

ABSTRACTS

INFLUENCE OF ENVIRONMENTAL FACTORS ON GENESIS OF MALIGNANT, PROFESSIONAL AND CONATAL DISEASES

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DERMATOPATHOLOGY (abs. 6-9)

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Leiomyosarcoma laryngis

Malignant mesenchymal neoplasms other than primary cartilaginous tumors in the larynx and trachea are extremely rare. Fibrosarcoma was originally considered the most common laryngeal malignant mesenchymal tumor. Other malignant mesenchymal neoplasms reported in the larynx include rhabdomyosarcoma, MPH, osteosarcoma, synovial sarcoma, liposarcoma, malignant schwannoma, angiosarcoma, malignant hemangiopericytoma, extraskeletal Ewing's sarcoma, and leiomyosarcoma. We reported a case of leiomyosarcoma of vocal cord in a male patient, 67 years old, with a polypoid mass in the left vocal cord. On histological examination we found: fascicle of spindle cells with vesicular, ovoid to cigar shaped nuclei showed orderly arrangement with occasional foci of necrosis. The nuclear-to-cytoplasmic ratio was increased with atypical nuclei. Focally there were giant cells with nuclear hyperchromasia and atypical nuclei, with presence of 1 mitosis per 10 high-power fields.

KEYWORDS: *Leiomyosarcoma; Laryngeal Neoplasms; Histological Techniques*

Morphological differentiation between regenerative changes in bronchial glands and squamous carcinoma

We found regenerative changes in bronchus at the site of former biopsy of bronchial glands. They had characteristics of necrotizing sialometaplasia (NS). The glandular changes of NS type can be misinterpreted as squamous carcinoma. In our researching we used 78 biopsy samples. They were divided into two groups: Group I (44 samples with regenerative changes in bronchial glands taken from re-biopsy), and Group II (34 samples with diagnosis of squamous carcinoma). In both groups presence of the same morphological parameters were observed and z-score with the error risk of 5% ($\alpha=0.05$) was applied. Morphological changes in bronchial glands at the biopsy site that had characteristics of regenerative changes were as follows: lobular form of the change (in 59.09% of cases), fibrin ($z=3.81$; $p=0.0001$), granulation tissue ($z=7.53$; $p<0.0000$), squamous cells in fibrin ($z=3.27$; $p=0.0011$), reparation defect in a cartilage ($z=2.76$; $p=0.0057$), granulocytes in epithelium ($z=2.91$; $p=0.0036$), columnar epithelium ($z=6.54$; $p<0.0000$), goblet cells on the squamous epithelium ($z=4.41$; $p<0.0000$), ciliated columnar cells on the squamous epithelium ($z=2.04$; $P=0.0409$), mucous in interstice ($z=6.27$; $p<0.0000$), cystic formations ($z=6.31$; $P<0.0000$). Morphological changes that had features of squamous carcinoma were as follows: infiltrative form of lesion (70.59% cases), squamous epithelium without fibrin ($z=-5.97$; $p<0.0000$), diskeratosis ($z=-3.47$; $p=0.0005$), nuclei polymorphism ($z=-2.10$; $p=0.0358$), nuclei hyperchromatism ($z=-5.81$; $p<0.0000$), polynuclear cells ($z=-2.49$; $p=0.0126$), mitoses ($z=-5.02$; $p<0.0000$), squamous cells in lymphatic vessels ($z=-3.85$; $p=0.0001$), necroses ($z=-4.66$; $p<0.0000$). The changes that disabled differentiation between regenerative glandular lesions and mucocpidermoid carcinoma were: granulocytes in stroma ($z=0.82$; $p=0.4111$), mucous defect ($z=-0.66$; $p=0.5094$), mononuclear cells in stroma ($z=-1.55$; $p=0.1205$), squamous epithelium (present in all the cases of both groups), nucleoli ($z=-1.80$; $p=0.0711$), squamous cells in connective tissue ($z=-0.53$; $p=0.5980$). The characteristics of bronchial gland changes at the former biopsy site were: lobular lesion, defect filled with fibrin or granulation tissue on the surface, isles of epithelial cells with cellular polymorphism, nucleoli, mitoses, intraepithelial and stromal granulocytes, presence of reparative defect in the cartilage, goblet and ciliated columnar cells, as well as interstice mucous and cystic formation. Characteristics of squamous carcinoma are: lesion with defect on the surface, with infiltrative form, consisting of squamous cells with expressed polymorphism, nuclear hyperchromatism, presence of polynuclear cells, numerous diskeratotic cells, frequent mitoses located in connective tissue stroma filled with lymphocytes.

