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# **CLINICOPATHOLOGICAL CORRELATIONS IN ONCOLOGY**

**GASTROINTESTINAL ONCOLOGY** (abs. 18-33)

**GENITAL FEMALE ONCOLOGY** (abs. 34-45)

**BREAST ONCOLOGY** (abs. 46-47)

**ENDOCRINE ONCOLOGY** (abs. 48-50)



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## Intraoral lipoma of the tongue: Report of the three cases

Intraoral lipoma is rarely found in the oral cavity. It is a benign fatty tumor, composed of adult fat cells, which are subdivided into lobules by septa of fibrous connective tissue. It appears most frequently in the subcutis of adults. Lipomas have been classified according to their histological features and growth patterns into simple lipoma, fibrolipoma, spindle lipoma, pleomorphic lipoma, myxoid lipoma, angiolipoma, lipoblastomatis, myelolipoma, hibernoma and atypical lipoma. Recurrence of these lesions is very uncommon as well as therefore we have a good prognosis. In the present study we described lipoma of the tongue in case of three male patients with the median age of 54 years (range: 33 to 70 years). All patients were operated in the Clinic of Maxillofacial Surgery of the Military Medical Academy, from January 1992 till October 2003. Clinical examination revealed a soft tissue mass located in the right side of the tongue, well demarcated and covered by normal mucosa, measuring 3x2 cm in one case and 4x2 cm in the other two cases. The wound was closed primarily and the healing was uneventful. Five years of follow-up showed no evidence of recurrence. Histologically examination of the lesion showed presence of a maturely adipose tissue.

**KEYWORDS:** *Lipoma; Tongue Neoplasms*

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## The significance of clinical findings and histological diagnosis of potentially malignant oral lesions

Although potentially malignant oral lesions (PMOL) may exhibit dysplasia or malignancy, in practice not all leukoplakias are biopsied. The same occurs with lichen planus often diagnosed only on the basis of the clinical aspects, which can lead to misdiagnosis. In addition, the biopsy technique and clinical data can modify the reliability of oral lesion histological diagnosis. In case of erosive lichen planus, a biopsy specimen of predominantly erythematous and ulcerated mucosal lesions should be obtained a few millimeters away from an ulcer so that the specimen's epithelium and connective tissue will be intact. A biopsy specimen of lesions with a hyperkeratotic component (e.g., leukoplakia, reticular lichen planus) should include an adjacent area of normal tissue. The aim of the study was to evaluate the discrepancy index between clinical and histological diagnosis of PMOL. Fifty-one patients with PMOL examined clinically and a biopsy obtained from each. The results of histological diagnosis were compared to the clinical diagnosis. We established the histological diagnosis incompatible with the clinical diagnosis when the clinical diagnosis was not confirmed. On the basis of incompatible diagnosis, we calculated a discrepancy index (DI) between the clinical and histological diagnosis. Clinically the homogeneous leukoplakia was the most frequent lesion followed by erosive lichen planus and reticular lichen planus. No cases of erythroplakia observed. Lesions were most frequently seen at the buccal mucosa, followed by the gingiva (alveolar mucosa) and tongue. The histological diagnosis showed that the majority of the lesions were benign keratosis followed by lichen planus. Three cases of epithelial dysplasia were mild. The DI between clinical and histological diagnosis was 17.6 %. The higher DI was found in erosive lichen planus. These data suggest that all PMOL should be submitted to a histologic analysis.

**KEYWORDS:** *Mouth Diseases; Diagnosis; Leukoplakia; Lichen Planus, Oral; Biopsy; Histological Techniques*



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## Histologic subclassification of the Warthin's tumor of the parotid gland: Analysis of 24 cases

## Esophageal cancer: Frequency and histopathological parameters

Warthin's tumor (cystadenolymphoma papillare; cystadenoma lymphomatosum papillare) is the second most common benign parotid salivary gland tumor. Nearly all Warthin's tumors occur in the parotid gland or periparotid region. These tumors are variable in their epithelial differentiation and the ratio of the epithelial tumor component to lymphoid stroma. The aim of this study was to perform histological analysis and present 3 subtypes: typical, stroma poor, and stroma rich Warthin's tumor. Twenty-four cases of Warthin's tumor from the files of Department of Oral Pathology, Faculty of Stomatology, Belgrade, (2003) were analyzed. In our group there were 15 male and 9 female patients (sex ratio: 1.66:1). Peak incidence was in fourth decade of life for men and fifth decade for women. Subtype 1 - typical Warthin' tumor (epithelial component 50%) was found in 14 cases (58%), subtype 2 - stroma poor (epithelial component 70%-80%) was found in 9 cases (38%), and subtype 3 - stroma rich (epithelial component 20%-30%) was found in 1 case (4%). In typical Warthin's tumors we also found the zones of fibrosis, bleeding and foreign body reaction. Stroma poor tumors consisted of fibrosis, calcifications, and focal necrosis.

**KEYWORDS:** Adenolymphoma; Parotid Gland; Histological Techniques; Cytodiagnosis

Esophageal cancer is relatively rare in most western countries, and represents the seventh commonest cancer globally. The incidence of adenocarcinoma of the esophagus has increased during the past 15 years, from five to ten percent to more than 50% today. Ten to fifteen percent of tumors arise in the upper segment, 50%-55% in the middle segment, and 30%-40% in the lower segment. More than 50% of patients have unresectable tumors at the time of diagnosis. We analyzed 49 patients affected with esophageal cancer for the observed 5-year period with aim to establish frequency, sex distribution and ratio, age distribution, localization (cancer site), histopathology diagnosis, histology grade, and type of the applied oncology treatment. During the period from 1998 to 2002 there were 49 patients with esophageal cancer. The disease was predominant in male population 77.55%. The male/female ratio was 3.45:1. The youngest patient was 52 years old and the oldest patient was 77 years old. Median age at diagnosis was 65 years. The most frequent localization was in the middle segment - 25 patients (51.02%). The lower segment was in the second place with 17 patients (34.69%). The upper segment is in the third place with 4 patients (8.16%). For 3 patients (6.13%) there were no data about localization. Only 1 patient had a radical surgical treatment (2.04%), 45 patients had endoscopical biopsies, and 3 patients had no histopathology diagnosis. The most common histopathology diagnoses are squamous cell carcinoma 63.27%, and adenocarcinoma 18.37%. Six patients were found with intraepithelial carcinoma (in situ). Histological grade of differentiation was found in only 28 patients (57.14%). Nineteen patients received specific oncology treatment - 15 received radiotherapy and 4 received chemotherapy (5-Fluorouracil + Cisplatin), and 30 patients were treated with symptomatic therapy. The analysis of the 5-yearperiod showed a low incidence (0.62% of all cancers). Esophageal carcinoma was 3.45 times more frequent among men than among women. The most frequent localization is the middle segment (51.02%). Only 1 patient had a radical surgical treatment (2.04%), and 97.96% had unresectable malignancy. At the time of diagnosis 61.22% of those patients were incurable. Squamous cell carcinomas are still the most frequent ones (63.27%), just like in other countries with the low risk where alcohol and tobacco have been implicated as a risk factor. Histological grades of differentiation were determined in only 57.14%.

**KEYWORDS:** Esophageal Neoplasms



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## Epidemiology of esophageal carcinoma on the 4-year endoscopic material examined at the Clinic of Gastroenterology and Hepatology, Clinical Center Niš

## Correlation of clinical symptoms and histologically confirmed gastric cancer

Esophageal carcinoma is relatively rare but extremely deadly malignant disease. More than 85% of esophageal tumors are esophageal squamous cell carcinomas. Adenocarcinoma is rare. Esophageal squamous cell carcinoma (SCC) shows significant geographic, racial, and socioeconomic differences, relating in part to the presence of certain high risk factors. The male/female ratio is 4-6:0 in most Western countries. The incidence of esophageal carcinoma increases with age. Etiology of esophageal SCC is related to different factors such as tobacco and alcohol consumption, nitrates, mycotoxins, hot liquid consumption, radiation exposure and constitutional genetic composition. Ten percent to 15% of tumors arise in the upper esophagus, 50%-55% develops in the midthoracic region and 30%-40% develops in the lower part. Adenocarcinoma represents 2%-8% of carcinomas of the upper esophagus and close to 20% of those of the lower esophagus. The aim of this study was to determine basic epidemiological characteristics of esophageal carcinoma on the 4-year endoscopic material obtained at the Clinic for Gastroenterology and Hepatology, Clinical Center Niš. During the 4-year period, from 2000 through 2003 we performed 13148 esophagogastroduodenoscopies on the Clinic of Gastroenterology and Hepatology (GEH). Biopsy was done in case of 60 patients suspected of esophageal neoplasm. Diagnosis of esophageal carcinoma was established in 38 patients (34 men and 4 women), average age 67.84 years (range: 47-82 years). Esophageal carcinoma was found in 38/60 (63.33%). Topographic distribution was: 23 (60.52%) in lower thoracic esophagus; 14 (36.84%) in midthoracic esophagus, and 1 (2.63%) in cervical esophagus. Considering gross features most common was fungating cancer 28 (73.68%), infiltrating carcinoma was found in 7 (18.42%), and ulcerating form in 3 (7.89%). Histologically most frequent was squamous cell carcinoma -22 (57.89%). Adenocarcinoma was found in 10 (26.31%), and signet ring cell carcinoma in 2 (5.26%). The four patients were diagnosed: infiltratio maligna esophagei, adenoma villosum cum alteratio maligna, Ca anaplasticum, and Ca intraepitheliale in situ. Our study supports present literature according to age and sex structure of patients. Also, our findings confirm the squamous cell carcinoma as the most frequent. Considering topographic distribution we found that the esophageal carcinoma is most often localized in lower thoracic esophagus. The esophageal carcinoma is rare in our region. It shows most often in older men and histologically this is squamous cell carcinoma, which may be related with bad habits as smoking and alcohol consumption, and bad dietary habits in our surroundings.

