fibroadenomas, from malignant origin of the tumor.

Keywords: lactating adenoma; breast; pregnancy; case report

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Idiopathic granulomatous mastitis: a case report

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Objective: Idiopathic granulomatous mastitis (IGM) is a rare chronic inflammatory disease of the breast of unknown etiology and it is a diagnose of an exclusion so the other granulomatous inflammation's causative agents must be excluded.
Case report: A 37-years-old patient complained of redness, warmth and swelling of the left breast. On examination there was a palpabile lesion of 3.5cm in diameter and the physician recommended MRI of the breast. Twenty days later, she came back with worsening symptoms, the lesion was punctated and sent for microbiology examination and it was sterile. In MRI, the inferior outer quadrant lesion was described as non-mass post-contrast signal intensity enhancement (PCSIE) measured 7 cm in diameter, which contained multiple ring-like zones of PCSIE and non-homogenic areas of edema. The retroareolar ducts were accented, the nipple was withdrawn with local skin edema. Core needle biopsy was performed and showed that breast lobular architecture was destroyed by presence of multiple granulomas. The centers of described granulomas contained focal microabscesses with neutrophils and eosinophils admixed with necrosis or there were granulomas without central necrosis. All of described granulomas were made of Langhans giant cells, epitheloid cells and foamy macrophages with monunucelar collarettes, all separated with fibrous tissue. PAS and Ziehl Neelsen stain showed no microorganisms present, so diagnose was made by excluding all granulomatous inflammation causes.
Conclusion: IGM can mimic breast cancer clinical signs so

CNB of lesion can be useful tool for distinction between benign and malignant lesions but also rare diseases.

Keywords: Breast Diseases, Granulomatous Mastitis, Inflammation

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Myocardial infiltration and acute abdominal pain as a result of un-recognized diffuse large B –cell

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Objective: Diffuse large B-cell lymphoma (DLBCL) represents aggresive lymphoproliferative desease with frequent extranodal presentation. This desease represents almost 30% of all globally diagnosed lymphomes. Most commonly infiltrated extranodal organes are stomach, then structures of waldeyer ring, then bones, testicles, ovaries, spleen, sallivatory glands, liver, kidney, and rarely other organs. In rare cases comes to infiltration of heart muscle by DLBCL. Choice of treatment is systemic immunochemotherapy based on Rituximab.
Case report: Female patient aged 54 years becomes hospitalized at gastrointestinal clinic of UCC of Nis due to acute abdominal pain, and shortly after all clinical protocols dies. After revision of medical documentation, we have discovered that she was pshychiatric patient, under which circumstances, hers presentation of symptoms is questionable. Autopsy has discovered presence of large quantities of free thoracic and abdominal liquid, and macroscopic detectable organ changes. Pathohystologic mycroscopic examination discovered tissue infiltration of almost all organs, and even heart muscle, giving the diagnose of non-Hodgkin large B-cell lymphoma, not otherwise specified (NOS), confirmed by immunohistochemistry cell markers: Vimentine -, CD20 +, antiCD45 +, CD163 +, CD38 -/+, CD56 -/+, Lambda +, Kappa +, CD3 +/-, CD68-, CD117-, S100-, CKAE1/AE3 - .
Conclusion: From this case report we can concur that DLBCL can remain undetected because of polymorphic unspecific clinical presentation and in rare cases even heart muscle can be affected.

Keywords: DLBCL, heart infiltration

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Sporadic Burkitt's lymphoma of the large intestine in elderly patient, case report

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Objective: Burkitt's lymphoma is highly aggressive non-Hodgkin's lymphoma. Three forms are distinguished: endemic, sporadic and the immunodeficiency associated. The sporadic form is the most common lymphoma in USA and Western Europe and accounts for less than 1% of all adult non-Hodgkin lymphomas. It is most often diagnosed in children and young adults. It is the most common form of lymphoma in the pediatric population.
Case report: A 77-year-old female patient was operated for ileus. The distal part of the ileum, the cecum with the appendix and the ascending colon were removed. A 9.5 cm circumferential ulcero-infiltrative tumor was found in the area of the cecum with complete infiltration of the appendix and the adjacent part of the small intestine. Ileocecal valve is preserved. In the surrounding adipouse tissue 17 lymph nodes were found, without tumors. Immunohistochemical stainings were positive for: CD 20 and BCL 6. Immunohistochemical stainings were negative for: CD3, cyclin-D1 and BCL2. The proliferative index (Ki-67) was 100%. After 40 days, the patient was operated again for ileus. A 110 cm long small intestine was surgically removed with fibrinous deposits on the serosa and diffuse and nodular infiltration by lymphoma cells. The patient died during postoperative

recovery.

Conclusion: Our case indicates that sporadic Burkitt's lymphoma of the large intestine can occur at an atypical age. Ileus was an absolute indication for operative treatment of the patient without a previous pathohistological diagnosis. Rapid and extensive postoperative disease progression indicate that operative treatment in these patients is a poor choice of treatment.

Keywords: Burkitt's lymphoma, large intestine, sporadic, ileus, elderly patient

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Unusual EMA and pan-keratin negative epithelioid sarcoma

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Objective: Epithelioid sarcoma is a rare malignant tumor that is positive for EMA and pan-keratin, with frequent loss of SMARCB1 expression.

Case report: We present the case of a 65-year-old patient with lower back pain and an ultrasound scan that showed an expansive formation in the abdomen with a diameter of 5.2 cm. Cytopuncture and core biopsy were performed under CT control. Cytologically, the smear showed a monomorphic population of poorly differentiated malignant cells. The cells formed clusters within which a homogeneous substance could be seen. Immunocytochemistry showed weak S100 positivity, while CK7 and CK20 were negative. It was concluded most likely to be a tumor of mesenchymal origin. Histology showed clusters of uniform cells with scant cytoplasm, which were immunohistochemically negative for S100, melan A, CD45LCA, CKAE1/AE3, EMA, CD 138, factor VIII, desmin, SMA, MSA, chromogranin and synaptophysin, while CD99 was positive. For additional processing, prof. Abbas Agaimy, MD, PhD, (University Hospital Erlangen, Germany) was consulted, who was of the opinion that „this is a SMARCB1-deficient malignant neoplasm with rhabdoid features and an unusual complete absence of EMA and pan-keratin expression." He was also of the opinion that „primary tumor site in other organs should be excluded, after which the diagnosis of keratin-poor epithelioid sarcoma can be accepted." The patient underwent surgery and adjuvant chemoradiotherapy, which led to remission.

Conclusion: Further research is needed to better understand the role of SMARCB1 loss of expression in tumor immunogenicity, aiming to develop optimal immunotherapeutics and new treatment strategies for these aggressive tumors.