KEYWORDS: *Bronchi; Biopsy; Regeneration; Carcinoma, Non-Small-Cell Lung; Diagnosis, Differential; Cytodiagnosis*



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Efficacy and safety of the transthoracic needle aspiration biopsy in diagnosis of pulmonary lesion

In the past several years, improved imaging and biopsy techniques have made possible to obtain tissue samples from most lung lesions, including very small nodules measuring less than 1 cm in diameter. During the same period, cytopathologists have developed remarkable accuracy in their interpretation of cytologic preparations and small tissue fragments, making it possible to use smaller (and safer) needles without sacrificing diagnostic accuracy. Several authors have demonstrated that carefully performed transthoracic needle biopsy (TNAB) can provide extremely high accuracy for the diagnosis of cancer. The use of fine needles has extended the applications of TNAB to perform safely the biopsy of deep lesions of the lung, hilus, and mediastinum. The purpose of the study was to evaluate diagnostic efficacy and the safety of TNAB in diagnosis of pulmonary lesion. We made a retrospective study of 47 consecutive patients (40 males, 7 females, mean age 60.8 years) with lung lesions underwent TNAB in the period of 4 years. The indications for performing TNAB were pulmonary nodules, masses, or infiltrates when there was a reasonable suspicion of malignancy. The lung lesions were detected on chest x-ray and CT. One patient had bilateral lesions. Before TNAB all the patients were submitted to fiberoptic bronchoscopy, which resulted non-diagnostic. Biopsies were performed under the local anesthesia with aspiration needle with minimum two passes, under fluoroscopic control. There were 80.85% positive biopsy results. Among patients with primary lung cancer histological type (squamous cell, small cell, adenocarcinoma) was determined in 25 (65.8%), undifferentiated type was present in 4 (10.6%) patients. There were 8 (21.6%) patients with benign lesions. There were no complications. When fluoroscopic guidance is used to perform the biopsy, CT is extremely useful for localization and for planning the most direct and safest approach to the lesion. The advantages of performing the biopsy under fluoroscopic guidance are that it is faster and less expensive. TNAB is safe and sensitive procedure in diagnosis of pulmonary lesions. Accurate histological diagnosis was obtained in most of our patients without complications.

KEYWORDS: *Biopsy Needle; Lung Diseases; Lung Neoplasms; Diagnosis; Sensitivity and Specificity; Cytodiagnosis*

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Cytopathological analysis of sputum in pig farmers

Many epidemiological and clinical studies have demonstrated an increased risk for the symptoms of respiratory disorders and alterations of respiratory functional tests in pig farmers. We have carried out a cytological sputum study of potential inflammatory and morphological epithelial changes of respiratory tract in pig farmers. We have also estimated the influence of pig farm exposition, smoking history, age and sex of farmers on these changes. Spontaneously produced sputum specimens were obtained from 133 randomly selected pig confinement operators and 120 control subjects, all clinically healthy, and grouped according to smoking habits and sex. Pig farmers worked on six pig farms housing 12383 pigs on average. Mean duration of work was 12.9 years (SD 8.8; range 2-29). The specimens were embedded in paraffin and multiple sections were stained with hematoxylin and eosin and tested for iron. There were no significant differences between pig farmers and control group in mean age, sex distribution, and smoking status ($p > 0.05$). All cytological findings were more frequent in pig farmers than in controls, but χ^2 test identified significant differences in the incidence of ACC and eosinophils ($p < 0.01$), and especially siderophages and respiratory spirals ($p < 0.005$). In the multivariate logistic regression analysis (Model 1) pig farming is the single, highly significant risk factor for siderophages and eosinophils only, and also operates in interaction with smoking. Smoking is the only single significant predicting factor for ACC, SM, ASM and respiratory spirals, but pig farming and somewhere other two variables operate in interaction with smoking. Pack-years is the only single predicting factor for all cytological findings (Model 2). Our findings support the supposition that some constituents of the pig farm environment might induce a hemorrhage, inflammation and an allergic reaction of respiratory tract. The findings of ACC, SM and, ASM represent signs of bronchial injury that might rise during development of chronic obstructive pulmonary disease, whose symptoms and functional alterations are still registered in pig farmers. In the only morphological study, thickening of the basement epithelial membrane of the lobar bronchi was identified in endobronchial biopsies of 27 pig farmers. Our study is the first extensive morphological study in the pig farmers.