**KEYWORDS:** Esophageal Neoplasms; Carcinoma, Squamous Cell; Epidemiology; Endoscopy, Digestive System

Gastric cancer ranks as one of the most frequent cancers despite decreasing incidence. In human gastric carcinogenesis different dietary and nondietary factors are involved, including genetic susceptibility of the host and *Helicobacter pylori* infection. Risk factors for gastric cancer are a family history of gastric cancer, *Helicobacter pylori* infection, blood type A, a personal history of pernicious anemia, a history of chronic atrophic gastritis, a condition of decreased gastric cancer and a prior history of adenomatous gastric polyp. The cancer usually involves the antrum, body or cardia with about equal frequency. The two main microscopic types are intestinal and diffuse. This research refers to 31 patients with histologically confirmed gastric cancer, hospitalized at the Clinic in Niš during last two years. There were 18 men and 13 women of median age 68.9 years. The youngest patient was 40 years old and the oldest 83. We were investigating appearance of some clinical symptoms and their correlation with histologically confirmed gastric cancer. Abdominal pain had 20 patients (64.52%) and it was at epigastrium and under the right rib, the most often after the meal. The same number had nausea. Anemia was found in 20 patients (64.52%). Vomiting had 18 patients (58.06%), a loss of appetite 16 (51.61%), and weight loss 17 (54.84%). Hematemesis as the first clinical symptom had 2 patients (6.45%). Diarrhea had 1 patient and constipation also one (3.23%). Two patients (6.45%) had personal history of gastric ulcers. Metastasis, in the moment of diagnosis, had 17 patients (54.84%) and they were located: in abdominal lymphonoduli at 10 patients (32.26%), in liver at 6 patients (19.35%) and in pancreas at 1 patient (3.23%). Ascites had 10 patients (32.26%). Two patients had family history of cancer. Clinical symptoms, which lasted more than sixth months, had 26 patients (83.87%). According to previous results, we can conclude that exist certain clinical symptoms, which can signify gastric cancer. Main clinical symptoms are abdominal pain and nausea. They are often followed by anemia, weight loss and loss of appetite. Although a stomach cancer diagnosis is unlikely in most cases, people should contact a doctor when they consistently experience them in more than a few months. Minor symptoms should be thoroughly investigated in people with predisposing conditions. The prognosis for patients with advanced gastric cancer remains poor that is why its early diagnosis is very important.

**KEYWORDS:** Stomach Neoplasms; Diagnosis; Signs and Symptoms, Digestive; Risk Factors



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## The epidemiological data about gastric cancers on 3 years endoscopy material

Gastric cancer still remains a major health problem and represents the second cause of death of all malignancies worldwide. High rates of incidence of gastric cancer are observed in Balkan countries. There has been a decrease in incidence of this cancer worldwide but the degree of this reduction varies considerably among different geographical areas. The aim of this study was to represent the epidemiological data about gastric cancers on our 3-year endoscopic material. This is a retrospective study of 10018 gastroscopies between 2000 and 2002. Diagnosis of gastric cancer has been established by endoscopic biopsies and histopathological examinations. Histological classification of gastric carcinoma into the intestinal type and diffuse type is based on the criteria proposed by Lauren. Malignant tumors were diagnosed in 136 patients. Gastric cancer was present in 127 (93.38%) patients - 86 men and 41 women. Two patients with recurrent cancer after partial gastrectomy and one after subtotal gastrectomy have been excluded from the study. Early gastric cancer was diagnosed in 3 (2.42%) male patients. Gastric cancer arose in the antrum in 51 (41.13%), in the corpus in 44 (35.48%) and in the cardia and fundus in 29 (23.39%) patients. Intestinal type according to the Lauren classification was present in 62 (51.24%) patients with the mean age 66.06 years (range: 43-83 years). Male/female ratio was about 2:1. The diffuse type was found in 47 (38.84%) patients with the mean age 61.94 years (range: 32-81 years). Male/female ratio was about 2:1. Unclassified or mixed type was present in 12 (9.92%) patients. The integration with Borrmann's gross types showed that 66.13% of the intestinal type carcinomas were polypoid of fungating, 20.97% were ulcerated, and 12.9% were infiltrative. The corresponding figures for diffuse carcinoma were 27.66%, 23.4%, and 48.94%. In comparison with the recent studies there is the small number of diagnosed early gastric cancers. Intestinal type is more common in elderly age group; diffuse type predominates in younger age group, particularly in women. Male/female ratio was 2:1 in both intestinal and diffuse type.

**KEYWORDS:** Stomach Neoplasms; Epidemiology; Gastroscopy

## Morphology of signet ring cells gastric carcinomas

Having on mind that several conditions mimic signet ring carcinoma (signet ring lymphoma, mucinophages, xantoma and detached of dying cells associated with gastritis) we performed this study. Surgical biopsies from 30 operated patients (total gastrectomy) were fixed in 10% formaldehyde during one day. Processed tumor tissue was embedded in paraffin. Sections were stained with histological (HE), histochemical (PAS, HID-AB pH 2,5) and immunohistochemical LSAB2 using antibody to cytokeratin (CK7) in dilution 1:50. From 30 investigated patients, out of which 16 signet ring cell carcinomas (SRCC) were found in women and 14 in men. Two youngest patients were in the group of patients aged from 20 to 25 years. The number of SRCC increased with age (50-54 years). Macroscopic type of SRCC was classified using Borrmann's criteria. Ulcerated infiltrating type was common (39%). Diffuse infiltrative carcinoma was the most frequent (61%), producing flat, plaque-like lesions. With extensive infiltration, a linitis plastica or "leather bottle" stomach resulted in Borrmann's type IV (one case). This type induced diffuse thickening and hardening of the gastric wall with the nature of scirrhous cancer. Almost 60% of the examined tumors consisted of isolated or small groups of malignant cells containing intracytoplasmic mucin. Superficially, cells lie scattered in the lamina propria, widening the distances between the pits and glands. The tumor cells had five morphologies: (1) nuclei pushed against cell membranes creating a classical signet ring cell appearance due to an expanded, globoid, optically clear cytoplasm (62%); (2) other diffuse carcinomas contained cells with central nuclei resembling histiocytes and showed little mitotic activity (18%); (3) small, deeply eosinophilic cells with prominent, but minute, cytoplasmic granules, containing mucin; (4) small cells with no mucin; and (5) anaplastic cells with little or no mucin. These cell types intermingled with one another constituting varying tumor proportions. Classical signet ring cells contained acid mucin and stained with Alcian blue at pH 2.5 (62%); small deeply eosinophilic cells contained PAS +, neutral mucin. Immunocytochemical staining with antibodies to cytokeratin (CK7) helped detect sparsely dispersed tumor cells in the stroma. Cytokeratin (CK7) immunostain detected a greater percentage of neoplastic cells. Histological detection of diffuse gastric cancer is sometimes very difficult. Because that, the authors recommend the use of combined methods for its diagnosis.