Keywords: core biopsy, cytopuncture, epithelioid sarcoma, SMARCB1

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Inflammatory myofibroblastic laryngeal tumor-case report

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Objective: Inflammatory myofibroblastic laryngeal tumor (IMT) is rare benign process which appears in lungs, but it is can also be diagnosed in other localizations such as ocular orbit, spleen, larynx. Although these tumors are histologically benign, they have tendencies to become locally aggressive, growing rapidly and and can be manifested by progressive symptoms. Main treatment is surgical excision. IMT is most often found on the vocal cords, even though it can be seen in the entire larynx.

Case report: Patient is 61 – year old female, admitted to the emergency center because of severe stridor breath-

ing. Patient reported that symptoms persisted for several days with worsening. The patient is a heavy smoker for 30 years, 30-40 cigarettes per day. Laryngeal imaging showed vocal cord swelling, myxomatotic tissue change, with sufficient breathing space, but due to inflammatory process, breathing is obstructed. Laryngomicroscopy with left and right vocal cord biopsy revealed presence of proliferation of spindle cells, localized in partially myxoid and collagenized stroma, and inflammatory plasmacytes and lymphocytes. Immunohistochemical analysis showed expression of vimentin and SMA, and Ki67 showed proliferate activity in about 10% of nuclei of tumor cells which confirmed pathohistological diagnosis of IMT.

Conclusion: Inflammatory myofibroblastic laryngeal tumor is a very rare neoplasm which can mimic malignant process. Immunohistochemistry plays main role in IMT diagnosis. Main choice of treatment is surgical excision with distance of surgical margins of at least 5mm each. Clinical follow-up is necessary with the aim of early detection of recurrence of the tumor.

Keywords: Inflammatory myofibroblastic tumor, IMT, larynx.

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Uniqe presentation of primary retrperitoneal PEComa with lymphoma-like symptoms: A case report

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Objective: Perivascular epithelioid cell tumor (PEComa) belongs to a family of rare mesenchymal neoplasms that can arise in various organs and are composed of cells that have myomelanocytic differentiation. We present histology and immunofenotype of PEComa of uncertain malignant potential.

Case report: A 73-year-old female patient presented with elevated body temperature, night sweats and loss of 20kg of body weight during a couple of months. CT scan found 162x89mm retroperitoneal mass compressing left kidney and spleen. Surgical biopsy was performed and diagnosed as granular cell tumor. Six months later MRI showed mass size increase to 200x120mm. Surgical excision was performed.

Tumor weighted 2011g, with dimensions of 240x190x80mm. Capsule was intact, focally thickened with solid and cystic parenchyma, containing extensive areas of hemorrhage and necrosis.

Histological examination showed moderately to prominently atypical, polygonal cells with hyperchromatic nuclei and abundant, eosinophylic cytoplasm that focally contains dark pigment, in trabecular and solid arrangement. Mitotic count is low. Stroma is scant with thin walled blood vessels, without lymphovascular invasion. The immunohistochemical staining showed positivity to Vimentin, CD68, NSE, HMB45, Melan-A, CD117, CDK4 and Desmin, with no immunoreactivity to PAX8, ER, SMA, CD163, SOX-10, CD34, Calretinin, Inhibin, myoD1, MDM-2, CK20, CK7, PanCK, S-100, Synaptophysin, Chromogranin. Ki-67 proliferation index was expressed in 5% of tumor cells.

Conclusion: PEComas are rare tumors with variable malignant potential. Though surgical resection is the treatment of choice for PEComas, some studies showed potential benefits to using mTOR inhibitors as target treatment or radiation courses for patient at higher risk to prevent metastases or recurrence.

Keywords: PEComa, retroperitoneum, immunohistochemistry

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An incidental finding of a desmoid tumor in an inguinal hernia

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Objective: Desmoid tumors are benign neoplasms originating from connective tissue. The etiology of desmoid tumors remains unclear, although they are frequently associated with genetic predispositions, hormonal factors, trauma, and previous surgical interventions. They present diagnostic challenge due to their rarity, diverse clinical manifestations, locally aggressive behavior, and high recurrence rates

Case report: A 46-year-old male presented with a noticeable bulge in the right groin for the past two months. Clinical examination revealed a soft abdomen with a palpable, painless right inguinal hernia, which was reducible. The patient underwent hernioplasty. Pathologist received a tissue specimen measuring 6.8x6.0x0.2 cm. Gross examination revealed a whitish, spherical formation measuring 3.0x0.8x0.6 cm within the hernia sac. Histological examination revealed unremarkable mesothelium, beneath which was unremarkable connective tissue with blood vessels lined by normal endothelium. The above-described spherical lesion revealed spindle cell proliferation without atypia or mitosis, embedded in collagenous stroma with a partially keloid appearance. Immunohistochemical staining was positive for Smooth Muscle Actin, Beta-Catenin (nuclear and cytoplasmic), and, focally, Desmin. Other markers including CD34, ALK, S100, Calretinin, Cytokeratin AE1/AE3, and Cytokeratin 5/6 were negative. Fluorescence in-situ hybridization analysis for MDM2 gene did not show amplification. The lesion was diagnosed as a desmoid tumor.

Conclusion: Desmoid tumors can be challenging to manage due to their unpredictable behavior, and variable response to treatment modalities including observation, surgery, radiotherapy, and systemic therapy. Management should involve a multidisciplinary approach due to many treatment options and a crucial clinical follow up after treatment.

Keywords: Desmoid tumor, Fibromatosis, Hernia, Immunohistochemisty

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Kaposi sarcoma: a case report

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Objective: Kaposi sarcoma (KS) is an uncommon angioproliferative endothelial neoplasm with distinctive clinicopathological, epidemiological and immunophenotypic characteristics. KS is the most common neoplasm in people with human immunodeficiency virus (HIV) infection. Its pathophysiology has been associated with the presence of a member of herpes virus type 8 family.

Case report: A 47-year-old male resorted to an outpatient clinic complaining of disseminated dermatosis. The patient referred multiple skin lesions that appeared two months earlier. Lesions were presented as erythematous livid plaques on the fourth finger of the left foot with rapid progression in a month to the trunk, right arm, right thigh, left lower leg, pubic region and right groin. HIV serology was positive. The method used for detection was chemiluminescence on Abbott's Alinity and the results were 1117.34 S/CO (reference value >1.00 S/CO). The patient also had positive anti-VZV IgG, anti-CMV IgG, anti-Toxoplasmosis IgG, anti-HBc, anti-HBs and TP antibodies.

A skin biopsy was performed as an excision biopsy from the right thigh. Histological examination demonstrated discrete nodules composed of intersecting fascicles of uniform spindle cells, intervening blood-filled spaces between spindle cells (slit-like and sieve-like). Endothelial cells formed a disorganized monolayer with dissolution of colla-

gen fibers. Immunohistochemistry was positive for CD34, CD31, D2-40, HHV8 with Ki-67 above 20%. These findings are compatible with pathological nodular stage KS.