KEYWORDS: *Sputum; Cytodiagnosis; Respiratory Tract Diseases; Agriculture; Occupational Exposure*



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Mediastinal cysts

Characteristics of skin basal cell carcinoma located in sun exposed areas

Mediastinal cysts are rare pathological entity and they consist 10 to 15 percent of radiological detected masses of this region. Cysts of mediastinum can be unilocular or multilocular, variable size up to 18 cm in diameter. In our study we include 163 patients, which were operated due to radiologically detected mediastinal tumor mass in ten-year period of time (from 1992 to 2003). From 163 diagnosed mediastinal masses 134 patients had solid tumors and we found cystic formations in only 29 patients. Among patients with solid tumors we found Hodgkin lymphoma in 37 patients, non-Hodgkin lymphoma in 27, metastatic carcinoma in 35, thymoma in 10, mesenchymal tumors in 15, thymic hyperplasia in 6, seminoma in 2, immature teratoma in 1, mesothelial cysts in 1, and colloidal thyroid goiter in 1 patient. We documented 48.3% mesothelial and 51.7% non-mesothelial cysts. Mesothelial cysts were found more often in women (64.3%) and non-mesothelial in men (66.7%). Median age of patients with mesothelial and non-mesothelial cysts was 38 and 39 years of age, respectively; the youngest patients in both our groups were 18 years old. Size of mesothelial cysts was from 2 cm to 11 cm (average: 6.4cm), and non-mesothelial from 1.5cm to 11 cm (average: 6.5 cm). Bronchogenic (33.3%) and dermoid (26.7%) cysts were the most frequent of non-mesothelial cysts, thymic cysts we found in 3 patients while parathyroid cysts had only 1 patient. Cystic tumors were diagnosed in 3 cases, from which 2 were cavernose lymphangiomas and 1 was cystic schwannoma. Though rare changes, mediastinal cysts are very diverse group of pathological changes. In our study mediastinal cysts were found in 17.8% of radiological detected masses in mediastinum. The approximate ratio of non-mesothelial and mesothelial cysts was 51.7%: 48.3%. They are more frequent in younger and middle-age population. Size of these changes differs as well as their localization. Non-mesothelial cysts were often found in men (66.7%) and mesothelial in women (64.3%). Bronchogenic (33.3%) and dermoid (26.7%) were the most frequent of non-mesothelial cysts. We have to emphasize that some mediastinal tumors can have cystic appearance. In our study cystic tumors constituted 20% of non-mesothelial cysts: cavernose lymphangiomas (13.3%) and cystic schwannoma (6.7%). Mediastinal cysts are rare and broad differential diagnostic group of changes in mentioned area of human body.

KEYWORDS: Mediastinal Cyst; Mediastinal Neoplasms; Diagnosis, Differential

Basal cell carcinoma (BCC) is a very common skin tumor of elderly persons. It most frequently occurs in sun-exposed and changed areas of the skin. Usually, the age-related changes coexist and make an important surgical problem. Aim of the study was to establish the main characteristics of the BCC located in the skin of face and neck, which may have practical importance in plastic surgery and in the postoperative treatment. 82 consecutive complete excisional BCC tumor biopsies of the sun-exposed skin of face and neck regions. Material was obtained from 39 female and 43 male patients, with an average age of 58.55 years (range: 33-85 years). The histological level of infiltration of BCC was usually the reticular dermis - 54.88%, followed by the infiltration into the papillary- reticular margin - 25.61%. The mean tumor thickness was 2.73 mm. The most common type of growing was infiltrative type, found in 45.12% of the cases, followed by nodular or noduloulcerative type, found in 35.37% of the cases. Among the tumors with histological infiltration into the subcutaneous adipose tissue, the most common growing type was infiltrative type - 72.73%, with the mean tumor thickness of 4.43 mm. In the largest majority of the cases (93.90%) the tumor was thicker than 1.5 mm. The mean facial skin thickness was around 1.5 mm, but with ageing it can be even smaller; also, accompanied by the harmful solar effect, it can cause a problem in obtaining the best cosmetic results after the total excision of thick tumors.

