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FNA application in cytological examination of the thyroid goiter

KEYWORDS: Thyroid gland; Goiter; Pathology; Needle biopsy, Retrospective studies

Palpable asymmetry and nodules of the thyroid gland may be clinically examined by a variety of methods: echosonography, radiography, radioactive isotopes, byochemistry (measuring the serum levels of T3, T4, TSH, TRH). Today the fine-needle aspiration (FNA) is also a necessary diagnostic procedure in analyzing thyroid lesions. FNA is a very usseful method in cytological diagnostics of different lesions in the thyroid gland, including the benign goiter. As the goiter is the most frequent lesion in the thyroid tissue, the FNA increasingly gains in significance as a diagnostic method. In the period of 2 years, 600 aspirates from thyroid lesionswere analysed for ther cytology. The aspirates were stained with: hematoxylin-eosin (HE), May-Grunwald-Giemsa (MGG) and Prussian blue. The cytological diagnostics included description of: the colloid (quantity, distribution, viscosity and activity) and the cells (number, shape, size, colour of the cytoplasm, size and shape of the nucleus, chromatin, mitoses, nucleo-cytoplasmatic index, nuclear inclusions and cellular arrangement). In the patients with the cytological diagnosis of goiter we analysed: 1) sex distribution, 2) age distribution, 3) correlation between clinical and cytological diagnoses and 4) goiter classification in accordance with cytological characteristics.The cytological characteristics of the aspirates from benign goiter are: 1. Eosinophilic diffuse colloid with many erythrocytes, rare lymphocytes and leukocytes and cellular elements from the thyroid gland; 2. Many follicular cells, slightly varying in size and shape, without atypia. The cytoplasm is light, basophilic, with a single centrally located oval nucleus. Slight anysonucleosis is sometimes present. The nucleo-cytoplasmatic relationship is saved. Chromatin is homogenous, intranuclear inclusions are not presented. Follicular cells are single or arranged in clumps or microbiopsy; 3. Rare Hurtle cells could be seen, they are round and bigger than follicular cells. The cytoplasm is light, eosinophilic and abundant. Nuclear polymorphism is not present. Oxyphilic cells are arranged around the colloid. The latter description is characteristic for the simple goiter, without degenerative changes. But, degenerative changes are very often in goiter. They can be hemorrhage, necrosis and fibrosis. Hemorrhage is the most frequent secondary change in goiter. The aspirate from goiter with hemorrhage is hypercellular with macrophageal domination. Of 600 analysed aspirates from 414 cases (69%) were diagnosed as goiter. This lesion was five times as frequent in females as in males (348 women, 66 men). By $\chi 2$ test a high sexual significance for goiter arising ($\chi 2=192,08$; $p<0,005$) was statistically conformed. The majority of the patients in our investigation were aged between 41 and 50 and the fewest (only 6 patients) were younger than 20 years of age. The youngest patient with goiter was 13, and the oldest was 77.8 years old. The patients' mean age was 46.5 yrs. By $\chi 2$ test the high age significance for the development of goiter ($\chi 2=494,30$; $p<0,005$) was statistically confirmed. Of 414 cytologically confirmed goiters, 222 had the clinical diagnosis of "nodular goiter", 127 "diffuse goiter", 46 "thyroiditis", 1 "anaplastic carcinoma" and 4 "tumors". Our conclusions are: 84% of cytologically diagnosed goiters had some clinical diagnosis, in only 1.5% of all patients (1 "anaplastic carcinoma" and 4 "tumors") a tumor was clinically suspected. We confirmed a high correlation between the clinical and cytological diagnosis. "Goiter" was the most frequent initial clinical diagnosis (474 patients; 300 diffuse goiters and 174 nodular goiters) In 349 cases or 73% the initial diagnosis was cytologically confirmed. According to their cytological characteristics, all goiters were classified in 2 categories: goiters with and without degenerative changes. Of all examined goiter cases, 174 (42%) were presented by degenerative changes-hemorrhage. Without hemorrhage were 240 goiters (58%). The $\chi 2$ test confirmed there is a statistical difference between the two goiter types, but it is not significant ($\chi 2=10.4$;$p<0.01$). In the diagnosis of goiter, FNA permits a substantial reduction or even elimination of other diagnostic procedures, such as imaging, with consequent saving in time and money. Furthermore, benign cystic lesions may be cured by FNA (a diagnostic and unexpected therapeutic value of FNA).

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Mycetoma of the foot caused by pseudoallescheria boydii - A case report