Conclusion: In the Balkan countries the prevalence rate of HIV-1 infection is low, under 0.1%. Diagnosis of KS by histopathological examination is the gold standard and we hereby demonstrate the importance of the right diagnosis.

Keywords: AIDS-related Kaposi sarcoma, HIV, Human Herpesvirus 8, Kaposi sarcoma

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Giant cell tumor of bone during pregnancy resembling primary bone sarcoma: A case report

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Objective: Giant cell tumor of bone (GCTB) is a rare, locally aggressive bone tumor with only 32 cases reported during pregnancy or postpartum. We report this case to emphasize the importance of a multidisciplinary approach in the diagnostics and management of GCTB during pregnancy.

Case report: We present a case of an 18-year-old female at 32 weeks of gestation misdiagnosed with a knee contusion and conservatively treated for 1 month in a non-referral center. An X-ray revealed an osteolytic lesion 52x43mm, with cortex invasion and periosteal reaction causing a pathological fracture of the left distal femur, highly suspicious of bone sarcoma, considering the patient's age, radiologic, and clinical features.

The biopsy revealed a highly cellular tumor composed of a myriad of multinucleated osteoclast-like giant cells amidst oval and spindled mononuclear tumor cells with dispersed nuclear chromatin and small nucleoli with focal hemorrhage. Tumor cells showed p63 and CD68 immunoreactivity. A diagnosis of giant cell tumor of bone was made. To preserve the patient's pregnancy, distal femur resection was performed with reconstruction of the defect according to the Campanacci technique. Grossly the distal femur resection measured 7x6x5cm containing an intramedullary soft, grayish tumor with a hemorrhagic appearance measuring approximately 6,5x6x4cm. Microscopically, the morphology was similar to that of the biopsy specimen, with recent hemorrhages, hemosiderin deposits, and necrosis present. Vascular invasion was identified.

Conclusion: A multidisciplinary approach is imperative for a correct diagnosis in cases of bone tumors during pregnancy offering the best treatment for preserving the mother and child's health.

Keywords: Giant cell tumor of bone, pregnancy, primary bone tumors, GCTB.

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Intramuscular granulomatous reaction after HPV vaccine injection

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Objective: This article describes a granulomatous reaction in a young woman as an adverse effect of a human papillomavirus (HPV) vaccine. The vaccine against HPV infection is recommended according to the Serbian National Immunization Program, for children and adolescents aged 9–19 years. The common side effects of HPV shots include pain, redness or swelling on the arm where the vaccine was administered, fever, dizziness or fainting, nausea, headache or fatigue and muscle or joint pain. A granulomatous reaction at the site of injection has rarely been described.

Case report: A 19-year-old female presented for clinical examination because of a palpable intramuscular tumor mass about 2cm in size on the upper arm. The lesion was

surgically excised. Histopathologic examination revealed an inflammatory granulomatous reaction with a necrotic/necrobiotic center surrounded by epithelioid histiocytes and lymphocytes. Immunohistochemical staining (CD68, LCA, S100, Cyclin D1, CD35, CD21, CK AE1/AE3 and Fascin) was performed. After a further clinical examination, we found that the patient had received an HPV vaccination.

Conclusion: We report a case characterized by the presence of a persistent nodule at the injection site of HPV vaccination, showing a granulomatous reaction with central necrosis, which should be considered an adverse effect of HPV vaccination due to the high vaccination rate in young women. Differential diagnoses should also be considered.

Keywords: granulomatous reaction, HPV vaccine, side effect

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Alveolar rhabdomyosarcoma in a patient with adenocarcinoma of the colon

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Objective: Rhabdomyosarcoma is a malignant tumor of striated muscle tissue. Alveolar rhabdomyosarcoma is a histological subtype that mostly occurs in children and adolescents, rarely in the adult population, with a high malignant potential and a frequent fatal outcome.

Case report: A 46-year-old man, undergoing chemotherapy due to a previously diagnosed mucinous adenocarcinoma of the colon, complains of pain in the left pectoral region of the chest. Computed tomography (MSCT) of the abdomen and chest was made with initial suspicion of metastatic lung deposits. MSCT showed soft tissue mass in left hemithorax at the level of VII, VIII and IX rib with pleural infiltration. A biopsy was performed and sent to pathology. Pathohistological analysis revealed the presence of scanty muscle and fat tissue with a neoplastic infiltration of strikingly pleomorphic, atypical cells, arranged in alveolar-like spaces with fields of weakly cohesive cells. Numerous anaplastic giant multinuclear tumor cells, as well as cells of rhabdomyoid morphology, with the presence of patchy necrosis, were also seen. Immunohistochemical analysis demonstrated diffuse positive expression of Vimentin, Desmin, CD99, focal expression of CKAE1/AE3, while the rest of the analyzed markers were negative (Actin, SMA, CD10, CD34, CD68, S100, TTF1, LCA, p63, WT1, CDX2, CD56). Based on micromorphological and immunohistochemical analysis, the diagnosis of alveolar rhabdomyosarcoma (ARMS) was established. The patient was referred to multidisciplinary tumor board for further oncological treatment.

Conclusion: Although rare, alveolar rhabdomyosarcoma can also occur in adulthood, as evidenced by our case. Therefore, a multidisciplinary approach is very important in diagnosis of these soft tissue neoplasms with a special focus on improving both diagnostics and adequate therapeutic treatment.

Keywords: Alveolar rhabdomyosarcoma, pleura, mucinous adenocarcinoma, pathohistology, immunohistochemistry

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Case report: Rare polypoid lesion of sigmoid colon

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Objective: Gastrointestinal leiomyomas are benign smooth muscle tumors that occur most frequently in the esophagus, while the colorectum is a rare site, accounting for about 3% of all gastrointestinal leiomyomas. Mostly they have sessile growth pattern, and are often not detected by colonoscopy.

Case report: We present the case of a 66-year-old patient who was initially admitted to the Institute of Gastroenterology due to severe microcytic anemia. Colonoscopy, gastroscopy, and abdominal ultrasound were performed, along with extensive gastroenterological treatment. A sigmoid polyp measuring less than 10 mm was verified by colonoscopy (NICE I), and it was removed. The resected material was sent for further pathohistological analisis. Histologically, the received biopsy sample showed the mucosa of the large intestine on the surface, that was polypoidally raised, under which in muscularis mucose there were clusters and bundles of bland looking spindle cells without atypia and mitoses. Necrosis was also absent. Immunohistochemically, the tumor cells were positive for SMA and Desmin, and negative for CK AE1/AE3 and CD 117. The histological and immunohistochemical profile corresponded to a gastrointestinal leiomyoma.

Conclusion: Although gastrointestinal leiomyomas are very rare, especially in the colon and rectum, they should be taken into account when making the correct diagnosis of stromal polypoid lesion, and it is necessary to exclude other mesenchymal tumors especially gastrointestinal stromal tumors (GIST).