KEYWORDS: Carcinoma, Basal Cell; Skin Neoplasms; Ultraviolet Rays; Cytodiagnosis



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Clinicohistological characteristics of spinocellular carcinoma of the skin

Squamous cell carcinoma (SCC) is the most common tumor appearing on sun-exposed sites in older people. Except for lesions on the lower legs, these tumors have a higher incidence in men than women. Implicated as predisposing factors, in addition to sunlight, are industrial carcinogens (tars and oils), chronic ulcers and oraining osteomyelitis, old burn scars, ingestion of arsenicals, ionizing radiation, and tobacco and betel nut chewing. The authors presented clinicohistologic characteristics of the skin in patients treated at the Clinic for Dermatology in Niš, from 2000 to 2003. The examined group comprised 240 patients with histologically verified squamous cell carcinomas of the skin. These patients were clinically examined by dermatologists and treated by X-ray therapy, after incisional biopsy and histopathological diagnosis. The majority of examined patients were with exophytic form of carcinoma (57%), then with ulcerous (34%), and rarely with the other macroscopic forms of carcinoma (9%). Pathoistological examinations of SCC of skin included the following parameters: histological type (and subtype), degree of differentiation of tumor cells by Broder's classification, examination of tumor edges, and immunological stromal reactivity of the patients to the presence of SCC. We found: free edges in 92%, differentiated type in 72%, nuclear gradus I in 12%, II in 75%, and III in 13%, and immunological mononuclear and desmoplastic reactivity in 66% of cases. Authors conclude that the incisional biopsy of skin epitheliomas is necessary not only to confirm clinical diagnosis in order to perform x-ray therapy, but to evaluate tumor edges, histological and nuclear grade, and immunohistological reactivity - all characteristics that are also very important for prognosis of this disease.

KEYWORDS: *Skin Neoplasms; Carcinoma, Squamous Cell; Histological Techniques*

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Spindle cell carcinoma of the forehead: A case report

Spindle cell carcinoma (SCSC) is a rare variant of squamous cell carcinoma (SCC) comprising up to 3% of SCC. Tumor is characterized by conventional SCC intermingled with invasive spindle cell (sarcomatoid) elements. The lesion is covered by dysplastic surface squamous epithelium. There is profound male to female ratio (11(1) and generally the tumor occurs in individuals in their seventh decade of life, although patients can present within a wide age spectrum. We report a case of 80 years old female patient with SCSC, involving forehead area. Grossly, tumor appeared as pedunculated, polypoid mass 31x20x10 mm in diameter. Histopathologically, tumor was composed predominantly of anaplastic spindle-shaped cells arranged in intermingled fascicles and of conventional SCC cells. The anaplastic spindle cells strongly resembled atypical mesenchymal elements. Immunohistochemically, both components of tumor strongly expressed the epithelial markers cytokeratin and EMA, and were negative for S-100 and mesenchymal cells markers. The SCSC may imitate a number of different mesenchymal processes such as malignant fibrohistiocytic tumors, leiomyosarcoma or fibrosarcoma. Histopathologically, it is difficult to distinguish this tumor from other spindle cell lesions. However, the positive immunostaining for epithelial cells markers is essential for correct diagnosis.

KEYWORDS: *Carcinoma; Skin Neoplasms; Head and Neck Neoplasms; Carcinoma, Squamous Cell*



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Cyclin A expression in actinic keratosis, Bowen's disease, and squamous cell carcinoma of the skin