**KEYWORDS:** Carcinoma, Signet Ring Cell; Stomach Neoplasms; Immunohistochemistry; Microscopy





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## Double duodenal villous adenoma: Case report

## Hystopatology finding in polypoid rectal lesions

Perry first described villous tumor of the duodenum (VTD) in 1893. Villous tumors account for only 1% of all duodenal tumors. Despite being relatively rare, VTD remain the commonest benign periampullary neoplasms. Patients with polyposis syndromes (usually familial adenomatous polyposis (FAP) and Gardner syndrome) have an increased incidence of VTD. The suggestion that VTD are premalignant lesions was made more than 40 years ago. The adenoma-carcinoma sequence (tubular adenoma, tubulovillous adenoma, villous adenoma, carcinoma in situ, invasive carcinoma) has been largely accepted as the pathogenesis of VTD. VTD cause symptoms due to their location, usually near the ampulla of Vater, presenting with biliary obstruction, pancreatitis, bleeding, duodenal obstruction, and intussusception. The diagnosis is based on radiographic barium contrast evaluation, fiberoptic endoscopy with full visualization of the duodenum and endoscopic ultrasonography. Although there is uniform agreement that VTD should be resected, there are many controversies about the radicality the resection. A 70-year-old woman was admitted to the Clinic in November 2003 with history of vomiting and intermittent jaundice. The physical examination revealed no abdominal tenderness, organomegaly, or abdominal masses. Laboratory and CEA and CA 19-9 levels were within the normal limits. There was no family history of either colon cancer or colon polyps. An upper gastrointestinal roentgenographic series revealed double mass 6 cm in the lower part of the descending duodenum. On endoscopy, two pedunculated lesions were seen adjacent to the duodenal papilla. The surface of the tumor was granular and white. A biopsy was performed, and a diagnosis of a tubulovillous adenoma of the duodenum was made. At laparotomy, the adenomas were identified by palpation, like "wandering" soft mass moving from D4 to D2. The bases of the tumors identified were on the anterolateral duodenal wall on the angle-junction of the D2-D3. The adenomas were resected by partial duodenectomy of the antero-lateral duodenal wall. Histologic examination of the resected specimen revealed. The postoperative course was uneventful. The patient was discharged on the 18th postoperative day. The treatment options are endoscopic snare excision or ablation, local submucosal excision (with or without sphincteroplasty and pancreatic duct septotomy in the case of periampullary VTD), full-thickness excision (when location of the VTD permits), and duodenectomy, with or without proximal pancreatectomy.

**KEYWORDS:** Adenoma, Villous; Duodenal Neoplasms; Digestive System Surgical Procedures

Polyps can be classified as nonmalignant hamartomas (juvenile polyps), hyperplastic proliferations of mucous (hyperplastic polyps) or adenomatous polyps. Only adenomatous polyps are determined to be precancerous, but only a few develop a carcinoma. Carcinomas are developed more often in sessile polyps. Histologically, adenomatous polyps may be tubular, villous or tubulovillous. Villous adenomas are presenting in sessile shape. The size of polyps is very important for the development of invasive carcinoma and is rare (less than 2%) if the lesions are smaller than 1.5 cm, middle (2%-10%) when lesion are between 1.5 and 2.5 cm and real (more than 10%) if lesion is more than 2.5 cm. Adenomatous polyps need 5 or more years to grow and have clinical expression. Rigid rectosigmoidoscopy was performed in case of 2571 patients at the Clinic of Gastroenterology and Hepatology, Clinical Center Nis, from beginning of 2000 to November 2003. We biopsied neoplastic lesions found in 114 patients, 41 women (35.97%) and 73 (64.03%) men, average age of 59.5 years (range: 34-85 years). The most common histopathological findings were rectal adenocarcinoma in 45.62% patients, tubular adenoma in 16.67% patients, tubulovillous adenoma in 14.03% patients, hyperplastic polyps in 13.16% patients, villous adenoma in 5.26%, inflammatory polyps in 5.25% patients. There were 10 female (66.66%) and 5 male (33.34%) patients with hyperplastic polyps 41.28 years of age, and the significant difference was  $p < 0.05$ . Adenoma tubular was found in 19 (16.67%), adenoma tubulovillous in 16 (14.03%), and adenoma villous in 6 patients (5.26%). Tubulovillous adenoma was found in 4 female (25%) and 12 male (75%) patients 45.82 years of age, and the statistic difference was  $p < 0.01$ . Adenocarcinoma was found in 53 patients (45.62%) and there was no statistically significant difference according to sex of those patients ( $p > 0.05$ ). Rectal carcinoma was more frequent in male patients but there was no statistically significant difference. Statistically, tubulovillous adenoma is frequent in men whereas hyperplastic and inflammatory polyps are more frequent in women. Rectosigmoidoscopy is very important method for diagnosing neoplastic lesion of rectum and sigmoid colon, but also as a complementary method with radiological or endoscopic methods - colonoscopy.

**KEYWORDS:** Rectal Neoplasms; Polyps; Adenoma; Adenocarcinoma; Biopsy



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## Colorectal cancer in patients younger than 40 years of age

Cancer of the colon and rectum is the first most commonly occurring gastrointestinal malignancy in our country and worldwide. Although primarily a disease of older patients, 4 to 8 percent of these cancers are found in patients younger than 40 years of age. Young patients with colorectal cancer have been reported to have a particularly poor prognosis, with five-year survival rates of 20 to 40 percent. This study was undertaken to review the experience with colorectal cancer in patients less than 40 years of age at the Institute of Pathology, to assess prognostic factors associated with decreased survival, and to detect any recent changes in either presentation of prognosis. The biopsy registry of the Institute of Pathology was reviewed over a 5-year period from 1996 to 2000. One child (12 years) and 14 patients younger than 40 years of age (2 brothers with Lynch's syndrome, 2 women with FAP, and 10 with sporadic type) with colorectal cancer were identified. Their hospital records were reviewed for demographic data, history (with particular attention to predisposing conditions), symptoms, tumor size and location, operation performed, pathologic characteristics and Dukes' stage, recurrence, and survival. The marked increase in the incidence of right-sided lesions (11 patients) was noted; the rectal localization was found only in 4 patients (2 with FAP); a preponderance of males (10 patients) was found among young patients. Dukes, classification-right sided localization: stage B (2 patients), stage C (6 patients), and Stage D (3 patients), two with liver and one with Krukenberg's metastases. Dukes' classification-left sided localization: stage B (2 patients) and stage C (2 patients). Five-year survival: 4 patients (2 of right-sided and 2 of left-sided). Histologically, the tumors of right-sided were both mucin-producing and poorly differentiated in 72% and of left side in 25%. The most common presenting symptoms were: abdominal pain, hematochezia, change in bowel habit, anemia, and weight loss. Cancer of the colon and rectum in patients less than 40 years of age is associated with a poor prognosis that is partially attributable to the occurrence of more aggressive, poorly differentiated tumors. However, both presentation with advanced disease and limited survival are associated with a prolonged duration of symptoms before definitive therapy. Young patients presenting with symptoms suggestive of colorectal malignancy, therefore, demand timely, complete investigation of the large bowel despite their youth.

**KEYWORDS:** Colorectal Neoplasms; Adult; Prognosis; Diagnosis; Survival Rate

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## Incidence of colorectal cancer during 4 years of follow-up

Colorectal cancer is the fourth commonest form of cancer occurring worldwide. It represents approximately 10% of cancer in men and women. The number of new cases of colorectal cancer worldwide has been increasing rapidly since 1970s. The majority of colorectal cancers arise from adenomas, dysplastic and nonmalignant masses in colon. There are significant regional variations regarding the incidence and localization of colorectal cancer. To determine the incidence, localization and other characteristics of colorectal cancer in the patients examined in Clinic of gastroenterology and hepatology, Clinical Center Niš, Serbia during four years of follow-up (2000-2003). The patients suspicious of having colorectal disease after clinical examination had undergone complete colonoscopy. Incidence of colorectal cancer was calculated for the four years period comparing the number of newly discovered cases with number of performed colonoscopies. Diagnosis was based on a clinical rectal examination including complete colonoscopy with biopsy for histopathological examination. Tumors with distal extension to 15 cm or less from the anal margin are classified as rectal more proximal tumors as colonic. Of 2917 patients examined by colonoscopy, diagnosis of colorectal cancer has been established in 105 (3.59%) patients, 42 women (40%) and 63 men (60%), aged 37 to 83 mean age 64.33 years. The commonest histology (99.05%) was adenocarcinoma. Rectal cancer was diagnosed in 50.48% of patients and colon cancer in 49.52% (cecum 1.9%; ascending colon 7.62%; transverse colon 7.62%; descending colon 8.57%, sigmoid colon 23.81%). The majority of colorectal cancers were localized in left colon (86.66%), comparing to right colon (13.33%). In 11.43% of patients adenomas with malignant alteration have been diagnosed. This fact directly supports adenoma-carcinoma sequence in patients with colorectal cancer. Colorectal cancer in southeast region of Serbia occurred mainly in seventh decade, predominantly in men. The most frequent localization is left colon, exactly rectosigmoid part of the colon. Colorectal adenomas are frequent precursors of colorectal cancer.