Keywords: Leiomyoma, Polyp, Sigmoid Colon

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Human alveolar echinococcosis mimicking hepatic malignancy

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Objective: To present the second recognized case report of human alveolar echinococcosis in Serbia caused by Echinococcus multilocularis.

Case report: A 57-year-old man was admitted to our hospital due to 10-day lasting symptoms of jaundice, nausea and stomach pain. He had no family history of gastrointestinal malignancy or liver disease. Laboratory tests showed very elevated liver enzymes, total bilirubin, and CRP. MRI showed an enlarged liver with heterogeneous, predominantly T2 hyperintense change, with zones of necrosis, enlarged hilar lymph nodes, and perilesional dilatation of intrahepatic bile ducts, primarily of infiltrative features, suspected to be a cholangiocarcinoma. The lesion of the liver underwent radical resection and was confirmed as alveolar echinococcosis by pathological examination. Histological criteria for diagnosis included the identification of multiple multilocular cysts covered with chitinous membranes, accompanied by numerous foreign body granulomas and broad areas of necrosis. Perineural propagation of echinococci and one hilar lymph node with wide necrotizing granulomas with chitinous membranes were also present. The patient had no surgical complications after the operation and was discharged with a 800 mg daily dosage of Albendazole.

Conclusion: Human alveolar echinococcosis is one of the most dangerous and potentially lethal parasitic zoonoses, with a mortality rate exceeding 90% in untreated patients. This case highlights the need for clinicians to include alveolar echinococcosis in the differential diagnosis of liver lesions, even in patients who have never lived in or traveled to known endemic areas, because of the high lethality of this disease and its infiltrating, metastatic, tumor-like behavior.

Keywords: echinococcosis, multilocular, liver

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Primary sclerosing cholangitis – A case report

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Objective: To show a case of primary sclerosing cholangitis (PSC).
Case report: A 72-year-old female patient was admitted to UC being disoriented and bradypsychic with symptoms of diarrhea, nausea, and vomiting that lasted five days while having a dry cough with pain in the upper abdomen for the last two weeks (heteroanamnesis). After CT of the endocranium and exclusion of acute neurological disorder, CT of the abdomen showed multiple hypodense abscess-like lesions in the right liver lobe. Laboratory showed increased values of bilirubin, ALT, AST, and APs. The following day, the patient had surgery, which showed multiple lesions in the S3, S4, and S8 segments of the liver. Cholecystectomy with S3 lesion biopsy (for ex tempore analysis which confirmed benign process) and subsequent resection were performed. Grossly, an off-white liver fragment, with a diameter of 15 mm, on a standard HE staining showed a classic "onion-skin" fibrosis around atrophic bile ducts, with fibrous scars in places of obliterated ducts, as well as large ducts rupture with prominent neutrophilic response (abscesses). Following surgery, the patient was in the intesive care unit for 5 days until stable and discharged on the 18th postoperative day.
Conclusion: PSC is a rare chronic and progressive cholestatic liver disorder. It is more common in men, and in half of the cases shows no symptoms at the time of diagnosis. 10-20 % of patients develop cholangiocarcinoma. Increased liver panel and bile-duct strictures detected using either MR or ER cholangiography, while excluding secondary SC, confirms diagnosis with no need for biopsy.

Keywords: Primary sclerosing cholangitis, "onion-skin" fibrosis, cholangiocarcinoma.

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Exogenous lipoid pneumonia associated with gastroesophageal reflux disease

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Objective: Exogenous lipoid pneumonia (ELP) is caused by inhalation or aspiration fatty substance and can include numerous of differential diagnoses. Clinical manifestations can vary.
We report the case of 68 year old women with ELP.
Case report: A 68-year-old woman non-smoker presented with fever, cough and shortness of breath. Her past medical history was significant for gastroesophageal reflux disease and diabetes mellitus. Pulmonary auscultation revealed crackles. A chest CT scan showed ground-glass opacities in the right lung. These opacities were predominating in the lower lobe where a foreign body was seen during the sec-

ond bronchoscopy but not removed. After that, an anterolateral thoracotomy with right lobectomy was performed. Macroscopically gross appearance of an ill-defined, pale yellow area of the lobe suggested lipoid pneumonia. The oil red staining demonstrate that the bronchiole and alveolar like structure filled with foamy histiocytes.

Conclusion: Medical history is often crucial in the diagnosis of ELP.

Keywords: Gastroesophageal reflux, egxogenous lipoid pneumonia, oil red.

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Radiological-pathological correlation of pulmonary cavitary lesions: report of three cases

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Objective: Diverse etiologies cause pulmonary cavitary lesions, but the most common causes in adults include malignancy and infection.

Case report: This study presents three cases hospitalized at the Institute for Pulmonary Diseases of Vojvodina to explain the etiology of pulmonary cavitary lesions detected on computed tomography scans. In the first case, a 66-year-old male patient was operated on due to an irregular hyperdense lesion of 3 cm in diameter with a smaller central zone of excavation localized in the right upper lobe. Histopathological analysis showed circumscribed areas of fine-grained acidophilic necrosis surrounded by palisade-arranged epithelioid cells with positive acid-fast bacilli on Ziehl–Neelsen staining. The second case is a 58-year-old female patient who had a lobectomy to clarify the etiology of an irregular hyperdense lesion with a centrally excavated zone localized in the right lower lobe with an approximate diameter of 2.2 cm. Histopathological findings corresponded to a partially necrotic squamous cell carcinoma. The third case represents a 67-year-old female patient with a radiologically suspected infiltrative lesion within complete atelectasis of the left lower lobe. The described lesion was poorly delineated and had a few smaller zones of hypodensity that could correspond to cavitations, followed by some calcifications. Actinomycosis was diagnosed after bronchoscopy and lobectomy, with the help of special stainings and characteristic histologic appearance.

Conclusion: Differential diagnosis of pulmonary cavitary lesions can be challenging, especially from radiological and pathological aspects. Therefore, these lesions should be cautiously evaluated by correlating pathological, radiological, and clinical findings.

Keywords: Actinomycosis, Pathology, Radiology, Squamous cell carcinoma, Tuberculosis

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Multilocular thymic cyst: a case report

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Objective: Benign thymic cysts are uncommon lesions, accounting for approximately 3% of all anterior mediastinal masses. They are typically multilocular and should be distinguished from congenital cysts for several reasons: they may recur after excision, they may be associated with thymic neoplasms such as thymoma or thymic carcinoma, and they may adhere to adjacent structures, mimicking invasive neoplasms during thoracotomy.