Intraepithelial lesions of cervix and their relationship with HPV infection

Recently, a new classification scheme based on the degree of epidermal involvement (keratinocytic intraepidermal neoplasia-KIN1, 2, and 3) has been proposed, but only few studies analyzed cell cycle proteins expression and none did so on cyclin A in AK regardless of the nomenclature used. Specimens of 12 AKs, 3 BDs, and 16 SCCs (5 well-, 6 moderately, and 5 poorly differentiated) were examined immunohistochemically with antibody to cyclin A using streptavidin-biotin technique. Nuclear staining was evaluated regarding the distribution of cyclin A positive cells and number of stained nuclei per 500 nuclei in areas with most pronounced immunoreactivity. Statistical significance of differences in cyclin, an expression between AK, BD, and SCC and in relation to level of differentiation, tumor size and maximal thickness was measured with t test, ANOVA, and multiple pairwise comparisons procedure. Cyclin A distribution in KIN1 lesions were basal, in KIN2 basal (2 cases) or basal-suprabasal (3 cases), and in KIN 3 basal-suprabasal (1 case) or full-thickness (4 cases). SCCs expressed cyclin A at the periphery in 5 cases (3 well- and 2 moderately differentiated), both peripherally and inside the tumor nests in 4 cases (2 well- and 2 moderately differentiated) and diffusely in 7 cases (2 moderately- and 5 poorly differentiated). Percentage of cyclin A-positive cells were 9.3% (KIN1), 9.9% (KIN2), and 18% (KIN3) and differences between KIN1 and KIN3 as well as between KIN2 and KIN3 were statistically significant ($p < 0.05$). Regarding SCC, cyclin A was found in 19.5% well-, 28% moderately- and 32.2% poorly differentiated tumors and the difference between moderately and poorly differentiated SCCs was not significant. Stratification of lesions to those up to 10mm, 11-20mm and over 20mm showed an increase in number of cyclin A-positive cells with larger tumor diameter but without statistical significance and comparison of SCCs up to- and over 4mm in maximal thickness did not reveal almost any difference (26.6% and 26.9%, respectively). Cyclin A is protein important in late S phase of cell cycle that corresponds well with grade, stage or clinical outcome in many tumor types (carcinoma of the larynx, breast, endometrium, thyroid, malignant melanoma). In our study, in situ epidermal tumors with full thickness atypia (KIN3) as well as poorly differentiated SCCs displayed significantly higher level of cyclin A-positive cells, irrespective of the tumor size and thickness, implying that it could be an independent factor in evolution of malignant epidermal lesions.

KEYWORDS: Keratosis; Carcinoma, Squamous Cell; Bowen's Diseases; Skin; Cyclin A; Immunohistochemistry

Incidence of intraepithelial cervical lesions is constantly increasing. Many proposal etiologic factors were included in their development, but probably the most important is HPV infection. The degree of intraepithelial lesions depends on carcinomatous potential of HPV. The low-risk HPV types 6 and 11 are found in benign cervical lesions (condylomata acuminata), the medial-risk HPV types 31, 33, and 35 are found in low-grade intraepithelial lesions (LSIL), and the high-grade lesions HPV types 16 and 18 are found in high-grade lesions (HSIL). Precancerous cervical lesions are the most frequent in the reproductive female period between 15 and 50 years of age. Especially is considerable the fact that the incidence of this lesions increases in young population. This study is based on prospective analysis of biopsied and operated material of 1331 female patients cured at gynecology and obstetrics clinic GOC "Narodni front". Formalin-fixed and paraffin-embedded tissue blocks were cut and stained with hematoxylin-eosin. Statistical analysis was performed by applying χ^2 , Kolmogorov-Smirnov test, and Student t test. Benign cervical lesions were the most frequent between 21 and 30 years of age ($D=0.331$; $p < 0.001$; and $D=0.66$; $p < 0.05$). Of all 81 lesions, condylomata acuminata was more frequent histopatological form then condylomata endophitica (4.94%), which was frequently associated with condylomata acuminata. Precancerous cervical lesion associated with HPV infection, condylomata plana HSIL, was the most frequent between 21 and 30 years of age ($D=0.348$; $p < 0.001$). Condylomata plana HSIL or carcinoma in situ was the most frequent between 21 and 30 years, too ($D=0.31$; $p < 0.01$). In 3.52% cases we notified progression of low-grade to high-grade lesion. The low-grade cervical lesions in 65.14% cases were significantly more frequent then high-grade lesion ($\chi^2=33.63$; $p < 0.001$; $DF=1$). We concluded that the intraepithelial lesions of all degrees are very frequent in all female population, however the most frequent between 21 and 30 years of age, confirming the fact that the high percentage of young women are infected with one or more human papilloma virus types.