KEYWORDS: Pseudallescheria; Foot dermatoses; Mycetoma; Pathology; Case report

Fungal bone infections make about 0.1-0.2% of all osteomyelitis cases caused by microorganisms. They have an endemic character in geographic regions with warm and wet climate (tropical and subtropical districts). In our country fungal bone infections are extremely rare. The disease most often affects the feet (mycetoma pedis). Clinical manifestations are tumorous proliferation, indurations, swelling, pain and dermal manifestations (erythema and ulceration). The bioptic material is presented by mycetoma as a chronic granulomatous inflammation. Histochemical stains - PAS, Grocott's hexamine-silver and Giemsa are very useful in the diagnostic procedure. However, the definite diagnosis is established by fungal cultivation on the laboratory media. To select the therapy, a highly sensitive and precise identification of microorganisms is necessary. We report a patient with mycetoma pedis who was diagnosed 7 months ago at the Institute of Pathology and the Institute of Microbiology, School of Medicine, Belgrade in the operative material from the Institute of Orthopedics and Traumatology "Banjica", Belgrade. The patient was a 50 years old woman. The clinical signs were: pain, indurations and local redness. She reported a very long (about 10 years) history of the symptoms, but lately the local disease was in progress (enlargement of the swelling and increased pain). The lesion had a local character and the patient was generally in good health. The biopsy sample was taken and sent for histopathology. The operative material was routinely stained with hematoxylin-eosin (HE). A granulomatous inflammation in the bone was histologically confirmed. The central part of the granuloma was unstructured, the eosinophilic mass surrounded with cellular elements. On the highest magnification this mass had the fiber structure and looked like the hyphae. The presenting cells were predominantly lymphocytes and plasma cells, but many leukocytes and epithelial cells were also found. All pathological characteristics pointed to a fungal infection in the form of mycetona pedis. A special staining for fungi was performed in the diagnostic procedure - PAS, Grocott's hexamine-silver and Giemsa and the diagnosis of mycetoma was confirmed. The definite microbiological analysis was the tissue inoculation on the Sabouraud dextrose agar laboratory media for fungal cultivation. Pseudoallesheria (Petriellidium, Allecheria) boydii was isolated. This fungus is a sexual staging of Scedosporium (Monosporium) apiospermum. The grains formed by P. boydii are large, up to 2mm white to yellowish, soft to firm, and round to lobulated. The hyphae are broad (up to 5 μm), septate, intertwined and show numerous intercalary chlamydoconidia. P. boydii is soil- and water-inhabiting fungus in our climatic region and the direct contact could be the door of the infection. The organism is of low inherent virulence and its clinical course is subacute or usually chronic (sometime taking a few years). After the microbiological verification of the fungal infection, the surgical treatment was performed. Seven months after the first operation, the patients had the same clinical signs (pain, swelling and local redness on the same foot). The diagnostic procedure was repeated and mycetoma was confirmed again. The surgical therapy was performed and antimycotic drugs were recommended. The bone infection with Pseudoallesheria (Petriellidium, Allecheria) boydii is very rare in our country and multidisciplinary approach is necessary in the diagnostic and therapeutic procedure.

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Grimelius' silver method in the diagnostics of birthmarks and malignant melanomas

KEYWORDS: Silver nitrate; Melanoma; Birthmark; Pathology; Retrospective studies

Birthmarks and malignant melanomas have attracted medical attention for decades because of their peculiar histologic and clinical features. They may occur at any age, most commonly in men and women over 40 years of age. Pearse's new concept that the melanoblast/cyte is included in APUD cell group I and that it is of neural crest origin , led us to answer the following questions: Could Grimelius' silver method, characteristics of the cells acronymosly named APUD (Amine Precursor Uptake and Decarboxylation) be used in the diagnostic-pathological work of birthmarks and all types of melanomas? Ten birthmarks of intraepidermal, intradermal and dermoepidermal localization and ten melanomas (5 with considerable amounts of melanin- melanotic type and 5 without melanin- amelanotic type) were studied. The surgical material was used. Samples of the tumors were fixed in 4% formaldehyde or in Bouin's fluid (acid aceticum 3 ml.). The following techniques for melanin were applied: Classical hematoxylin-eosin stain (for cytologic appearances); Grimelius silver (for melanin cell granules), blanched by hydrogen peroxidase. a) A freshly prepared 0,03% (w/v) aqueous silver nitrate solution buffered to pH 5.6 was used. This silver solution was prepared by mixing 10 ml of 0.2 M acetic acid-sodium acetate buffer, pH 5,6 with 87 ml glass of redistilled water and 3 ml of a freshly prepared 1% (w/v) aqueous silver nitrate solution. The slides were placed in this solution at room temperature, then incubated, either for 24 hours at 37º C (variant I) or for 3 hours at 60º C (variant II). b) The silver solution was drained off the slides (not the sections) and these were then immersed for 1 minute in a freshly prepared aqueous reducing solutions of 1% (w/v) hydroquinone and 5% (w/v) sodium sulphite (crist.) at 40 to 45ºC. c) The sections were rinsed in distilled water, dehydrated, cleared and mounted in Canada balsam. Silver granules in the cytoplasm were stained pale brown, brown-black to black. Birthmarks of all localizations were argyrophilly positive. Grimelius silver reaction could show melanin in melanotic and hematoxylin-eosin amelanotic types. From field to field melanin cell granules were Grimelius reactive. Independent of the melanin quantity, the granules were stained from brown to black. The most important result was that Grimelius reactive cells inside the tumors which in the hematoxylin-eosin stain were amelanotic. The consequent blanching of Grimelius reactive cells by hydrogen peroxidase confirms that the melanin cell pigment was in question. Pigment formation and deposition are often a striking feature of birthmarks and malignant melanomas. The amount of melanin varies in this tumor. In some melanomas considerable amounts of melanin are found only within the tumor cells, but also within melanophages present in the stroma. Not infrequently is melanosis sparse. Sometimes it is completely absent from all the regions of a malignant melanoma in the hematoxylin-eosin stain (melanotic melanoma). Occasionally it is plentiful in the tumor but scanty or absent in its metastases. Or, the metastases may contain much melanin, though the primary tumor appears melanotic. Having in mind that malignant melanomas can mimic various types of carcinomas and sarcomas, as well as their radioresistant feature, a correct diagnosis is therefore of great significance. The staining of the sections of malignant melanomas, melanotic in the hematoxylin-eosin stain, by Gremlius' silver reaction facilitates the diagnosis of amelanotic melanoma and helps in the appropriate treatment of these patients. Grimelius' silver method is a very sensitive method for the identification of all birthmarks and both melanotic and amelanotic melanomas. Silver granules in the cytoplasm are stained pale-brown, brown, brown-black to black, proportionally to the quantity of melanin.