Case report: We present the case of a 70-year-old woman who underwent surgery on the aortic and mitral valves at our institution. During the chest opening in the anterior mediastinum, a tumor nodule was discovered, which was surgically excised entirely. The tumor nodule measured 8 x

6 x 4.5 cm, exhibiting a grayish-yellow color and a smooth surface. Upon sectioning, it appeared multicystic with cystic spaces filled with brownish paste-like material. Histologically, multilocular cystic formations were surrounded by connective tissue capsules with focal calcifications. The cystic spaces were lined by flattened and focally cylindrical epithelium with goblet cells and filled with abundant finely granular material, numerous foamy macrophages, and blood. Additionally, a marked giant cell reaction with numerous giant multinucleated cells resembling foreign body types with cholesterol crystals was observed within the cyst wall. Smaller foci of thymic tissue were also noted.

Conclusion: Multilocular thymic cysts are rare acquired lesions of the thymus, likely resulting from inflammation but may also be associated with neoplasia. Complete surgical resection and meticulous histopathologic examination are recommended for all patients suspected of having multilocular thymic cysts.

Keywords: cardiac surgery; mediastinum; thymic cyst.

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Pleural synovial sarcoma in a one-and-a-half year-old child: a case report

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Objective: Synovial sarcoma of the pleura is a very rare entity, particularly in pediatric population.

Case report: A one-and-a-half year-old female child presented with two weeks long cough, dyspnea and high fever. She was treated with antibiotics for presumed pneumonia. Chest X-ray showed shadowing of the right hemithorax. Multislice computed tomography (MSCT) showed expansive tumor mass 10 x 10cm in this region, pushing liver caudally and trachea and heart to the left. Biopsy showed a lesion composed of spindle cells arranged in a fascicular growth pattern, with nuclear atypia and areas of necrosis. Immunohistochemistry demonstrated positivity with CKAE1/3 (focally), vimentin, TLE-1, CD99, bcl-2, CD56, and negativity for alfaSMA, H-caldesmon, CD117, desmin, myoD1, myogenin, S-100, SOX10, CD34, CD31, CK7, CK20, napsinA, and TTF-1. Fluorescent in situ hybridization for SS18:SSX rearrangement showed positive result and diagnosis of pleural synovial sarcoma was made. Neoadjuvant chemotherapy was given, followed by surgical resection of tumor.. Histopathological examination of the resected specimen showed therapy response with necrosis in 93% of the tumor. After a 5-month follow up, there were no signs of recurrence or metastases.

Conclusion: Our case represents a rare presentation of synovial sarcoma of the pleura in a one-and-a-half-year-old child. This tumor is highly aggressive, especially due to localization, but in our case had an excellent treatment response. Synovial sarcoma of the pleura should be considered in differential diagnosis of mesenchymal pleural tumors, especially in children and adolescents.

Keywords: mesencymal neoplasm, pleura, synovial sarcoma

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Harmonization of PD-L1 testing in non-small cell lung cancer (NSCLC): challenges in daily practice

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Objective: Tumor expression of Programmed death-ligand 1 (PD-L1) is an important but imperfect predictive biomarker for treatment with immune checkpoint inhibitors. High tumor PD-L1 expression, detected by immunohistochemistry (IHC) typically on formalin-fixed paraffin-embedded (FFPE) histological specimens, is linked to better response. Multiple PD-L1 IHC assays have been approved by the FDA. However, different antibodies show different limitations in terms of sensitivity.

Case report: We present a 63-year-old male whose chest CT revealed a spiculated nodule on apicoposterior segment of the upper lobe of the left lung. First atypical resection, then sublobar anatomical resection with dissection of hilar and mediastinal lymphatics due to high operative risk was performed and histological examination revealed mixed-type adenocarcinoma (solid and acinar type). IHH showed positive napsin A and TTF1 stains. PD-L1 testing on Ventana BenchMark GX with SP263 antibodies showed a negative result (0%).

Four years later control CT showed an infiltrating mass on the edges of the earlier performed resection. Histological examination demonstrated relapsus of previously diagnosed adenocarcinoma. PD-L1 testing was performed again on Dako Autostainer Link 48 with Kit 22C3 pharmDx. Examination showed positivity in 80% of tumor cells.

Due to a discrepancy with previous results, we repeated PD-L1 testing on first tested FFPE with negative results now with Dako Autostainer Link 48 with Kit 22C3 pharmDx, tumor cells showed 60% positivity and on relapsing adenocarcinoma we used Ventana BenchMark GX with SP263 antibodies. Tumor cells showed 80% positivity.

Conclusion: We showed a consistent discrepancy in PD-L1 results when different antibodies were used.

Keywords: Adenocarcinoma of Lung, CD274 protein, human, Immune Checkpoint Inhibitors, Immunohistochemistry

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Liquid biopsy for the detection of EGFR mutations in lung cancer: A case report

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Objective: Activating gene mutations of the epidermal growth factor receptor (EGFR) are a predictive biomarker for therapy with tyrosine kinase inhibitors (TKIs). Liquid biopsies are minimally invasive procedures based primarily on the molecular examination of circulating cell-free tumor DNA (ctDNA) isolated from body fluids.

Case report: An 82-year-old woman, a non-smoker with neuropsychiatric comorbidity, came to the Institute for Pulmonary Diseases of Vojvodina in September 2021 due to severe weakness and dyspnea. Computed tomography (CT) of the chest showed a massive bilateral pleural effusion, an irregular hyperdense lesion apically in the left lung, and mediastinal lymphadenomegaly. Cytology of the pleural fluid (cell block) confirmed lung adenocarcinoma. This sample was limited for EGFR, but insufficient for PD-L1 and ALK testing. DNA was isolated from the cell block using the Cobas® DNA Sample Preparation Kit. Due to the low DNA concentration, the Cobas® EGFR Mutation Test V2-based real time PCR analysis was not successful. A liquid biopsy was performed. ctDNA was isolated from 2 mL EDTA blood plasma using the Cobas® cfDNA Sample Preparation Kit. The EGFR test revealed the presence of deletion in exon 19. In November 2021, treatment was started with erlotinib, a first-generation TKI, at a dose of 150 mg/day. Due to the deterioration of the patient's performance status, the multidisciplinary tumor board decided to discontinue erlotinib in February 2022.

Conclusion: Tissue biopsy remains the gold standard for all molecular tumor tests. However, liquid biopsy may be an alternative approach for EGFR testing when an adequate histological or cytological sample is not available.