**KEYWORDS:** Colorectal Neoplasms; Adenoma; Incidence; Colonoscopy



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## Epidemiological, macropathological and mucinohistochemical characteristics of colorectal cancer in district of Niš

The aim of this work was to examine the characteristics of colorectal cancer in this area. Patients with histological diagnoses of colorectal cancer from 2000 to 2001 were retrospectively examined. The data source was the medical record database of the Institute of Pathology. The inquiry included 253 patients, 95 women and 158 men. The mean age at diagnosis was 64.29 with SD=11.82. Men were younger (63.53 years) than women (65.41 years). Predominant segment of colorectum was rectosigmoid with 74% of all cancer locations. Predominant gross pathology finding was ulcerous-vegetative cancer, followed by ulcerous, simple vegetative, and finally infiltrative cancers as the most rare. Predominant micropathological finding was well, moderately, and nondifferentiated adenocarcinoma. On histochemical field there was a decrease of neutral mucins with different percents and disturbance of acid mucins: increase of sialomucins and decrease of sulfomucins. Hyposecretion to asecretion is common finding in severely dysplastic cancers. Patients with right side colorectal cancers demonstrated a more advanced stage than the left side cancer patients. The colorectal cancer characteristics in the district of Niš were not remarkably different from those seen in Western countries in age, primary tumor site distribution, and gross pathology and histology type. Certain differences were evidenced in sex ratio. It was expected that left sided lesions was mostly repeated in men and right in women. In our examination men were predominant in both patients' population - with left and right side colorectal cancers.

**KEYWORDS:** *Colorectal Neoplasms; Epidemiology; Pathology*

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## Clinical and micromorphological correlation of ulcerative colitis

For the evaluation of ulcerative colitis (UC) a number of clinical, endoscopic, and histological activities are necessary for an optimum therapeutic approach and the analysis of therapy effects. The aim of our study was to present clinical and micromorphological correlation of ulcerative colitis. Our prospective, 3-year study included 117 patients who were examined and treated for ulcerative colitis at the Gastroenterology and Hepatology Clinic of the Clinical Center in Niš. We verified a significant correlation between clinically and endoscopically established UC activity. Neither clinical nor endoscopic activities were in correlation with the age of the patients, the duration and the extensiveness of UC. When we correlated the age of the patients, the duration and the extensiveness of UC with the histological level of activity, we didn't find any statistical significance ( $p > 0.001$ ). The correlation of the clinical and histological levels of activity showed statistical significance. The correlation of the endoscopic and histological levels of activity showed statistical significance. The clinical level of activity and the extensiveness of UC were in significant negative correlation with the secretion of sulfomucin but not sialomucin. The age of the patients, unlike the duration of the disease, was in significant correlation with the level dysplasia ( $p < 0.001$ ). Clinical activity and the extensiveness of UC were in statistically significant correlation with the dysplasia level. Regular clinical and histopathological controls of the patients are required, because in "seemingly" clinical and endoscopic inactive UC there may be histopathological activity, which demands adequate therapeutic treatment.

**KEYWORDS:** *Colitis, Ulcerative; Diagnosis; Endoscopy; Histological Techniques*





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## Histopathological changes in gallbladder mucosa in cholelithiasis

Cholelithiasis produces diverse histopathological changes in gallbladder mucosa, namely acute inflammation, chronic inflammation, glandular hyperplasia, granulomatous inflammation, cholesterosis, dysplasia, and carcinoma. Gallbladder carcinoma shows an unusual geographic and demographic distribution. It is relatively uncommon in Europe, but more frequent in Israel, Chile, Bolivia, etc. Chronic cholecystitis, choledochal cystitis, high body mass index, female gender, age, nicotine and industrial exposure to carcinogens are associated risk factors. The frequency of gallbladder cancer in all operations of the biliary tract is about 1% to 3%, reflecting biliary tract malignancy as more common. Preoperative imaging, including ultrasound and computed tomography (CT), may reveal signs indicative of the presence of malignancy. However, most patients are not diagnosed prior to surgical intervention. The aim of this retrospective study was to see histopathological changes in gallbladder mucosa in cholelithiasis. Between January 2003 and December 2003 we diagnosed and operated 285 patients: 88 (30.87%) were men and 197 (69.13%) were women with cholelithiasis at the Surgical Clinic in Nis. After operation all gallbladders were sent for histopathological analysis to the Institute of Pathology Nis. Diagnoses were mostly established by ultrasound. After postoperative analysis we found out that 269 (94.39%) out of 285 patients had chronically gallbladder inflammation, 102 (35.79%) had fibrosis, 37 (12.98%) had atrophic mucosa, 2 (0.70%) had dysplasia, 9 (3.16%) had hyperplasia, 19 (6.67%) had atrophy associated with polyposis, and 100 (35.09%) had only chronic cholecystitis without the precancerous lesions. Out of 285 analyzed gallbladders gallbladder carcinoma was concomitantly found in 16 (5.61%): 15 (5.26%) were adenocarcinomas and 1 (0.35%) was carcinoma anaplasticum. Gallbladder carcinoma appeared more frequently among patients with to chronic cholecystitis and cholelithiasis. Chronic cholecystitis with cholelithiasis is precancerous stage of gallbladder. We consider that it is necessary to send all operated gallbladders to histopathologic analysis.

**KEYWORDS:** *Cholelithiasis; Gallbladder; Mucous Membrane; Histological Techniques; Gallbladder Neoplasms*

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## Gallbladder polyposis

Benign epithelial tumors of the gallbladder are adenomas and mixed tumors. Gallbladder epithelial changes that do not have malignant potential are: adenomatous hyperplasia, primary papillary hyperplasia, and cholesterol polyps or inflammatory polyps. Benign mesenchymal tumors are rare and include leiomyoma, hemangioma, and lipoma. Premalignant lesions are: intestinal and squamous metaplasia. Malignant lesions of the gallbladder are: epithelial (adenocarcinoma, squamous cell, adenosquamous, oat cell), mesenchymal embryonal rhabdomyosarcoma, leiomyosarcoma, malignant fibrous histiocytoma), miscellaneous (carcinosarcoma, characinoid, lymphoma, melanoma). They may be multiple or localized. The study was performed to determine importance of localized overgrowths involving the gallbladder. During the 2-year period we detected 189 patients with localized overgrowths in the wall of the gallbladder, using ultrasound. Ultrasound findings include diffuse or segmental thickening of the gallbladder wall as echogenic foci with or without associated acoustic shadowing projecting within the lumen of the gallbladder, single or multiple. Some of them were operated and histologically evaluated. Ultrasound examination included 189 patients with localized overgrowths of the wall of the gallbladder. There were 52.96% female patients. Single polyps were found in 71.96% and stone disease in 23.81%. Polyps smaller than 5 mm were seen in 50.79%, and they were controlled by ultrasound at the beginning once a month and later every three months. Other patients (49.21%) were suggested to undergo operation, but only 38.71% of them, (19.05% of all) underwent surgical treatment. Adenocarcinomas were found in 2.12%, or 5.48% of operated patients. Cholesterol polyps were in 76.71% and adenomatous hyperplasia was found in 17.81% of operated patients. The other forms of the tumors were not detected. Determination of premalignant lesions, intestinal and squamous metaplasia, and early malignant lesions are important because they can successfully be operated.

**KEYWORDS:** *Gallbladder Neoplasms; Polyps; Ultrasonography; Metaplasia; Hyperplasia*



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## Compatibility of colposcopy, cytology, and histopathology in grading of precancerous cervical lesions

Uterine cervix can be visualized and the majority of lesions originating from the cervix may be readily seen. However, the incidence of precancerous cervical lesions rises, especially in younger women. Cervical carcinoma is the most common malignant neoplasm of the female genital tract and the second most frequently diagnosed cancer in women. Among all the malignant tumors diagnosed in women, approximately 12% is cervical carcinoma. In recent years, the frequency of invasive cervical carcinoma decreased. In contrast, the frequency of carcinoma in situ increased for 2% annually. The aim of this study was to determine: (1) validity of colposcopic image in grading of visible cervical lesions; (2) significance of cytology in assessment of grade in precancerous cervical lesions; and (3) compatibility of Pap classification and histopathologic classification of precancerous cervical lesions. At the Department of Early Cancer Detection, Clinic of Gynecology and Obstetrics Niš, 100 patients with abnormal colposcopic and cytologic findings were examined from February 2003 to December 2003. Directed biopsy of the cervix with histopathologic verification was performed in each patient. The highest concordance (90.32%) of colposcopic and histopathologic findings was observed in patients with high-grade squamous intraepithelial lesions (HSIL) and the lowest concordance (48.70%) in patients with low-grade squamous intraepithelial lesions (LSIL). LSIL was referred to as benign lesion in 46.15% of cases. The highest concordance (75%) of cytologic and histopathologic findings was in HSIL and the lowest one (23.30%) in LSIL. An agreement between benign findings existed in 69.23% of cases, while histopathologic finding was normal in 30.76% of cases with abnormal cytologic finding. The average agreement of cytologic with histopathologic finding was 55.58%. Colposcopy is subjective diagnostic method with high sensitivity (96%) and low specificity (57%). Because of low specificity, the scoring system for colposcopic findings is important, when we decided on the necessity of cervical biopsy, and it contributes to the decreasing of unnecessary biopsy. Colposcopic scoring system and expected histopathologic finding showed good overall agreement (76%) with the highest value (90.32%) in the group of HSIL. Exfoliative cytology has low sensitivity (64%) and high specificity (88%) with low negative predictive value (60%) and high positive predictive value (90%). An agreement of Pap classification with histopathologic classification is moderately good (55.58%). For this reasons, it is necessary to introduce and apply the uniform cytologic and histopathologic classification of precancerous cervical lesion.