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Hemangiomas and vascular malformations of maxillofacial region - Necessity for accordance of clinic and pathohistologic terminology

KEYWORDS: Hemangioma; Arteriovenous malformations; Diagnosis; Terminology

Modern knowledge on vascular lesions urge us to reestablish two crucial clues for the needs of the clinical praxis: accordance in attitudes for adequate diagnosis establishment, that clearly define principles of treatment of these biologically different lesions and priority of other diagnostic methods usage over the results of histopathologic analysis. Former classifications of vascular lesions are mostly based on a disorder of the embryologic development of the vascular tissue and its histologic structure, but nowadays, the worldwide accepted classification is the one proposed by Mullicken and Glowacki (1982), that defines the cellular features of vascular anomalies and correlates them with the clinical behavior. Correlative studies of surgical specimens, radiologic findings and natural history demonstrate that there are two major categories: 1. hemangioma; 2. vascular malformation "fast flow" - arteriovenous fistula (AVF) "slow flow" - capillary, venous, lymphatic or combined forms. Hemangiomas are vascular lesions that usually are not visible at birth, but they are characterized by an intensive postnatal growth (the proliferative phase) for the first 8-12 months of life, followed by a slow regression (involutive phase) from 5-8 years which lasts up to the early adolescency. In their proliferating phase hemangiomas are composed of rapidly dividing endothelial cells forming syncytial masses with or without lumina. During the involutive phase, the endothelial cell activity diminishes and the cellular parenchyma is replaced by fibrofatty tissue. Recent papers show that the angiogenic peptide basic fibroblast growth factor (bFGF) is elevated in the serum and urine of infants with proliferative hemangiomas. They only rarely cause bone or cartilaginous hypertrophy. Clinical studies confirm that 50% of small hemangiomas and those which do not cause complications involute by the age of five years, 70% by the age of seven years and 30% by the age of twelve years of life. Most hemangiomas do not reqiure management, but only watchful waiting until involution occurs; some are treated conservatively by corticosteroids and eventually interferon-alpha-2a, and surgical treatment is indicated only at those which do not involute, which cause visual problems and respiratory obstructions, large hemangiomas with thrombocytopenia and ulcerated hemangiomas prone to bleeding. It is generally accepted that smaller ones can be excised without esthetic and functional risks because of psychosocial reasons. Vascular malformations by definition are present at birth, but most of them are clearly seen in the nursery or during infancy, and they do not involute. They mostly grow proportionately with the child, although they may expand secondary to trauma, infection, hormonal changes or embolic or surgical treatment. The histologic evaluation of vascular malformations shows no evidence of cellular proliferation, but a rather disturbed development with progressive dilatation of vessels due to abnormal mural structure because of a lack of the muscle layer. Vascular malformations are able to produce significant hypertrophy, distortion and destruction of craniofacial skeleton. With its success rate of 95%, the laser is a therapy of choice in the management of capillary malformations; the surgery is limited to excision and primary reconstruction of the remaining tissue defect. Venous malformations are treated by sclerotherapy, intratumorous ligation to reduce bulky mass, preoperative embolisation and surgery, which is indicated for large and symptomatic lesions and when the nourishing vessel is present. Lymphatic malformations are treated surgically, but persistent notion exists that these lesions have the potential for neoplastic growth and recurrence after excision. The only therapy that carries any hope for long-term success in the case of arteriovenous malformations is a total resection of the tissue involved with it, but it has to be preceeded by preoperative superselective embolisation. It is clear, of course, that in accordance to this nowadays most acceptable clinical classification, anamnestic data, clinical examination and radiographic investigation - ultrasound, Doppler, angiography, CT and MRI - even preoperatively solve the dilemas about differential diagnosis, which determines a particular way of treatment. So, vascular lesions belong to that small group of cases where intraoperative or postoperative decision about further treatment does not depend on histopathologic analysis, but this fact does not cease the necesity for consistent and unique clinical-surgical, radiologic and pathologic terminology.