Keywords: Cell-Free Nucleic Acids, EGFR, Lung Neoplasms

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Lung cryptococcosis as an sign of an underlying immunocompromised condition – case report

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Objective: Fungal infections are emerging as a significant challenge to public health, especially with the rise in immunocompromised individuals worldwide. The radiological presentations of this condition encompass a diverse array of potential diagnoses, extending to include malignant diseases among them.
Case report: We present the case of an asymptomatic fifty-six-years-old male patient who underwent for surgical treatment as a diagnostic and therapeutic procedure for radiologically verified lung mass. Computed tomography revealed the presence of a 19 mm soft tissue excavated lesion in the upper lobe of the right lung. Additionally, discrete changes in density resembling ground glass opacities were observed in the remaining lung parenchyma. Imprint smear stained with MGG, GMS and PAS, as well as in histological samples stained H&E, GMS, and PAS showed necrotizing granulomatous inflammation with presence of rounded/oval shaped, fungi ranging from 2-15 μm which were GMS and PAS positive. Based on cytological, histological and molecular (PCR) analysis, fungi belongs to the Cryptococcus neoformans species. Due to the patient's poor general condition and the detected infection, further tests were conducted, confirming the presence of HIV infection.
Conclusion: Fungal lung infections are among the potential alternative diagnoses for suspicious lung lesions indicative of malignancy. Histological verification stands as the preferred diagnostic method for such lesions. Imprint cytology smears prove beneficial in revealing granulomatous inflammation and yeast organisms. Confirming the morphological diagnosis requires microbiological culture and molecular identification of the causative organism.

Keywords: cryptococcosis; mycoses; immunocompromised host; pulmonary fungal infections

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Pathological rib fracture as a presentation of Langerhans cell histiocytosis

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Objective: Langerhans cell histiocytosis (LCH) is a rare clonal proliferative disease caused by the aggregation of Langerhans cells in various organs. LCH most commonly affects the skeletal system, with the mandible being the most frequent site (30%), and the ribs being the least affected (6%).
Case report: A thirty-seven-year-old patient presented with left-sided chest pain persisting over the past 6 months. Computed tomography examination revealed an osteolytic lesion measuring 15 mm in diameter with a soft tissue component and a pathological rib fracture, located in the middle axillary line of the left fourth rib. Skeletal scintigraphy demonstrated a solitary focus of pathological hypercalcification in the fourth rib. A bone marrow biopsy ruled out hematological diseases, prompting the recommendation for partial rib resection to clarify the lesion's etiology. For histopathological analysis, a 4 cm segment of the rib was excised, focusing on a central thickening disrupting the bone structure upon cross-section. Microscopic examination revealed infiltration of tumor tissue within residual bone tissue. The tumor tissue consisted of histiocytoid large cells with oval to slightly elongated nuclei, irregular nuclear membranes, nuclear grooves, and abundant pale-eosinophilic cytoplasm. Immunohistochemical staining showed

positivity for CD1a and S-100, consistent with Langerhans cells. Additionally, dense infiltrates of eosinophilic granulocytes were observed between clusters of Langerhans cells and bundles of connective tissue.

Conclusion: LCH is a rare disease with variable manifestations. A solitary rib lesion with a pathological fracture is an uncommon presentation and can be easily misdiagnosed.

Keywords: chest wall; Langerhans cell histiocytosis; pathological fracture

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Mediastinal mixed germ cell tumor with a rare component – case report

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Objective: The range of microscopic entities found in germ cell tumors is highly diverse. The presence of a polyembryoma component is uncommon in gonadal locations and even more so in extragonadal sites, with only a handful of cases reported worldwide.

Case report: A twenty-five-year-old patient was admitted to the hospital for the treatment of an undiagnosed mediastinal mass. Among his symptoms, he reported chest pain over the past 10 days. The computed tomography scan revealed a soft tissue mass measuring 10x7.3x10.5 cm in the anterior mediastinum. Following appropriate preoperative preparations, the patient underwent surgical treatment with video-assisted thoracoscopy, followed by medial sternotomy in order to perform tumor excision. Macroscopically, the tumor appeared partially encapsulated with a nodular surface. Upon cross-section, it displayed a distinctly heterogenous appearance with multiple cystic formations. Microscopic examination revealed that the tumor comprised several components: immature teratoma (50%), mature teratoma (25%), polyembryoma (20%), and seminoma (5%). The polyembryoma component consisted of embryoid bodies composed of embryonal carcinoma cells (positive for CD30 and OCT3/4), situated within "amnion-like" cavities surrounded by a yolk sac tumor component (positive for Glypican 3 and AFP). Tumor infiltrates were identified within samples of mediastinal pleura. Considering the histopathological findings, adjuvant chemotherapy and radiotherapy of the mediastinum are considered necessary.

Conclusion: We have reported the clinical presentation, histological and immunohistochemical finding of a mixed germ cell tumor with a polyembryonic component. The treatment of patients with germinal tumors depends entirely on a detailed histological examination of the tumor tissue.

Keywords: germ cell tumor; mediastinal neopasms; immunohistochemistry

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Epithelioid hemangioendothelioma of the lung – case report

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Objective: Epithelioid hemangioendothelioma is a rare tumor with a wide range of differential diagnostic pathological entities, encompassing granulomatous pathology to primary lung cancers. Despite significant advancements in molecular diagnostics in recent years, which have facilitated more precise diagnosis and classification of soft tissue tumors, these tumors continue to pose a diagnostic challenge for both pathologists and clinicians.

Case report: The sixty-seven-year-old female patient was hospitalized to clarify the etiology and potential surgical treatment of the lesion in the lungs. The mass was discovered incidentally on a chest X-ray. Chest computed tomography showed a peripheral nodule in the VI segment

of the left lung. An atypical resection was performed with video-assisted thoracoscopy. Histopathological findings on frozen sections indicated that the lesion was benign. During the definitive histopathological examination, tumor tissue consisted of weakly to moderately cellular solid sheet-like arrangements of tumor cells, with uniform, round to slightly oval nuclei and a small amount of cytoplasm. The immunohistochemical profile of the tumor cells favoured tumors of vascular origin, as evidenced by positivity for CD31, CD34, D2-40, CD10, and vimentin, while showing negativity for KRT AE1/AE3, KRT7, EMA, TTF-1, Napsin A, ER, PR, and S-100. Based on the histomorphological features and the results of the immunohistochemical analysis, final diagnosis was consistent with epithelioid hemangioendothelioma. At the latest follow-up, conducted three months after surgery, the patient showed no signs of disease.

Conclusion: We present a case of a rare primary low-grade lung sarcoma, which will contribute to the limited literature available on this pulmonary entity.

Keywords: epithelioid hemangioendothelioma; primary pulmonary sarcoma; vascular tumors

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Pericardial cyst: case report

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Objective: A pericardial cyst (PC) is an uncommon benign dilatation of the pericardial sac surrounding the heart. PC is typically considered a congenital anomaly with most patients diagnosed via incidental findings on routine chest imaging and have been diagnosed in all ages. The incidence is 1 in 100,000 persons. Rarely PC can become symptomatic and require treatment or intervention.

Case report: A 60-year-old female presented with substernal pain radiating to the bilateral shoulders. A chest X-ray was suggested and performed which showed a round, rounded mass near the heart that was suggestive of a pericardial cyst. The dimensions of the cyst were 35x35x30cm. Surgical resection of the cyst was performed through a thoracotomy. The obtained material was sent for histopathological diagnosis. The delivered material corresponds to a pericardial cyst with a diameter of 35x35x30 cm and a wall thickness of 0.5 mm, a smooth outer and inner surface, which is filled with clear liquid fluid. The wall of the cyst is made of fibrous tissue lined with simple cuboidal mesothelial cells.