**KEYWORDS:** Cervix Dysplasia; Cervical Intraepithelial Neoplasia; Colposcopy; Cytodiagnosis; Biopsy

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## Rare metastatic sites in cervical carcinoma

Cervical carcinoma belongs to the group of tumours characterized by expansive local growth. Dissemination of this malignancy occurs predominantly by lymphatic route, while hematogenous dissemination is verified in only 2%-3% of the cases and in autopsy material in 3%-20%. Predilection sites for metastases are the lungs, liver and bones, while metastases in other organs are encountered only rarely. At the Clinic of Oncology in Niš in the last 16 years hematogenous dissemination of cervical carcinoma was a rare diagnostic finding, most commonly within the general disease progression and after secondary and tertiary therapy. The following two examples illustrate a completely atypical mode of dissemination of this cancer. CASE NUMBER 1: A woman born in 1947, presented in January 2003 to her physician with severe headaches and neurological events. CT helped in diagnosing an expansive process in the occipital left hemisphere, surgically treated at the Clinic of Neurosurgery (histopathology: *metastasis carcinomatis*). Due to vaginal bleeding occurring immediately after the operation, she was referred for gynecologic examination, after which a neoplastic process FIGO stage IIIB was diagnosed, and histopathology confirmed *Ca planocellulare invasivum cervicis uteri HG2 NG2*. Before specific oncologic therapy was instituted, brain CT was repeated (a month after surgery) and numerous metastatic changes were detected on that occasion. Rapid and severe disease advancement, as well as the patient's general condition required further symptomatic therapy. CASE NUMBER 2: A woman born in 1946 was surgically treated in August 1999 for cervical carcinoma FIGO staged IIA. Histopathologic finding postoperatively confirmed *Ca planocellulare non kerathodes HG2 NG2*. Metastatic deposits were not detected in the lymph nodes (0/19). Postoperative irradiation was not applied; instead, regular follow-up controls by a radiologist were instituted in the following two years. Due to pain below the rib cage and in the left abdominal portion she visited her gynecologist, when the local relapse was diagnosed in the small pelvis on the left. Except for the gall bladder calculosis, all other tests were in the normal range. After the council decision palliative chemoradiation was administered. Eleven months after irradiation she was admitted as an urgent case to the surgical clinic with obstructive icterus. Cholecystectomy and choledochoduodenostomy were performed. Histopathology: within the gall bladder wall, plaques of poorly differentiated planocellular carcinoma were found. After this surgical intervention, general patient status abruptly deteriorates, with signs of terminal malignant disease, and specific oncologic therapy was not indicated.

**KEYWORDS:** Cervix Neoplasms; Carcinoma, Squamous Cell; Neoplasm Metastasis



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## Pathohistologic evaluation of curettage specimens with endometrial adenocarcinoma

The biologic differences between adenocarcinoma that arise in the settings of high or low estrogen exposure have stimulated the hypothesis of two pathogenetic types of endometrial adenocarcinoma (i.e., type I: estrogen related or endometrioid type, and type II: non-estrogen related or non-endometrioid type). The important information that can be ascertained in the evaluation of curettage specimen containing adenocarcinoma includes the following: histologic type, histologic grade, nuclear grade, identification of other processes in the endometrium, and distinction of carcinoma arising in the endometrium from those representing metastatic or local spread. These data help to guide subsequent therapy. The aim of this study was pathohistologic evaluation of curettage specimens containing endometrial adenocarcinoma; new attitudes in the histopathologic diagnosis of endometrial adenocarcinoma and its significance in therapy were also referred to. Routinely processed curettage specimens of 141 patients (mean age 60 years, range 39-89 years) with endometrial adenocarcinoma were evaluated for following morphologic parameters: histologic type, histologic grade, nuclear grade, combined grade, and associated lesions. The incidence of adenocarcinoma of endometrioid type was significantly higher ( $p < 0.05$ ) than the incidence of adenocarcinoma of non-endometrioid type. Endometrioid adenocarcinoma and its variants made 75% of all endometrial adenocarcinoma. The frequency of histologic, nuclear and combined grade 1 (41.35%; 36.54%; 40.39%) and grade 2 (38.46%; 40.38%; 33.65%) was relatively equal in endometrial adenocarcinoma of endometrioid type. The frequency of histologic, nuclear and combined grade 3 (20.19%, 23.08%; 25.96%) was lower than the frequency of grade 1 and grade 2. An agreement of histologic with nuclear grade was presented in 76.92% of endometrioid type adenocarcinoma. Correction of histologic grade required less than 7% of endometrioid type adenocarcinoma. Endometrial changes in adenocarcinoma surroundings were possible to identify in less than 5% of curettage specimens. The most endometrial adenocarcinomas were tumors with a favorable prognosis. The precise evaluation of all histopathologic parameters makes possible the selection of endometrial adenocarcinoma with a more aggressive biological potential from those with a favorable prognosis, which provides the basis for adequate treatment of patients.

**KEYWORDS:** Endometrial Neoplasms; Adenocarcinoma; Histological Techniques; Curettage

## Stage III endometrial cancer: Analysis of prognostic factors

Endometrial carcinoma is the most common malignancy of the female genital tract and the fourth most common cancer site, accounting for 6% of all cancers in women, exceeded only by breast, lung and colon/rectum. In approximately 75% of the cases, the tumor is clinically confined to the uterus at the time of diagnosis. The overall survival rate for endometrial cancer is 84%. Endometrial cancer is usually treated with primary surgery followed by adjuvant radiotherapy. This study was performed to assess the prognostic factors and patterns of actuarial disease-free survival in stage III endometrial carcinoma treated with surgery and adjuvant radiotherapy. A retrospective review of 31 stage III endometrial carcinoma patients treated between 1990 and 1998 at the Clinic of Oncology, Clinical Center Niš, was performed. All patients underwent surgery, followed by adjuvant radiotherapy. The log-rank test was performed for the 5-year disease-free survival. There were 21 cases with endometrioid adenocarcinoma and 10 with papillary forms. There were 3 patients with grade 1 tumors, 19 with grade 2 and 9 with grade 3 tumours. Thirteen cases had less than 50% inner myometrial invasion and 18 cases more than 50% inner myometrial invasion. Ovarian metastases were present in 21 patients, vaginal invasion in 6 and pelvic lymphonodal metastases in 4 cases. Out of 21 cases with endometrioid adenocarcinoma form 15 had 5-year disease free survival (71.43%); out of the remaining 10 cases with papillary tumor forms there were 7 cases with 5-year disease free survival (70%). Out of the histologic grade 1 cases, all 3 cases had 5-year disease free survival (100%). Out of 19 grade 2 cases, 13 had 5-year disease free survival (68.42%); out of 9 grade 3 patients, 6 had 5-year disease free survival (67%). Out of 13 cases with myometrial invasion of less than 50%, 11 had 5-year disease free survival (84.62%); out of 18 cases with myometrial invasion of more than 50%, 11 had 5-year disease free survival (61.11%). The log-rank test utilized demonstrated that the histologic type of the tumor, histologic grade and depth of myometrial invasion correlate with 5-year disease free survival, though not significantly. Our results differ from the literature information. The difference probably reflects insufficient number of cases in our series.