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Mitochondria and mitochondrial encephalopathy lactic acidosis and stroke-like episodes (MELAS)

KEYWORDS: MELAS syndrome; Muscle biopsy, Ultrastructure, Mitochondrial diseases

Why do we need mitochondria? In each of our cells, the mitochondria (singular: mitochondrion) make up the equivalent of a car's engine. These tiny biological machines combine the food we eat with oxygen to produce energy to keep our bodies going. The energy produced by the mitochondria is stored in the form of a chemical called adenosine triphosphate, or ATP. Mitochondria have some of their own DNA, ribosomes, and can make many of their own proteins. The DNA is circular and lies in the matrix in punctate structures called "nucleoids". Each nucleoid may contain 4-5 copies of the mitochondrial DNA (mtDNA). In addition to making energy, mitochondria are also deeply involved in a variety of other activities, such as making steroid hormones, detoxication and others. Each cell in our body contains, on average, between 500 and 2,000 of these hard-working machines. When the mitochondria aren't functioning properly, an "energy crisis" can develop in tissues such as muscles, brain and heart, which normally are heavy energy consumers. Even a person with 15% normal mitochondria might have enough to be healthy. However, aging patients may show a more severe disease phenotype. Mitochondrial DNA (mtDNA) is a Double-stranded, circular molecule, except for D-loop which is triple stranded (Contains extra 7S DNA) and encodes for 37 genes In each mitochondrion there are 2 to10 copies of mtDNA. mtDNA encodes 13 mitochondrial peptides, (peptides are in the mitochondrial respiratory chain complex), 2 rRNAs, 22 tRNAs. Other mitochondrial proteins encoded by nuclear DNA mtDNA inherited maternally. Tissues are differentially sensitive to the levels of mtDNA mutations. The mutation rate of mt DNA is 10 to 100x higher than nuclear DNA, mitochondria lack an adequate DNA-repair mechanism. Risks of having affected offspring differ between different mtDNA mutations. Mutations in nuclear DNA coding for mitochondrial components can cause defects in oxidative phosphorylation alter control of replication & expression of mitochondrial genome leading to multiple mtDNA deletions or reduced amounts of mtDNA. Mitochondrial diseases are the result of either inherited or spontaneous mutations in mtDNA or nDNA which lead to altered function of the proteins, or RNA molecules that normally reside in mitochondria. Over 30 mitochondrial DNA point mutations and over 100 mtDNA rearrangements have now been identified as etiological factors in human disease. Mitochondriopathies are heterogeneous in their molecular pathogenesis and in their clinical presentations. Defects, often present in the form of point mutations, lead to mitochondrial dysfunction which may present with neurological symptoms. One of the recognized syndromes in this class of disorders is MELAS - mitochondrial encephalopathy lactic acidosis and stroke-like episodes. MELAS disorder is caused by mutation: A-to-G at nucleotide 3243 (A3243G) in the mitochondrial tRNA (Leu-UUR) gene. Maternal or occasional sporadic and non-inherited mutation (tRNA Leu) is the most frequent mtDNA mutation (16/100,000 in the adult population), varied clinical presentations as Leigh syndrome or MELAS. Genetic counseling: % of affected offspring increased with mutant load in maternal blood. When maternal mutant load 1% to 19% - 20% chance of affected offspring, and mutant load > 20% - 50% chance of affected offspring. The ratio of mutant to normal mtDNA in each tissue, along with other factors, may determine the severity of the disease in an individual. Two biopsy samples of the skeletal muscle were fixed in glutar-aldehyde and postfixed in osmium-tetroxide. The specimens were dehydrated in a graded series of alcohol and embedded in EPON. The ultrastructural analysis of the sections was performed on Philips electron microscope 208S. By the ultrastructural analysis of the skeletal muscle in a 3-year old patient with Leigh syndrome we evaluated the subsarcolemmal accumulations of abnormal mitochondria of various shapes and sizes with aberrant crystal architecture. The characteristic electron microscopy findings of the skeletal muscle in a 42-year old patient with MELAS included abnormal mitochondria and mitochondria with paracrystaline inclusions. Rectangular crystalline inclusions are located in the outer mitochondrial compartment (usually in the intracrystal space) and are made up of parallel arrays of plates or filaments with periodical constrictions between them. Mitochondrial plasticity plays an important role in the adaptation of cells to changing energy demands. This is particularly true in the skeletal muscle, that reacts to aerobic endurance training by increasing the number of capillaries and mitochondria. It is concluded that, although ultrastructural changes in the mitochondria may represent unspecific findings, the electron microscopy of muscle biopsy specimens is a useful screening method to select the specimens for further biochemical analysis and to obtain an early and more precise diagnosis of the disease.

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A fixative for detection of lymph nodes and its role in elaboration of resected material with colon and breast carcinomas