KEYWORDS: Cervical Intraepithelial Neoplasia; Papillomavirus Infections; Condylomata Acuminata



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Coincidence of HPV infection and pathological changes of the vulva

Changes induced by HPV can be classified in three groups: condyloma (condylomata acuminata), intraepithelial neoplasm (VIN), and malignant lesions (condylomatous, basaloid, and verrucous type of squamous carcinoma). Condylomas can be in coexistence with VIN. The frequency of VIN, as a premalignant lesion, shows increasing tendency. The average age of the patients with VIN is 40 years, decreasing to 25-30 years of age in last few years. For the development of premalignant and malignant lesions, the most important are HPV 16 and 18 in the presence of other cocarcinogens. VIN is graded as VIN I, VIN II, and VIN III and this classification is based on the amount of intraepithelial dysplastic changes. Among all primary tumors of the vulva, squamous carcinoma is found in 76%, with frequency peak at the age of 55 and 77 years. In younger women it is found together with VIN and HPV infection (40%). The aim of this study was to evaluate the frequency of these lesions and the presence of HPV in them. We used surgical material (biopsies and operations) of 67 patients treated in gynecology and obstetrics clinic GOC "Narodni front", Belgrade in 2001 and 2002. The results were statistically analyzed using average value, standard deviation, Student t test, and Kolmogorov-Smirnov test, for small samples. The criteria for statistical significance were $p < 0.05$, $p > 0.01$, and $p < 0.001$. The obtained results showed that 20% of 46 benign cases of vulval lesions was condylomata acuminata; most of them were found in women in the age from 31 to 40 years. We found 17 cases of premalignant lesions: VIN I in 2, and VIN II and VIN III in 6 cases. VIN with condyloma acuminata was found in 2 cases (11.76%). In 7 cases of VIN (41.18%) the beginning of the invasion was found with VIN III. VIN, all stages, was predominantly found in patients older than 60 years of age. Invasive carcinoma was found in 13 cases, 6 (42.86%) G1, N1 5 (35.71%) G2, N2, and 2 (14.29%) G3, N3. Invasive carcinoma was also found in patients older than 60 years ($D=0.619$, $p < 0.01$). One of all invasive carcinoma was metastatic tumor (7.14%). The results showed that the most frequent (46) were the benign lesions (68.66%, $\chi^2=24.34$, $DF=2$, $p < 0.001$), premalignant lesions were found in 17 cases (27.37%) and malignant in 14 cases (20.89%). Significant number of cases was in the age group from 41 to 50 years ($D=1.193$, $p < 0.05$). Distribution of morphological changes of the vulva according to the age of patients showed for benign lesions to be most frequent in the age from 31 to 40 years, and premalignant (VIN I, II, and III) in patients older than 60 years. In the age group over 60 years invasive carcinoma was found in histological grade 1 (42.86%).

KEYWORDS: Vulvar Neoplasms; Papillomavirus Infection; Condylomata Acuminata; Carcinoma, Squamous Cell; Cervical Intraepithelial Neoplasia

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Histological grading and staging in chronic B and C hepatitis

Chronic hepatitis B and C are certainly the most explored fields in the area of hepatology in recent decades. We investigated the distribution of histological activity indexes (necroinflammatory activity of acini and the extent of interface hepatitis) and fibrosis and individual histopathological characteristics (the presence/absence of lymphoid aggregates/follicles, alterations of bile ducts, fatty change, acidophilic bodies, and sinusoidal activity) respectively in similar histopathological types of chronic B and C hepatitis, separately and by comparison in the function of progression of disease. We examined 38 punctured liver tissue specimens from patients with chronic hepatitis B, and 36 punctured liver tissue specimens from patients with chronic hepatitis C of different aggressiveness and staging. All specimens were formalin-fixed and paraffin-embedded, and stained with basic hematoxylin-eosin and Gomori's reticulin staining. Statistical analysis: the basic statistical analysis, the rank-box analysis, and the linear correlation analysis were used. The histopathological characteristics of both diseases do not differ essentially although there are certain quantitative differences. In both diseases fibrosis indexes have the higher estimates variability, so that this index should be avoided as a sole independent criterion index to evaluate fibrosis. For the fibrosis index determination, the correlation with both other indicators is necessary. If all three indexes are used for estimation, then the total sum of their estimates could be used as a relevant statistical parameter. In both diseases there is a high grade of estimates variation of all types of individual histopathological characteristics. The histopathological diagnosis of chronic B and C hepatitis based on combined, associated morphologic characteristics and on the higher frequency of certain individual characteristics has a prognostic significance. Based on results got to it may be said that the estimation system itself is conditionally inadequate, due to a wide spectrum of possible variations. It has been considered that the continuous necroinflammatory process is the main cause of the fibrogenesis mechanisms responsible for the progression of the liver disease in both diseases, but the necroinflammatory lesion and the progression of fibrosis are not always correlated, what suggests the existence and the influence of various cofactors including host and viral factors.