**KEYWORDS:** Endometrial Neoplasms; Neoplasm Staging; Prognosis; Disease-Free Survival; Carcinoma; Adenocarcinoma



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## Chronic myometritis is a reason for postpartum hysterectomy

Non-specific myometritis is very rare, except in states of puerperal infections. In acute state, it appears like endometrio-myometritis, and it is usually caused by streptococcus hemolyticus (type A), chlamydias, eventually by viruses, and rarely by gonococci. Massive chronic inflammation of myometrium is rarely seen, and usually as complication of placental rests or post-abortive infections. Histologically, it is characterized by fibrosis, lymphocytic, plasma cell, as well as histiocytic infiltration of muscular mass. Patient, 24 year old woman, which finished her second pregnancy per vias naturalis, next day started with metrorrhagia, unstoppable even after few curettages. Suspecting on placenta accreta, and because of atonic uterus, subtotal hysterectomy was performed. Macroscopically, uterus was enlarged, limp, with 12 cm thick wall, rough endometrial surface, partially crepe like. Histologically (HE, van Gieson, Gomory), it was noticeable devastation of myometrium caused by diffuse reduction of muscular bundles and atrophy of residual myocytes. Significant was domination of fibrocolagenic and mixomatous tissue with numerous of lipocytes and intense dilatation of blood and lymphatic capillaries. Adjacent to large blood vessels (ligamenta viva uteri), instead of smooth muscle tissue, existed only bundles of collagenous fibre. Inflammatory infiltrate was surrounding and invading the fields of atrophic myocytes, fibro-vascular components and perivascular spaces. The infiltrate consisted of lymphocytes, plasma cells and histiocytes, as well as significant presence of eosinophil leucocytes. Groups of lymphocytes and eosinophils were present in lumen of dilated capillaries and arterioles. This clinically unrecognizable, asymptomatic myometritis, evolved possibly during the postpartum period of previous pregnancy, and acquired its character of auto-aggressive process against smooth muscular cells of myometrium, which is documented by presence of cell types important in immune reactions (lymphocytes, plasma cells, eosinophils). Profuse bleedings are consequence of eradication of contractile muscular bundles, adjacent to the large blood vessels, and atony of uterus is caused by the absence of adequate muscular mass in myometrium, and by interposing of fibro-myomatous tissue between and inside of muscular layers.

**KEYWORDS:** *Myometrium; Inflammation; Puerperal Infection; Hysterectomy; Histological Techniques*

## Decidual changes in adenomyosis of uterus during the pregnancy as indication for Cesarean section

Adenomyosis is the part of endometriosis, usually localized in inner two thirds of myometrium of posterior wall of uterus. However, there is continuity between adenomyosal fields and endometrium. Adenomyosis causes enlargement of uterus, and histologically it consists of focuses of endometrial glands, surrounded with cytogenetic stroma. According to literature, those focuses are followed by hypertrophy of myometrial muscular cells. Sterility is the frequent complication found in the patients with adenomyosis. Patient, 31 years old, at the end of 10<sup>th</sup> lunar month pregnancy, was labored by cesarean section because of atonic uterus. Immediately after removal of placenta, massive bleeding occurred, and suspecting on placenta accreta, subtotal hysterectomy was carried out. Besides, the patient was treated of sterility for a long period. Macroscopically, in enlarged uterus, endometrial surface was meat like, with hemorrhagic focuses inside myometrium. Histologically (HE staining), inside myometrium, broad areas of adenomyosis with few endometrial glands, filled by pink secrete, were noticed, as well as an abundance of large decidual cells, spreading to endometrial rests, which also contain trophoblast cells, but without signs of placenta accreta. Smooth muscular cells, around adenomyosis foci, were atrophic, and decidual cells spread radially through myometrium dividing it into smaller groups of muscular cells. Distant parts of myometrium were atrophic and permeated by fibrous tissue. In opposite to other authors, who registered muscular cells hypertrophy around the decidualy changed adenomyosis foci, in presented case we noticed its atrophy. Atrophy of muscular cells and dissection of their bundles, as well as broad fields of decidual cells between them, lead to decreasing of myometrium muscular mass and breaking of nexus connections between myocytes, important for synchronized normal myometrium contractions, finally caused atony of uterus. The false impression of placenta accreta, was made because of direct connection between decidual changes in stroma of endometrium with the same of adenomyosis foci in myometrium.

**KEYWORDS:** *Endometriosis; Pregnancy; Cesarean Section; Histological Techniques*





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## Epithelial ovarian cancer: Tumor cell type and tumor grade

## Low malignant potential ovarian tumors: Our 14-year experience

Epithelial ovarian cancer is the sixth most frequent form of cancer in women worldwide and the fourth most frequent cause of cancer death among women in USA. At the same time it is the second most common gynecologic malignancy and the most frequent cause of death from gynecologic cancer in the developed countries. At the time of diagnosis two-thirds of patients will present with advanced disease (FIGO stage III-IV). Following primary surgical cytoreduction, the current standard treatment for patients with advanced ovarian cancer involves the systemic administration of a paclitaxel and platinum-containing chemotherapy regimens. Despite the fact that it is one of the most chemosensitive cancers, the prognosis remain poor with 5-year survival rate of approximately 15% to 20% in stage III and less than 5% in stage IV patients. Prognosis depends on FIGO stage disease, age, tumor grade and size, as well as number of residual lesions after primary cytoreductive surgery. The aim of this study was to determine the frequency of different tumor cell types and tumor grade in epithelial ovarian cancer patients. We performed a retrospective review of all patients with celomic origin ovarian malignant tumors treated from January 1991 to the end of 2001 in Department of Gynecology Clinic of Oncology in Niš after primary radical or cytoreductive surgery performed elsewhere. The World Health Organization histologic typing of ovarian neoplasms was used and the tumors were assigned a histologic grade of differentiation. In total of 421 cases with ovarian cancer, 344 women (81,7%) had epithelial ovarian cancer. One hundred ten tumors were serous (32%), 55 were mucinous (16%), 26 were sero-mucinous (7.6%), and 25 were endometrioid carcinomas (7.3%). The others were non-differentiated (10/344 or 3%), clear cell 8/344 (2.3%), and malignant Brenner tumor 4/344 (1.2%). Seventy-nine tumors (23%) were unclassified and 27 patients (7.8%) had borderline tumors of different histologic type. Tumor grade 1 was noted in 35 cases (10.2%), grade 2 in 91 (26.5), and grade 3 in 54 ones (15.7%). In 46.6% patients (151/344) tumor grade wasn't identified. The prognostic significance of histology has been well established in ovarian cancer. On the basis of our data, we concluded that there were differences in tumor cell type.

**KEYWORDS:** *Ovarian Neoplasms; Neoplasm Staging; Neoplasm by Histological Type; Neoplasms, Glandular and Epithelial; Prognosis*

This ovarian malignancy is defined by an epithelial tumor with a stratification of the epithelial lining, but with a lack of frank stromal invasion, as well as increased mitotic activity and nuclear atypia. Those tumors account for 10% to 20% of all epithelial ovarian tumors and tend to present at an earlier stage and at a younger age. Borderline ovarian tumors behave indolently in the overwhelming majority of cases, and the prognosis is therefore usually outstanding. Five-year survival for FIGO stage I is over 95%. Earlier reports on the mortality of even 20% in advanced stages were not confirmed in the last decade. The aim of this study was to determine the frequency of ovarian tumors with low malignant potential, the mean age, FIGO stage disease and survival rates due to tumor cell subtypes in the patients with the same therapeutic approaches. We performed a retrospective review of all patients with celomic origin ovarian malignancies treated from January 1985 to the end of 1998 at the Department of Gynecology, Clinic of Oncology in Niš, after primary radical or conservative surgery performed elsewhere. The World Health Organization histologic classification and the staging FIGO (International Federation of Gynecology and Obstetrics) classification were used. All the patients received the same chemotherapy regimen, six cycles each of them. In total out of 273 cases with epithelial ovarian cancer, 23 women (8.40%) had borderline tumors. The median age of the patients at the time of surgical procedure was 52.2 years (range 30-72). Fifteen tumors (15/23, or 65.21%) were serous, and 8/23 (34.79%) was mucinous. Eleven out of 23 patients (47.8%) had FIGO stage I disease, stage II 2/23 (8.7%), and 2/23 patients (8.7%) had stage III disease too. FIGO stage disease was not possible to determine in 9/23 (39.13%) cases due to insufficiently radical surgery. Five-year survival rate was 86.96% for all cases, but for serous tumors it was 80% and for mucinous tumors it was 100%. In the presented series, low malignant potential ovarian tumors had lower incidence (8.4%) than in the other authors' reports (10-20%). The average age at the time of diagnosis was 52.2 years, one decade more than in the other authors' series. In spite of their indolent course, 13.04% of borderline ovarian tumors ended fatally. Serous subtype had lower 5-year survival rate 80%, in contrast to mucinous tumors, which had 100% 5-year survival rate.