KEYWORDS: Lymph node; Tissue fixation; Breast neoplasms; Colorectal neoplasms

The status of lymph nodes is of substantial importance for establishing the state of colon carcinoma as well as brest carcinoma, being the most important single prognostic factor for the patient`s life expectancy. As per the recommendation of the Cancer Committee of the American Pathology College, the minimum of 12 lymph nodes with colon cancer and 10 lymph nodes with breast cancer must be detected in the resected material for a successful determination of the stage of the disease. Traditionally, lymph nodes are detected by inspection, palpation and serial section of pericolic and axillary fat tissue. Objective of the research: to examine the value of a cheap fixative, which may help in quick visualization of the lymph nodes in a material, and compare it to the traditional method. Methodology: a prospective analysis has been carried out on 32 samples gained from colon carcinoma resection and 22 samples from axillary dissection. Initially, the material was elaborated using traditional methodology with complete extraction of the lymph nodes. Subsequently, the material was placed in a fixative for detection of lymph nodes for a period of 12 hours.100 ml of the fixative contained 65ml of 95% alcohol, 20ml of diethyl ether, 5ml of glacial acetic acid and 10ml of buffered 10% formaldehyde solution. After the said time, the material was inspected and the previously undetected lymph nodes appeared lime-white and clearly visible. All the lymph nodes were subject to analysis through the optical microscope and the results processed using descriptive statistics. In the material gained through traditional resection of colon carcinoma, between 1 and 48 lymph nodes per case were detected (median 20, SD=11.32). 0 to 21 lymph nodes per case were detected using additional fixation (median 4, SD=4.23). The size of the lymph nodes detected using additional fixation varied between 0.5mm and 5mm. In 7 cases, the number of lymph nodes detected traditionally was smaller than 12. Upon additional fixation, there was an increase to 12 or more in two cases, enabling thus a satisfactory determination of the stage of the disease. In each of the two cases, one lymph node with metastasis of carcinoma was detected using the additional method though this additional lymph node didn't modify the TNM stage of the disease. In the breast carcinoma, in the material gained from axillary dissection using traditional methodology, 6 to 26 lymph nodes per case were detected (median 15, SD=6.26). Between 0 and 4 lymph nodes per case were detected using additional fixation (median 0, SD=1.10).The size of the lymph nodes from additional fixation varied between 0.5mm and 3mm.In 4 cases where the number of lymph nodes was smaller than 10, no lymph nodes were found using additional fixation. Conclusion: additional fixation enables detection of all lymph nodes in a material, which helps determine the stage of the colon or breast carcinoma. Therefore, we recommend this method to be used as a routine

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Histological and radiological reparative changes in alveolas following teeth extraction

KEYWORDS: Tooth extraction; Regeneration; Wound healing; Pathology; Radiography

Congenital oligodontia is a very common developmental anomaly of the orofacial system in animals. As it could be easily confused with changes that occur in the alveoli after the teeth extraction, it became interesting to small animal practitioners. We have used the total of 15 German shepherd dogs, 10 months old and of 20-27kg body mass. The animals were fasted 24 hours prior to the operation. The extraction of 1st premolar from the right side of maxilla and 2nd premolar from the right side of maxilla was then performed. For x-ray of the maxilla we have applied the retro alveolar technique and extra oral films. After eight months, the dogs were sacrificed and sections of pieces of the alveolar bone were taken for histological analyses. Decalcination of the bone samples was performed by the decalcinate for compact bones consisting of formic acid and sodium-acetate. Analyses of individual elements that are important for radiological diagnostics of teeth aplasia included the dynamics of the alveolar space filling, the appearance, form and loss of calcinous shadow of lamina dura, diameter of inter dental space and contour of the alveolar limbus. At the end of the experiment, eight months after the extraction, histomorphological examinations of the alveolar tissue sections were performed in order to estimate the microstructure of this regions and to analyze the dynamics of their filling. Each alveolus was examined in three levels. The intensity of the osteogenesis in the alveoli of extracted teeth was judged by the presence of the osteoblastic tissue, trabeculae and intensity of the periostal reaction. The degree of maturity of the newly formed bone tissue was judged by the presence of the bone marrow. The analyses of the experimental data revealed the possibilities of radiological and histological diagnostics in monitoring the changes on the alveoli following the teeth extraction or loss. We observed the differences in the length of the time necessary for reparation of radicular spaces of different premolars from the maxilla. There are also differences in duration of the reparative process between the alveoli of the upper and lower jaw.

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Autoimmune myelofibrosis associated with juvenile Sjögren's syndrome. A case report

KEYWORDS: Myelofibrosis; Sjogren's syndrome; Autoimmune; Pathology; Case report

Myelofibrosis is characterized by an increased reticular content in the bone marrow (BM). It is often associated with malignant disease and chronic infections. But, association of myelofibrosis with autoimmune diseases has more rarely been described, especially in young adults. A 21-yr-old woman was presented with 14-years history of xerostomia, xerophtalmia and recurrent parotid gland enlargement. The diagnosis of primary Sjögren's syndrome (SS) was performed 5 years ago. Autoimmune features included positive ANA and RF with polyclonal hypergammaglobulinemia. Hepatosplenomegaly and lymphadenopathy were absent. The total blood count was normal, but 6-months ago leukopenia has been detected (WBC $3.3x10^9$/l). BM aspirate was unsuccessful. BM biopsy specimens revealed severe hypocellularity with increased fibrosis (grade 3 to 4), intrasinusoidal hematopoiesis and sparse nonparatrabecular, loose aggregates of lymphocytes. There were no dysplastic cells in erythroid, myeloid or megakaryocyte lineage nor clusters of megakaryocytes. The diagnosis of autoimmune myelofibrosis associated with SS was made. Our patient will be carefully followed up as SS patients are at risk of developing both SLE and lymphomas. The absence of morphologic and clinical features of myeloproliferative and lymphoproliferative disease is the clue for distinguishing autoimmune myelofibrosis from better known causes of BM fibrosis.