KEYWORDS: Hepatitis B; Hepatitis C; Histological Techniques; Prognosis



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Histopathological findings in the gastric mucosa of patients with hepatitis C

The hepatitis C virus infection affects primarily the liver, sometimes spreading into other organs. HCV genome was found in the extrahepatic cells of the circulating T and B lymphocyte types and in the antigen-presenting cells. The attention to a role of HCV in the occurrence of gastritis was drawn in view of the persisting histopathological finding in the gastric mucosa for a considerable time after the helicobacter pylori eradication in patients with hepatitis C. In our pilot study on the correlation of hepatitis C and gastritis, liver and gastric biopsies (antral and corpus regions) were taken from 10 HCV-positive patients, who had histopathological findings of hepatitis varying in the degree of inflammation and fibrosis, without helicobacter pylori and without subjective gastric discomfort. In 8 HCV patients, the gastric mucosa findings showed a very mild, nonspecific inflammation without gastric atrophy and sometimes with mildly expressed foveolar hyperplasia. It is noteworthy that one patient had a proliferated connective tissue in the liver of micronodular cirrhosis type, joined with nonspecific gastritis, which lessens the importance of portal hypertensive gastropathy in case of hepatitis C. In 2 HCV patients (20%), the findings showed an intensive diffuse lymphocyte inflammatory infiltrate, lymphoid accumulations, lymph follicles, lymphoepithelial lesions, atrophy of gastric glands, and intestinal metaplasia of foveolar epithelium. These two patients had to be fully clinically investigated for HCV infection. The obtained results pointed to the importance of the histopathological analysis of the changes in the gastric mucosa in HCV patients.

KEYWORDS: *Hepatitis C; Gastric Mucosa; Gastritis*

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Helicobacter pylori and histopathological changes in gastric mucosa of duodenal ulcer patients

Antral cell is target for *H.pylori*. Gastritis begins as an acute superficial inflammation followed by the involvement of lower glandular layers and atrophy of mucosae and intestinal metaplasia. In case of duodenal ulcers localization is predominantly in the antrum (active superficial gastritis). We analyzed the frequency of inflammatory changes in presence of *H.pylori* in patients with duodenal ulcers. Prospective study in Clinic of gastroenterology and hepatology, Clinical center Nis, included 197 patients. In control group there were 60 patients, 33 men (55%) and 27 women (45%) without endoscopically found pathological changes in the mucosa of the stomach, and who, according to used Sydney classification (1990), did not match endoscopic criteria for macroscopic diagnosis of gastritis. The second group included 137 patients with duodenal ulcer, 92 men (67.15%) and women (32.85%). *H.pylori* was present in 118 (58.33%) of examined patients. In the group without endoscopically found changes the most frequent findings were chronic active gastritis (76.67% in antrum, and 71.70% in corpus), chronic atrophic gastritis (10% in antrum, and 8.30% in corpus), and intestinal metaplasia (8.36% in antrum and corpus). *H.pylori* colonized antral and body mucosa in 26 (43%) and in 25 (42.6%) patients, respectively. In patients without endoscopic changes and histological findings of chronic active gastritis we found equal presence of *H.pylori* in antral and corpus mucous ($p=0.0031$). Patients with interstitial metaplasia of antral and corpus mucosa were *H.pylori* negative ($p=0.0483$). In 3 of 6 patients without endoscopic changes of antral mucosa and presence of chronic atrophic gastritis *H.pylori* was found, and only in 1 of 5 patients in body mucosa. Chronic gastritis and chronic active gastritis are statistically significant in patients with duodenal ulcers vs. control group of patients ($p<0.001$). There is significant correlation between *H.pylori* presence and chronic gastritis, in patients with duodenal ulcers ($p=0.0476$). In the investigation male sex is more frequent. In patients without endoscopic changes the most common findings was chronic active gastritis. In patients with interstitial metaplasia *H.pylori* was not found. We concluded that eradication therapy for *H.pylori* is not necessary in absence of macroscopic changes. If there is presence of histological changes like gastritis in any stage and *H.pylori* is also present, then eradication therapy is needed. The findings of *H.pylori* in almost half of patients in our examination show high incidence of *H.pylori* in nonulcerous dyspepsia.