Conclusion: The general prognosis is excellent for PC, not unexpected when one considers that the vast majority of patients are asymptomatic. Spontaneous resolution of lesions has even been reported.

Keywords: pericardial cyst, chest X-ray, histopathological diagnosis

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Solid pseudopapillary neoplasm-case report of the youngest patient

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Case report: Solid pseudopapillary pancreatic tumor, also called Frantz tumor after the author, represents 1-2% of pancreatic neoplasms. It is considered for tumor with low malignant potential, of unclear etiology. It occurs more often in women in the third and fourth life decade. In children, it usually affects the head of the pancreas, while the pancreatic body or tail in adults. The tumor is most often manifested as a palpable mass in the upper part of the abdomen, accompanied by pain, nausea and vomiting. However, it is most often discovered accidentally, by radiological examinations, where it presents as a clearly limited, encapsulated lesion, usually with areas of cystic softening.

A fourteen-year-old girl had a resection of the pancreas' head with a tumor formation, duodenum and part of the jejunum. Macroscopically, the tumor mass measuring 10x7x6 cm was partly solid, partly cystically altered, fulfilled with dark and bloody content. Pathohistologically, a solid pseudopapillary tumor was verified, consisting of uniform round epithelial cells without atypia that are distributed in pseudopapillary and partly solid areas, permeated with cholesterol crystals and dystrophic calcifications in a moderately abundant connective vascular stroma, without

necrotic areas. Pathohistological verification is necessary for confirmation of diagnosis. This case report is also a report of a rare neoplasm of the youngest patient who was diagnosed with a solid pseudopapillary tumor at the Center for Pathology and Histology of the University Clinical Center of Vojvodina.
After surgical resection, the prognosis of this disease is excellent.

Keywords: Frantz tumor; pancreatic neoplasm

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Progressive mucinous histiocytosis in a child – a report of a rare entity

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Objective: Non-Langerhans cell histiocytoses are heterogeneous disorders, some of which may predominantly affect the skin. The most common form in children is juvenile xanthogranuloma, while other forms are very rare and may be hereditary such as progressive mucinous histiocytosis.
Case report: We present a case of a nine-year-old girl with painless skin papules lasting for five years before the examination. Papules first appeared on the forearms and then on the face. Several papules were excised for histopathological examination. Papules were composed of a variable number of epithelioid or spindled cells with clear or light eosinophilic cytoplasm, without prominent nuclear pleomorphism. Cells showed loose or lobular arrangement in the superficial and mid-dermis and were embedded in a myxoid stroma. On immunohistochemical analysis, tumor cells showed positivity for CD68, Factor XIIIa, and Fascin, but were negative for CD163, S-100, CD1a, and Langerin. Diagnosis of progressive mucinous histiocytosis was made. Further clinical examination showed no other organ was affected. Close clinical follow-up and examination of close relatives were suggested.
Conclusion: Progressive mucinous histiocytosis is a hereditary or sporadic disease, that predominantly affects skin without propagation to visceral sites. It often occurs in childhood, has a slowly progressive course, and may be treated surgically. Histopathological and immunohistochemical analyses are necessary for final diagnosis.

Keywords: non-Langerhans cell histiocytosis, pediatric skin tumors, myxoid histiocytosis

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Unusual presentation of pediatric carcinoma of unknown primary origin: a case report

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Objective: Pediatric carcinomas are often the first manifestation of various hereditary syndromes. In addition to being rare, these diseases have a different clinical presentation in children compared to adults, which often delays diagnosis. This report aims to indicate the importance of pathohistological diagnostics in such cases.
Case report: We present a case of a 14-year-old boy with clinical suspicion of lymphedema of unclear etiology due to unilateral elephantiasis and hydrocele. Deep vein thrombosis, hereditary angioedema and filariasis were excluded. Whole-body nuclear magnetic resonance imaging did not detect a tumor but only inguinal lymphadenopathy. Biopsy of the inguinal skin and subcutaneous tissue showed carcinomatous lymphangiosis of mucinous "signet-ring cell" carcinoma of unknown primary origin. Immunohistochemical evaluation pointed to a gastrointestinal origin of the primary tumor, including "goblet cell" carcinoma of the appendix (CK20+, CDX2+, Villin+, Synapthophysin+/-) but subsequent gastroscopy and colonoscopy with serial biopsies did not reveal the tumor. Additional immunohistochemical analysis showed loss of nuclear expression in

more than 30% of tumor cells for MSH6/MSH2 and MLH1/PMS2 suggesting microsatellite instability-high (MSI-H) cancer. There was no clinical improvement during chemotherapy and the patient died after one year of follow-up as a result of complications from pulmonary embolism and massive pleural effusions.

Conclusion: Although an incidental finding, the pathohistological analysis of the biopsy sample proved to be superior to other diagnostic methods in the detection of metastatic carcinoma in this case. Proven MSI-H in tumor tissue explains its early onset and in correlation with the assumed gastrointestinal origin are together a hallmarks of Lynch syndrome.

Keywords: pediatric carcinoma, microsatellite instability, Lynch syndrome

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Sacrococcygeal teratoma with Yolk sac tumor in newborn– case report

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Objective: To present a case report of a 7-day-old female newborn with a mature sacrococcygeal teratoma with a component of the yolk sac tumor.

Case report: A term newborn was delivered by cesarean section with a large mass in the sacrococcygeal area. After the seventh day of birth, a complete resection of the tumor was performed. Macroscopic examination revealed that it was a large tumor covered with skin, measuring 9.5 x 8.5 cm, partly solid and partly cystic, with a colorful appearance. Microscopically, the prominent component of the tumor was mature nervous tissue composed of neurons, nerves and ganglion cells. We found mucus producing cylindrical epithelium resembling gastrointestinal epithelium as well as cuboidal epithelium resembling ependyma. Other components in the tumor included skin, cartilage, smooth and striated muscle tissue, mesenchymal tissue, gastrointestinal glands, retina, and numerous calcifications. In several foci, we observed necrotic tumor tissue composed of atypical cells with hyperchromatic to vesicular pleomorphic nuclei, acidophilic nucleoli in a glandular, alveolar, and microcystic arrangement. Schiller-Duval bodies were observed. After the performed immunohistochemical analysis (AE1/AE3 +, Glypican3 +, AFP+, GATA3 +, PLAP+ , Ki67 85%) the diagnosis of Yolk sac tumor was confirmed.

Conclusion: Yolk sac tumors are rare and highly malignant tumors that occur in children as well as in young adults. In conclusion, a sacrococcygeal mass, especially in children or neonates, requires rapid clinical evaluation and confirmation by histopathological examination.