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Sjogren's syndrome - Histopathological analysis of salivary glands

KEYWORDS: Sjogren's syndrome; Salivary glands; Pathology; Retrospective studies

Sjogren's syndrome is a clinicopathologic entity characterized with dry eyes (keratoconjunctivitis sicca) and dry mouth (xerostomia) resulting from immunologically mediated destruction of the lacrimal and salivary glands. The disease may occur as isolated (primary form), also known as sicca syndrome, or in association with other autoimmune diseases (secondary form). The most common among other autoimmune diseases are rheumatoid arthritis and systemic lupus erythematosus. We analyzed 12 cases with the clinical diagnosis of Sjogren's syndrome at the Institute of Pathology, Faculty of Medicine in Skopje, from the period between 1999-2002. 11 cases were sent from the Clinic of Maxillofacial Surgery and 1 was sent from the Clinic of Rheumatology, associated with systemic lupus erythematosus. The obtained bioptic material was routinely processed and stained with standard hematoxylin-eosin, histochemical stainings Van Gieson and PAS, as well as immunohistochemical analyses using the method Avidin-Biotin peroxidase (Hsu). We used monoclonal antibodies for CD79, CD20, CD43, kappa and lambda light chains. In the obtained bioptic material (12 cases) with the clinical diagnosis of Sjogren's syndrome, morphological changes supporting this diagnosis were found in 5 cases. The following morphological criteria were used for partial or total confirmation of the clinical diagnosis: periductal and perivascular lymphocytic infiltration, which may be extensive and form lymphoid follicles with germinal centers, hyperplasia of the epithelial cells lining the ducts, which may result in their obstruction, atrophy of the glandular acini, fibrosis and hyalinization of the interstitial tissue, atrophy and replacement of the parenchyma with fat, the intensity of the lymphoid infiltrate may appear as lymphoma. The heterogeneous population of these cells and partially preserved lobular structure of the gland differentiate this lesion from lymphoma. In our material the female:male ratio was 3:2, and the age of the patients was between 40-60 years, which corresponds to the literature data. The histological criteria were not met in the remaining 7 cases sent as Sjogren's syndrome, and they were diagnosed as chronic syaloadenitis, normal morphology and one case of MALT lymphoma with associated atrophy of the salivary gland. The definition of Sjogren's syndrome saying that it is a clinicopathological entity points to the necessity of establishing a correlation between the histopathological findings and the clinical symptoms and history of the disease. The histopathological findings, obtained by modern techniques (immunohistochemistry), may confirm or exclude the clinical diagnosis.

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Morphological features of liver giant mitochondria

KEYWORDS: Liver; Mitochondria; Pathology; Retrospective studies

Mitochondria, double membrane organelles present in all cells, display a variety of shapes, including spheres, rods and long filamentous structures. Being sensitive indicators of cellular pathology, they respond to an injury by a marked increase in size. In certain cases, mitochondrial enlargement results in formation of giant mitochondria (GM). Formation of GM may be detected by light microscopy in a high proportion of alcoholics, and rarely in nonalcoholic liver diseased . As to connection between GM and apoptosis there are two types of mitochondrial enlargement- simple swelling and formation of GM. Formation of GM may be a prerequisite for free radical- mediated apoptosis. We performed staining with Masson trichrome (MT) on 1445 routine liver biopsy samples in order to determine the presence of GM, morphological features of GM, and also to compare the presence of GM with the presence of Mallory bodies, macrovesicular steatosis and apoptotic bodies. Chi-square test was used for statistical analysis. The main criteria was that on MT stains GM are larger than nucleolus and stain bright red. The study revealed the presence of GM in 51 routine liver biopsy samples (3.6 %), liver cirrhosis being the most frequent form (ALD-alcoholic liver disease related). GM can also be found in chronic viral hepatitis (9.8 %), primary biliary cirrhosis (7.8 %) and many other forms of the liver disease. GM are much often visible in macrovesicular steatosis. There is no statistically significant connection between liver steatosis and the presence of GM. During the morphological investigation on GM, we noticed that in 66% of the samples round-shaped GM were present, in 16 % spindle-like, and in 18 % both round and spindle- like GM. As to the distribution of hepatocytes with GM within the liver acini, we noticed that 79 % of round, 85 % of spindle-like and 75 % of both round and spindle-like GM are distributed around portal areas. GM are much often visible in macrovesicular steatosis than in any other form of the liver steatosis. 13.7 % of all samples with GM contained also Mallory bodies, 9.8 % contained both Mallory bodies and macrovesicular steatosis, and 21.6 % contained apoptotic bodies.

Although GM are mostly visible in all forms of ALD, these organelles are also present in various forms of the liver disease. Their presence, shape, size and distribution are of no importance in routine evaluation of liver biopsy samples.

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Fibrocystic breast disease in the analysed material of the Institute of Pathology, Medical Faculty Priština from 1993-1997

KEYWORDS: Fibrocystic disease of breast; Retrospective studies; Age distribution

The term "fibrocystic breast disease (FBD)" refers to a spectrum of very polymorph disorders of breast structures caused by a long term hyperestrogen influence of the ovaries. Clinically, the disease is usually seen before the age of 40. It can be rarely seen at menopausal women. The aim of our research was to determine the frequency of FBD in breast biopsies, the frequency of FBD in the breasts without and with carcinoma, location of FBD and its age distribution. Our analysed material included 29586 biopsies, of which 805 or 2.72% were breast lesions. FBD was diagnosed in 239 cases or 29,69% of all breast lesions or almost 55% of all benign breast lesions. FBD was more frequent in the left than in the right breast. Its bilateral localisation was registered in only 6 (2,51%) cases. In more than 50% cases it was located in the lateral upper parts of the breasts. The mean age of the women with FBD and without the breast carcinoma was 38.91 years (min=16, max=84). The mean age of the women with FBD associated with the breast carcinoma was 52,24 years (min=30, max=75).