KEYWORDS: *Helicobacter pylori; Gastric Mucosa; Duodenal Ulcer; Gastritis; Histological Techniques*



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Is density of *Helicobacter pylori* colonization in correlation with the degree of gastritis activity, atrophy, and intestinal metaplasia?

The aim of this prospective study was to examine the relationship between the density of *H. pylori* colonization in gastric mucosa and the degree of severity of certain histologic parameters of gastritis, such as inflammation activity, atrophy, and intestinal metaplasia. Upper gastrointestinal endoscopy was performed in 350 *H. pylori* positive patients. The rapid urease test and histologic examination were used for detection of *H. pylori* on endoscopic gastric mucosal biopsies. Classical hematoxylin-eosin method and histochemical staining methods (AB-PAS and HID-AB) were used for histologic assessment of gastritis according to modified Sydney system. *H. pylori* colonization density was determined semiquantitatively in the interval from 0-3 (0, absence of *H. pylori*; 1, small number of *H. pylori* focally; 2, large number of *H. pylori* focally or small number, diffusely; 3, large number of *H. pylori* diffusely). Results of the study showed that along with the increase of density of *H. pylori* colonization there was a tendency of increasing the gastritis activity score in the gastric antrum ($p < 0.01$) and in the gastric corpus ($p < 0.01$). A statistically significant decrease of the score of antral atrophy and intestinal metaplasia was determined with the increase of density of *H. pylori* colonization in the gastric antrum ($p < 0.01$ for atrophy; $p < 0.05$ for intestinal metaplasia). The average value of atrophy score in the corpus did not statistically differ much according to the degree of density of *H. pylori* colonization in the gastric corpus. It can be concluded that *H. pylori* plays the most important part in the occurrence and maintenance of the chronic active inflammation in gastric mucosa. Differently from atrophy of the gastric corpus, atrophic and metaplastic milieu in the gastric antrum is an inadequate environment for the survival of *H. pylori*. However, the question is what the distribution of *H. pylori* colonization and its density are like in the gastric corpus under the conditions of significant expansion of antral type of mucosa toward the corpus (pseudopyloric metaplasia). In order to answer this question, wide endoscopic and histologic prospective studies are needed.

KEYWORDS: *Helicobacter pylori*; Endoscopy Gastrointestinal; Gastritis; Metaplasia; Gastrointestinal System; Gastric Mucosa

Effect of solitary and combined influence of heavy metals during chronic intoxication on reproductive ability and speed of preadult development of *Drosophila melanogaster*

Heavy metals have an important place among environment contaminants. Most of them are proved to be toxic, genotoxic, and carcinogenic. We investigated the solitary and combined influence of heavy metal compounds (copper and chromium) on reproductive ability and length of preadult development of *Drosophila melanogaster* (DM). In our investigation of the effects of copper and chromium we used following: I - control line nourished in standard nourishment medium; II - line nourished on standard medium enriched with 0.05% copper (II) sulfate; III - line nourished in standard medium enriched with 0.05% potassium bichromate, and IV- fly line nourished in standard medium enriched with both compounds of heavy metals. Small flies were exposed to mentioned compounds during two generations. Following analyses were done in every experimental line: average number of adult descendants per one female, length of the reproductive period, length of the reproductive period and length of duration of preadult development period (from egg stadium to the appearance of the first adults). The obtained results showed that the average number of adult descendants per one female, with flies from II and III line was within the limits of control (I) line. However, flies from line IV have significantly less number of descendants in relation to control line ($p < 0.001$), as well as to lines II and III ($p < 0.001$). The length of reproductive period in all experimental lines was about 22 days. Although the average value of duration of reproductive period was identical, maximal value of this parameter was lower in the line IV. In the same line the significant differences in the length of preadult development were observed. Compared to flies from lines I, II and III, this period was in average two days longer and disclosed after 14.02 days. Copper and chromium in concentration of 0.05%, added solitary to nourishment medium, enables normal reproduction and preadult development of flies (DM). 2. Combined performing of copper and chromium induces strong toxic effect, resulting in significant reduction of the number of the descendants, in decreasing of maximal value of the length of the reproductive period and in the extending of the period of preadult development. Our study pointed out the synergistic toxic effect of heavy metals copper and chromium.

KEYWORDS: Metals Heavy; Reproduction; *Drosophila melanogaster*; Copper; Chromium