Keywords: sacrococcygeal teratoma, Yolk sac, newborn

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Lymphangiomatosis of the small intestine

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Objective: Lymphangioma is nonencapsulated benign proliferation of lymphatic vessels. In most cases it is usually identifiend in infants and children around the head and neck, trunk or extremities. Lymphangioma cavernosum in the abdominal cavity is a rare benign tumor, account for 6% of gastrointestinal tumors in children. Variable clinical presentation, from asymptomatic to abdominal pain mass effect. May present as an incidental finding during surgical precedures performd for other conditions. Rarely complications include obstruction, infarct and perforation of small intestine. Complete surgical resection is considerd the main method of treatment.

Case report: Our patient is a 14 year old girl, which appears to the pediatrican due to an increase in body temperature and pain in the lower abdomen. On the first ultrasound, a cystic change in the projection of the ovary was observed, and laboratory analyzes show inflammation (CRP 305, Le 12.2). After the given antibiotic therapy, the general condi-

tion improves. On the second ultrasound more clearly circumscribed hypoechoic areas were observed in abdomen, largest diameter up to 44mm. Surgical excision of the small intestine was performed and pathohistological examination, which showed dilated and anastomosed thin-walled blood and lymphatic vessels lined with endothelial cells of regular micromorphology.

Conclusion: Lymphangiomatosis of the small intestine is a rare benign neoplasma which cane mimic a malignant process. The treatment of choice is surgical excision with clean margins. Postoperative follow-up is necessary to detect recurrence.

Keywords: lymphangioma, small intestine, abdominal pain

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Cytological diagnosis of metastatic pleomorphic sarcoma in the ascites fluid- case report

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Objective: Presentation of cytological diagnosis of metastasis of sarcomatoid malignancy in the ascites fluid and pathohistological confirmation.

Introduction: Sarcomas are unusual findings in cytological samples of body fluids and make up 3%-6% of malignant effusions. Morphological characteristics of sarcoma in cytological and pathohistological findings can be a great diagnostic challenge.

Case report: A 74-year-old woman, one month after a laparoscopic cholecystectomy, was hospitalized in a serious general condition, with advanced ascites. After drainage of the ascites fluid, the material was cytologically analyzed. In the cytological sample, in addition to inflammatory and mesothelial cells, numerous clusters of pleomorphic tumor cells with moderately abundant and partially basophilic and small vacuolated cytoplasm were found. Nuclei were eccentrically placed, focally with prominent nucleoli. Numerous multinucleated cells were observed. Diagnostics, according to the type of secondary deposit of non-small cell carcinoma, was completed with cytoblock and immunocytochemistry staining. Only an intense reaction was found for vimetin, while reactions for CK7, CK20, estrogen, progesterone, EMA, CK5/6-, CDX2 were negative. In the differential diagnosis, cytologically, poorly differentiated sarcoma or sarcomatoid carcinoma was considered. After the MSCT examination, a biopsied change was observed in the liver. Pathohistologically, pleomorphic neoplastic cells were positive for vimentin, CD68, SMA, and focal S100. A primary undifferentiated pleomorphic sarcoma of the liver was diagnosed.

Conclusion: We analyzed rare localization of undifferentiated pleomorphic sarcoma in the liver with deposits in the ascites fluid. Its diagnosis can be difficult in exfoliated cytological samples, due to the epithelioid, mesothelial and sarcomatoid morphology of the tumor cells.

Keywords: Malignant effusions, Pleomorphic sarcoma, Citology

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Neurological, cardiac and musculoskeletal anomalies in fetuses with aneuploidy

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Objective: Defining the frequency of neurological, cardiac and musculoskeletal anomalies during macroscopic analysis of fetuses with Down, Edwards, Patau, Turner, Klinefelter and 47 XXX syndrome.

Introduction: Aneuploidies represents disorders of the number of chromosomes within the human genome. The most common are: Down's, Edwards', Patau's, Turner's, Klinefelter's and 47 XXX syndrome. Neurological, cardiac and musculoskeletal anomalies are characteristic for all these syndromes.

Material and Methods: This research of retrospective character was conducted at the Center for Pathology and Histology of the University clinical center of Vojvodina. Autopsy reports were used as a source of data. The follow-

ing data were collected and statistically analyzed: maternal age, fetal sex and gestational age, the type of aneuploidy as well as neurological, cardiac and musculoskeletal findings. The study included 90 fetuses with autopsy performed in a three-year-period.

Results: Out of 90 fetuses, 32 were female, while 58 were male. The largest number of fetuses had Down syndrome - 56 (62.2%), followed by 15 fetuses with Edwards syndrome (16.7%), 7 with Klinefelter syndrome (7.8%), 5 with Turner syndrome (5.6%), 4 with 47 XXX syndrome (4.4%) and Patau syndrome, which was present in only 3 fetuses (3.3%). Of all anomalies analyzed, musculoskeletal were the most common, cardiac were found to a significantly lesser extent, while the least present were neurological.

Conclusion: The study confirmed the presence of anomalies in the analyzed syndromes, of which the following are represented: musculoskeletal, cardiac and finally neurological.

Keywords: aneuploidy; anomalies; syndrome; fetus

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Core needle biopsy of liver nodal lesion- from few cells to diagnosis

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Objective: The objective of this case report is to demonstrate difficulties that can arise in small biopsies and the importance of having an idea of a possible diagnosis.

Case report: Liver neoplasms whether primary or metastatic are quite common. About a quarter of all metastases are found in the liver, most commonly carcinoma metastasis, but other tumors such as sarcomas, melanoma, and lymphomas can metastasize to the liver as well. Minimally invasive small biopsies, e.g. FNA and CNB, are safe, quick, cost-effective procedures that facilitate the diagnosis of numerous visceral changes.

We present a case of an FNA biopsy of solitary liver neoplasm in a 70-year-old man, found during a routine diagnostic for abdominal discomfort the patient had a couple of months before the procedure. On HE, pleomorphic tumor cells were embedded in the myxoid stroma with fragile blood vessels. Tumor cells had a sparse, eosinophilic cytoplasm and focally with granular brown pigment. Tumor cells showed positivity on Vimentin, S-100, SOX10, and PRAME, but a loss of staining for Melan A, HMB-45, and MiTF was observed. Pigment in tumor cells was stained with Masson Fontana.

Based on tumor morphology on HE, immuno- and histochemistry diagnosis of metastatic melanoma was made. The patient had no history of previously diagnosed melanoma.

Conclusion: Small biopsies are a powerful tool in providing material for pathohistological and molecular testing with minimal patient discomfort and few rare complications. However, considering that the small tissue fragment delivered through these procedures is just a minor part of a neoplasm can raise a question of adequacy and representativity of a sample, as well as the sufficiency of cytological and architectural characteristics to establish the right diagnosis.

Keywords: FNA biopsy, melanoma, liver metastasis

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