**KEYWORDS:** *Ovarial Neoplasms; Neoplasm Staging; Prognosis; Survival Rate*





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## Disseminated ovarian carcinoma revealed by umbilical metastasis (Sister Mary Joseph's nodule)

## Morphological features of malignant Brenner tumor

Approximately 5% of visceral malignancies eventually develop cutaneous metastases, but only in less than 1% of cases do it so as a presenting sign of an undetected cancer. Chest wall and the abdomen are the most common sites of cutaneous metastases, whereas umbilicus presents very rare localization, usually as a consequence of an extensive intra-abdominal tumor spread with a poor prognosis. We present a case of a 46-year-old female patient that was first operated for a nodular mass of 2 cm diameter, clinically diagnosed as an umbilical hernia. Histopathological examination revealed predominantly solid, irregular tumor islands (with rare tubular-glandular structures), composed of medium-sized cells, showing moderately pleomorphic nuclei and numerous mitoses, including the atypical forms. Tumor infiltration occupied space between the eroded epiderm to the superficial parts of the subcutaneous fat tissue, and could be found in many dilated dermal lymphatic channels. Immunohistochemically, tumor cells were positive for cytokeratin 7 and CA-125 antigen and negative for cytokeratin 20. Diagnosis of metastatic adenocarcinoma was made and, after ultrasonographic and computerized tomography examination, which disclose bilateral ovarian enlargement, total hysterectomy with bilateral salpingo-oophorectomy was performed. A 17 cm-long part of the sigmoid colon was resected (due to a tumor infiltration of the colonic wall) as well as was great omentum with enlarged lymph nodes. Histopathological evaluation of specimens from all excised tissues showed tumor structures of architectural and cytological characteristics similar to those seen in a cutaneous metastasis infiltrating both ovaries, omental lymph nodes and sigmoid colon wall (serosa and outer muscular layer). Tumor cells were found in lumina of lymphatic channels of the myometrium and uterine cervix also, but endometrial, cervical, and colonic mucosae were without any atypism. Immunohistochemical profile was identical to the one seen in umbilical metastasis and diagnosis of primary ovarian carcinoma of endometrioid type was made. Metastatic nodules to the umbilicus could be produced by lymphatic and venous propagation or contiguous extension from a peritoneal surface, and rarely after laparoscopy (iatrogenic). In our case presence of tumor nests on peritoneal surface and in numerous lymphatic channels indicated that more than one mechanism could be involved in a single patient. Absence of neoplastic changes in mucosa of the colon and the endometrium and immunohistochemical profile excluded other possible sites of origin of umbilical metastasis, including the exceptional urachal adenocarcinoma metastatic to the ovary, which was positive for cytokeratin 20 and negative for cytokeratin 7.

Brenner tumors are uncommon adenofibromas in which the epithelial component consists of nests of transitional cells resembling those lining the urinary bladder. They constitute to 2% of all ovarian tumors. Brenner tumors are occasionally encountered in mucinous cystadenoma. The vast majority of these tumors are benign, but borderline and malignant counterparts have been also reported. Female patient, 52 years of age, had lower abdominal pain, pelvic pressure, gastrointestinal complaints and urinary frequency. A combination of solid and cystic areas, confined to the right ovary, without spreading beyond ovary, was discovered during surgical therapy. Encapsulated mass, 8 cm in diameter, solid and cystic was found. On cut surface, tumor had light gray and light yellow color. Histologically, the fibrous stroma, resembling that of the normal ovary was marked nests of epithelial cells resembling the epithelium of high-grade urothelial carcinoma, with the infiltration of tumorous stroma. The degree of histologic atypia was high: neoplastic cells exhibited considerable pleomorphism (variation in size and shape) and deeply stained (hyperchromatic) nuclei, which were abnormally large for the size of the cell. Frequently mitotic figures also were observed. Glandular cystic spaces were lined by columnar mucin-secreting cells (with areas of necrosis and hemorrhage). Two years after surgical treatment and chemotherapy, the patient died with generalized metastases.

**KEYWORDS:** *Brenner Tumor; Ovarian Neoplasms*

**KEYWORDS:** *Ovarian Neoplasms; Neoplasm Metastasis; Umbilicus; Immunohistochemistry; Cytodiagnosis*



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## Characteristics of Krukenberg ovarian tumor

A special form of malignant tumor of the ovary was described by Krukenberg (1896) who regarded it as mucoid fibrosarcoma. Subsequent observers established that the tumor was a metastatic carcinoma. Krukenberg tumor is usually secondary to carcinoma of the stomach (70%), and less often to carcinoma of the bowel (15%), breast (6%) or other organs. The importance of Krukenberg tumor in clinical practice is that this secondary tumor frequently produces symptoms through the primary carcinoma is unsuspected. The stated facts are the reason for this report. We reported three women (22, 36, and 39 years old) with abdominal enlargement lower abdominal pain. During surgical treatment, bilateral, solid ovarian tumors lobulated in contour and of moderate (two cases) or large size (one case) were detected; the cut surface was moist, myxomatous, and of cystic consistency, with hemorrhagic and necrotic areas. Formaldehyde-fixed and paraffin-embedded tumors tissue were cut and stained with HE, PAS and HID-AB pH 2.5 methods. The tumors were cellular in structure and of diffuse and indefinite pattern. On close inspection, polyhedral and round epithelial cells were intermingled with the fibrous tissue stroma, or arranged in cords or small groups. The larger cells had a mucoid, spongy or vacuolated cytoplasm and the nucleus was placed at the periphery of the cell imparting a signet ring form. The staining reactions of mucin were positive, making the cells more easily recognizable than in preparations stained by hematoxylin and eosin. The mucin-containing cells resembled the cells seen in certain varieties of carcinoma of the stomach. The signet ring cell gastric carcinoma of the corporal localization was discovered in all three patients, during suggested endoscopy. The route of dissemination of carcinoma from the primary site in the formation of a Krukenberg tumour was vascular. In spite of total gastrectomy, pancreatectomy and splenectomy, the patients died within one year after the diagnosis of Krukenberg tumor had been established.

**KEYWORDS:** Krukenberg Tumor; Ovarian Neoplasms

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## Pathology of placentas from the assisted reproductive program

According to some investigations histopathological characteristics of placentas from the assisted reproductive programs differ from naturally conceived pregnancies. Assisted reproductive techniques carry more factors for the misdeveloping of the trophoblast and the embryo (ovulation induction, media, micromanipulation etc). The aim of our study was to analyze the histopathological characteristics of placentas from the assisted reproductive programs. We collected specimens from 24 placentas - 12 of the mothers who conceived in an assisted reproductive program (8 from in vitro fertilization and 4 from intrauterine insemination) and 12 of the parturients who conceived naturally. Samples from central and peripheral parts of placentas were fixed in 10% formalin and routinely processed and stained with hematoxylin and eosin. We found distinct pathological pictures, villous edema, fibrin deposits, calcifications, syncytial knots and leucocyte accumulations, especially in the group of placentas from mothers in assisted reproductive program. We found high statistically significant difference between two groups of placentas when comparing them for villous edema ( $\alpha=0.001$ ). Also a statistically significant difference for microcalcification was present ( $\alpha=0.04$ ) but not for syncytial knots and fibrin deposits ( $\chi^2=0.67$ ,  $p>0.25$ ). Placentas of mothers who conceived in an assisted reproductive program differ from those of mothers who conceived naturally - it is a statistically significant higher incidence of villous edema and microcalcification in placentas from the assisted reproductive program.

**KEYWORDS:** Placenta; Reproductive Techniques, Assisted; Placental Diseases



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## Correlation between different histological grading methods in breast cancer

Histological grading is an important parameter for the risk assessment in patients with breast cancer. This study assessed the prognostic significance of three different types of histological grading methods (Elston, Contesso, Helpap) in a retrospective sample of 292 patients. Contesso method assessment was made on a two microscopes with different field areas (0.238 mm<sup>2</sup> and 0.345 mm<sup>2</sup>). Four-micrometer thick hematoxylin-eosin stained slides were investigated. Mitotic figures were counted in representative areas of the tumor in 10 HPF at 400x magnification. Survival analysis was evaluated by univariate (Kaplan-Meier) and multivariate (Cox model) analysis. Univariate and multivariate analysis showed that all three methods had high prognostic value to overall survival (OS) and disease free survival (DFS). Using univariate analysis was confirmed that Elston method was the best reflected on OS and DFS ( $p < 0.0001$  and  $p < 0.001$ ). The field area of the microscope had a minor influence on the mitotic count and on the results of the Contesso method. The histological grade is an important prognostic factor in breast cancer with the Elston method giving the best results.