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Relationship between Helicobacter pylori gastritis and paediatric coeliac disease

KEYWORDS: Helicobacter pylori; Coeliac disease; Child; Pathology

Association of coeliac disease (CD) and gastritis with or without Helicobacter pylori (HP) infection in children is intereseting primarily for its relation to host factors. In order to examine this relationship, data on 73 CD patients (43 female, 30 male), median age 5.8 (range 0.6-19.0) years; who had simultaneous small intestinal and gastric antral biopsies, were analysed. Diagnosis of CD was based on non-revised ESPGHAN criteria and Helicobacter pylori colonization on urease test (commercial and home made) and microscopic detection of helicobacter-like organisms in Gram stained antral biopsy smears and modified Gram stained paraffin sections with/without culture and/or serology. Helicobacter pylori infection was associated with gastritis in: 47.9 % of CD patients - 12.3 % had normal villi, 12.3 % partial atrophy, 23.3 % subtotal/total atrophy. Helicobacter pylori gastritis associated with CD is not so uncommon. Gluten withdrawal and normalised small intestinal histology are not sufficient in lowering frequency of Helicobacter pylori associated chronic gastritis in coeliac disease patients.

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Retrospective study of mesenchymal malignancy in maxillofacial region

KEYWORDS: Mesoderm; Pathology; Maxillofacial surgery; Differential diagnosis

During the last ten years at the Clinic for Maxillofacial Surgery at the MMA there were 35 patients with mesenschymal malignancy, making less than 0.5% of all patients with a malignant disease of the head and neck region. The gender distribution is equal - 18:17. The patients were 5-75 years old. The males expressed the disease mostly at the age of 25 and 45, while the females expressed it at 25 and 60 years of age. These patients were followed for 2-28 years. Six of them died, 8 are in stable remission and 5 with poor prognosis at the moment, while there is no relevant data for half of them, although it is certain to presume them to be classified either in the first or the second one of these three categories. There were 31.43% malignant schwannomas, 28.57% rhabdomyosarcomas, 11.43% malignant fibrohystiocytomas, 5.57% leiomyosarcomas, 5.7% osteosarcomas, 5.7% chondrosarcomas, 5.7% liposarcomas, 5.7% dermatofibrosarcomas and 2.86% malignant haemangiopericytomas. In the maxillofacial region, the mesenchymal malignancy mostly developed on the alveolar process of the upper jaw (35%) and parotidomasseteric region (31.5%); neck (10.5%); scalp (7%) and premaxilla (7%), while in the rest 8% of the patients the malignancy appeared in other regions of the face. On the first admission, 28.57% of the patients were at the T-1 stage, 31.43% in T-2 and 31.43% in T-3 stage, and 8.57% in T-4 stage of the disease. The largest malignancy measured over 20 cm at the face. Lokoregional cervical secondary deposits developed in 34.29% of the patients, and 11.43% developed distant metastases in the lungs, liver and brain The histopathological diagnosis has been established just in one, inoperable patient (2.86%) by the probatory excision, while the other patients underwent a radical surgical treatment once (34.29%), twice (25.71%), up to ten times (31.43%) and over ten times (5.71%). The second surgical intervention was performed one, up to three or up to five years after the initial operation in 28.57%, 41.28% and in 17.14% of the patients respectively. The postoperative irradiation therapy was applied in 6 (17.14%) patients, chemotherapy in 7 (20%) and both of them in one (2.86%) patient. Two patients (5.71%) with a previously operated and by later revision of specimens confirmed benign tumor (epulis; fibrous dysplasia), developed a malignant alteration to malignant fibrohistiocytoma after one year. In three (8.57%) patients originally diagnosed as rhabdomyosarcoma, malignant haemangiopericytoma and leiomyosarcoma, the additional revision of former specimens definitely confirmed the diagnosis of malignant schwannoma after five, fourteen and two years, that was after the fifth, twelfth and second operation. The youngest patient, a 5-years old boy, a few months after a removal of the left eye due to retinoblastoma, was operated because of the invasive osteosarcoma of the right orbita. Few months later he died. Three females (3/18) were in the third trimester of pregnancy, but it makes 100% of all pregnant patients operated because of a malignancy in our Clinic. The first one had rhabdomyosarcoma of the infratemporal region, the second one a malignant fibrohistiocytoma of the parotidomasseteric region and the third one a malignant schwannoma in the parotidomasseteric region, too. All the three patients died within one year after the delivery. A mesenchymal malignancy in the head and neck region is rare, but with significant mortality.

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Multifocal appearance of different malignant entities: a case report