**KEYWORDS:** Breast Neoplasms; Survival Analysis; Prognosis; Histological Techniques

## The correlation of histopathologic and mammographic findings in the detection and early diagnostics of breast carcinoma

In the Institute of Oncology in Sremska Kamenica, 30 women were examined for breast carcinoma. In all cases, mammography pointed to malignancy, which was later proved by ex tempore and definitive histopathology analysis. The aim of the study was to compare the results obtained by mammography and histopathologic analysis of breast carcinoma in order to determine significant morphologic parameters in the diagnostics of malignancy in this organ. The authors analyzed and compared the values obtained in histopathologic and mammographic investigations; degree of tumorous changes, spreading into axillar lymph nodes, extempore, definitive histopathologic diagnosis, and tumor score. Most parameters of the study conform to world literature standards, especially category of life age of developing breast malignancy, tumor differentiation, and possible metastasising into axillar lymph nodes, which also depends on carcinoma type. In our study, most detected tumors were ductal carcinomas. Mammographically suspect and positive axillas were histopathologically verified. Tumor dimensions did not depend on the differentiation (score), frequency of metastasising or the number of involved nodes, but the type of carcinoma affected the tumor dissemination. All the tumors diagnosed extempore were later verified by definitive histopathologic analysis, whereas false positive or false negative cases were missing. We concluded that the mammographic findings were not precise in the differentiation of tumor dissemination, while pathoanatomic and histopathologic analysis of same region gave more reliable parameters. Mammography is still an invaluable diagnostic method in early detection of malignant breast lesions but only combined with histopathologic findings. There is a positive correlation between these two methods.

**KEYWORDS:** Breast Neoplasms; Diagnosis; Mammography; Histological Techniques; Carcinoma



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## Fine-needle aspiration of thyroid papillary cancer

Fine needle aspiration (FNA) cytology has a high sensitivity for the diagnosis of thyroid nodules. Significant number of thyroid papillary cancers can be detected by fine needle aspiration biopsy. Papillary carcinoma is the most frequent malignancy of the thyroid. During the period of two years we obtained 600 thyroid aspirates. The smears were stained with HE and MGG. Following diagnostic guidelines were used: tumor cellularity of smears, papillary arrangement of cells, tumor cells larger than normal follicular cells with slight anisocytosis, ground-glass nuclei, presence of intranuclear inclusions, and scanty or absent colloid. There were 19 (3.5%) cytological diagnoses of papillary carcinoma. Tumor was more frequent in female patients (74%). The youngest patient was 13 years old boy; the oldest was 74 years old woman. The median age (51.2 years) was higher than expected. Classic cytological characteristics were found in 89% aspirates. Only 1 (one) papillary carcinoma contained psammoma body. In 5 cases (26.3%) degenerative changes (hemorrhage and necrosis) were presented. Also, in 2 smears (10.5%) papillary carcinoma was associated with Hashimoto's thyroiditis and oxyphilic lesion.

**KEYWORDS:** *Biopsy, Needle; Carcinoma, Papillary; Thyroid Neoplasms*

## Thyroid carcinoma - histopathological and immunohistochemical features

Thyroid-specific malignant tumors are rare neoplasms, derived from follicle cells (papillary and follicular carcinoma), and from parafollicular, calcitonin-producing C-cells (medullary carcinoma). Biological behavior and prognosis of thyroid carcinoma depend on specific features of patients (age, gender), tumor (histology, extent, aneuploidy), and treatment. Total of 300 patients with thyroid carcinoma operated in the Center for Endocrine Surgery, Institute for Endocrinology, Clinical Center of Serbia, from 2001 through 2003 was evaluated. The surgical specimens were investigated by routine histopathological method (HE), some special methods of staining (Congo red) and relevant immunohistochemical markers (thyroglobulin, calcitonin). Papillary carcinoma was the most frequent type of follicle-cell derived carcinoma (240 cases, 80%). Its histology usually revealed papillae - delicate stalks of epithelial cells situated on basal membranes covering stromal fibers and thin capillaries. The main criterion for diagnosis of papillary thyroid carcinoma was the occurrence of hypochoemic, "ground-glass" nuclei. Often the tumors contained round laminated calcifications (psammoma bodies). The diagnosis of follicular carcinoma (3 cases, 1%) was based on two criteria: 1) true infiltration of the venous vessels outside the tumor capsule, and 2) infiltration through the tumor capsule into the surrounding parenchyma. Oxyphilic cell type carcinomas, which were diagnosed in 24 cases (8%), showed large, polygonal cells with abundant oxyphilic cytoplasm and capsular and vascular invasion. Undifferentiated (anaplastic) carcinoma (15 cases, 5%) revealed sheets of polygonal and spindle cells, with frequent appearance of giant cells, numerous mitotic figures, and large areas of necrosis and hemorrhage. Thyroglobulin was present in more than 95% of papillary and follicular carcinomas. Anaplastic thyroid carcinomas were mostly immunonegative for thyroglobulin. Medullary (C-cell) thyroid carcinoma (18 cases, 6%) was composed of solid nests and infiltrating formations of polygonal and spindle-shaped cells. Amyloid deposits within the stroma were found in more than half of the tumors. Nearly all medullary carcinomas were immunopositive for calcitonin. Generic neuroendocrine markers (neuron-specific enolase - NSE, synaptophysin, chromogranin A), as well as carcinoembryonic antigen - CEA were also positive in cases of medullary carcinoma, with variable frequency and intensity. Although the histopathological criteria for diagnosis of different types of thyroid carcinoma are well known, immunohistochemistry is strongly indicated in many cases. Two main discriminatory immunohistochemical markers for tumors with follicular and parafollicular origin are thyroglobulin and calcitonin, respectively.

**KEYWORDS:** *Thyroid Neoplasms; Carcinoma; Histological Techniques; Immunohistochemistry*



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## Adrenal neoplasms - histopathological and immunohistochemical features

Primary adrenal neoplasms may be derived from adrenal cortex (most frequently adenoma and carcinoma) or adrenal medulla (pheochromocytoma, neuroblastoma). Differential diagnosis between adrenocortical adenoma and carcinoma, and in some cases even between primary and secondary adrenal tumor, still remains the challenge for pathologist, although applying of immunohistochemistry may be helpful. The aim of the study was to make histomorphological and immunohistochemical analysis of surgically resected adrenal tumors from the Center for Endocrine Surgery, Clinical Center of Serbia over the period from 1999 to 2003. Paraffin-embedded cut sections were stained by both hematoxylin-eosin and PAS. The expression of inhibin, melan A, chromogranin A, synaptophysin, S-100 protein and ACTH was examined using the PAP method, with appropriate antibodies being applied. Among 198 adrenal tumors histopathological diagnosis were: adrenocortical adenoma (96 cases), adrenocortical carcinoma (20 cases), "border-line" cortical tumor (1 case), pheochromocytoma (45 cases), mixed corticomedullary tumor (1 case), myelolipoma (6 cases), malignant schwannoma (1 case) and metastases (18 cases). Adrenocortical adenomas were composed of cells similar to those populating the normal adrenal cortex, sometimes with some degree of pleomorphism, and with the cytoplasm ranging from eosinophilic to vacuolated, depending on their lipid content. Mitotic activity in adenomas was generally inconspicuous. Adrenocortical carcinomas were poorly demarcated lesions containing areas of necrosis, hemorrhage, and cystic change. Their histology revealed well-differentiated cells resembling those seen in cortical adenomas or bizarre, pleomorphic cells, sometimes difficult to distinguish from those of an undifferentiated carcinoma metastatic to the adrenal. Pheochromocytomas were composed of polygonal to spindle-shaped chromaffin cells and their supporting, sustentacular (S-100 protein immunopositive) cells, compartmentalized into small nests, or "Zellballen", by a rich vascular network mitotic figures in these tumors were infrequent. In one case the diagnosis was compound pheochromocytoma (e.g., pheochromocytoma - ganglioneuroma). One mixed corticomedullary tumor showed cords and nodules of adrenal cortical cells intimately admixed with pheochromocytes. Immunohistochemical investigations highlighted these two cellular components: the adrenocortical cells revealed inhibin and melan A immunopositivity, whereas the pheochromocytes were strongly reactive with chromogranin A, synaptophysin, and ACTH, and the sustentacular cells with S-100 protein. Among metastatic tumors we proved 4 renal cell carcinomas, 7 adenocarcinomas, 3 bronchogenic carcinomas (1 squamous cell, 1 small cell and 1 large cell) and 4 poorly differentiated carcinomas of unknown origin. The correct diagnosis of adrenal neoplasm may be given by experienced pathologist after keen microscopy, and high-quality immunohistochemistry.

**KEYWORDS:** *Adrenal Gland Neoplasms; Immunohistochemistry; Histological Techniques; Microscopy*