KEYWORDS: Multiple neoplasms; Maxillofacial; Pathology; Retrospective studies

It is well known that one either benign or malignant tumor can appear multifocally, as well as that histologically different tumors can exist coincidentally. A few studies have attempted at answering how many different concomitant tumors can appear in the human body. This paper presents a 78 years old male, a retired chemistry engineer grown by the seaside, with several tumors of different malignancy degree and morphologically benign or semimalignant cutaneous lesions. Over the last 25 years he underwent three surgical excisions of epitheliomas of the scalp, body and limbs. The last time was two years before his first admission to the MMA, when an epithelioma of the right frontoparietal region had been removed, and the defect covered with a free skin graft. His admission was proposed by the consultation board, for a surgical treatment of the tumor sized 4 cm in the right parotid salivary gland, followed by paralysis of the frontal and paresis of buccal branches of facial nerve. The patient was also presented by one palpable lymph node in the right submandibular region up to 2 cm in diameter and one crust 1 cm wide on the left leg. Along with the laboratory finding of 22.48 leukocytes and histopathologic frozen-section analysis, the right-sided radical parotidectomy and suprahyoid dissection of the neck were performed. The histopathologic analysis did not confirm the preoperatively suspected metastatic tumors, but a malignant mixed tumor of the parotid salivary gland, while in four carotid (one of them analyzed by frozen-section) and one submandibular lymph node a chronic nonspecific lymphadenitis was found. The excised cutaneous lesion from the leg was verified as senile hyperkeratosis. According to the decision of the consultation board, the postoperative irradiation therapy was applied in 21 fractions and the total dose of 45 Gy. Nine months later the patient was admitted again, this time with an exulcerated, 5 cm in diameter cutaneous lesion of interscapular region, that appeared two months earlier. Because of the WBC count of l23.60 (12.6 neutrophils, 78.8 lymphocytes and 0.8 monocytes), the peripheral blood smear and myelogram were performed, On the basis of these findings and in the absence of pathologic lymphadenopathy and organomegaly, the chronic lymphoproliferative disease in the form of chronic lymphocytic leukosis, grade A was diagnosed (although the reactivity following the neoplastic process could not be excluded), but specific hematologic treatment wasn't indicated. The excised cutaneous tumor from the back was histopathologically confirmed as the infiltrative G-2 squamocellular carcinoma. Nine months later the patient was readmitted, presented by multifocal cutaneous lesions on the face and neck, that appeared two months earlier. There WBC count was 30.28 accompanied by an identical finding in the peripheral blood smear, without radiographic changes on the skull bones and lungs, and also without clinical and ultrasonographic lymphadenopathy and organomegaly. The patient was operated and together with the right-sided tarsorraphy, nine cutaneous lesions were remove, with a: partial amputation of the upper pole of the left auricle destroyed by a 3.5 cm exulcerated tumor. On histology, the FIRST lesion was diagnoserd as a malignant mixed tumor involving the subcutaneous tissue and cartilage. The SECOND, 2 cm sized lesion excised from the left temporoparietal region and directly sutured, was established as senile keratosis. The THIRD 1 cm lesion excised from the forehead and directly sutured was defined as chronic dermatitis. The FOURTH, 6 cm exulcerated lesion excised from the left parietal region close to midsagittal line and the defect covered with free cutaneous graft was on histology established as a squamocellular G2 carcinoma. The FIFTH, 2 cm large lesion excised from the right frontoparietal region and the defect covered with free cutaneous graft was diagnosed as seborrheic keratosis. The SIXTH sample of two lesions, 1 cm and 2 cm in size, excised together from the right zygomatic region and directly sutured, were on Histopathologic analysis define as sebaceous adenomas. The SEVENTH, exulcerated lesion of 7 cm together with the periost excised from the right parietal region, the defect reconstructed with transpositional cutaneous flap based on the occipital artery, the secondary defect covered with free cutaneous graft, was histologically diagnosed as corneal squamocellular G-1 carcinoma. The EIGHTH, 2 cm sized lesion excised from the left supraclavicular region and directly sutured, was on histopathology established as baseocellular carcinoma. The NINTH, 1 cm large lesion excised from the right supraclavicular region and directly sutured was diagnosed as an adenoid type of the baseocellular carcinoma. The Oncologic Consultation Board suggested further surgical, hematologic and clinical follow-up. The patient came five times for monthly controls in a good general condition, without relapses, regional or distant metastases. We were later informed that the patient suddenly died during the sleep seven months after the surgery. All the three surgical treatments performed at the MMA were completed without complications and the treatment of chronic lymphocytic leukosis. Histopathologic examinations of the removed tissues and revisions of the former specimens undoubtedly excluded the spreading of one and the same tumor in different regions, but proved multifocal appearance of tumors of the same embryologic - ectodermal origin in very different structures. The authors found no evidence in the available literature of a similar case of associated cutaneous tumors, malignant mixed tumor of the salivary gland and chronic lymphocytic leukosis.

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Actinomycosis pedis - A case report

KEYWORDS: Actinomycosis; Foot diseases, Case report

Actinomycosis is a chronic suppurative infection localized chiefly to the neck, lungs or abdomen. The lesions, which spread by contiguity, are markedly indurated and contain multiple abscesses that drain to the surface by sinuses. The discharge from the sinuses typically contains grossly visible yellowish colonies called sulfur granules. Most human infections are caused by Actinomyces israelii. A case of a 32 years old female with soft tumor lesion on her left foot is reported. We have analyzed two soft tissue specimens using the standard histologic staining with hematoxylin eosin. The first one was ellipsoid excision of skin with dimensions: 30x15 mm and the second one a soft tissue fragment with dimensions: 20x15x5 mm. Both specimens exhibited the same histologic features. Under the superficial stratified squamous epithelium there were granulomas showing central suppurative necrosis surrounded by granulation tissue and intense fibrosis. The granulomas contained bacterial colonies consisted of interwined radiating filaments (rays) capped by eosinophilic hyaline material (clubs) creating a sunburst pattern. An inflammatory infiltrate composed of polymorphonuclears, eosinophils, lymphocytes and plasma cells with marginally localized giant cells was present.