INTRODUCTION: The vast majority of uterine cervical carcinomas are human papillomavirus (HPV) related neoplasms. In women with a cervical cancer and a distant lesion the histologic distinction of metastatic cervical cancer versus another primary tumor can be difficult and has important clinical implications. OBJECTIVE: To study the presence of HPV DNA in primary cervical cancer and in second neoplasms in the same patient. MATERIAL AND METHODS: Four patients with squamous cell carcinoma (in bone, lung, lateral neck lymph node and pleural fluid) and two with adenocarcinoma (in ascitic fluid) and a past history of uterine cervical cancer (diagnosed 1 to 11 years before) were studied. HPV DNA detection was performed both in the cervical tumors and in the second neoplasms (formalin fixed, paraffin embedded tissues) using a PCR based technique with GP5+/6+ primers for detection of the HPV L1 gene followed by reverse line blotting hybridization for genotyping. RESULTS: In five patients DNA of the same HPV type was found in the cervical tumor and in the second neoplasm (HPV16 in 4 squamous cell carcinomas and HPV18 in one adenocarcinoma), thus allowing to classify the second tumors as metastatic. In the remaining patient HPV DNA was not detected in any of the tumors tested. CONCLUSIONS: In women with a past history of an HPV-related cancer and a second neoplasm detection and typing of HPV DNA is helpful in the differential diagnosis between metastases and a second unrelated malignancy.

PP4-16
EFFECTIVENESS FOR EVALUATION OF LYMPHATIC INVASION IN ENDOMETRIOID ADENOCARCINOMA OF THE UTERINE CORPUS

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Backgrounds: Lymph-vascular involvement is one of the important prognostic factors in the patients with carcinoma of the uterine cropus. Conventionally, it has been determined morphologically using hematoxylin and eosin sections. In addition to that, various immunohistochemical stains have been attempted in order to confirm the accuracy of diagnosis of lymph-vascular involvement with section stained H&E. Recently, D2-40 immunostaining was demonstrated as the best immunohistochemical marker for the endothelium of the lymph vessel. The aim of this study is to clarify the effectiveness of immunohistochemical staining with D2-40 in determination of lymphatic invasion. Methods: We investigated that 40 patients with adenocarcinoma confirmed to the uterine corpus, who were underwent radical hysterectomy. The stages of tumors were 26 cases in pT1b, 14 cases in pT1c, and 7 cases were positive node among 40 cases. From each material, one section containing the deepest invasive part was selected for examination and stained with H&E and D2-40 immunohistochemically. Lymphatic invasion was evaluated by either H&E staining or D2-40. The concordance of these results was assessed using the kappa statistic (κ). Additionally, the relationship between lymph vascular involvement and lymph node metastasis was examined by using Fisher's exact test. Results: The evaluation of lymphatic invasion with H&E staining resulted in 24 positive cases (positivity of 60%) and 16 negative cases (negativity of 17.5%). The result with D2-40 immunostaining showed 7 positive cases (positivity of 17.5%) and 33 negative cases (negativity of 82.5%). The concordance between H&E and D2-40 was moderate (57.5%, κ=0.53). The negative cases in the evaluation with H&E staining were always negative in the evaluation with D2-40. As a result, lymph vascular involvement might have been over-estimated by H&E staining. The correlation between lymphatic invasion and lymph node metastasis showed statistical significance, in both results with H&E and D2-40 (p=0.011 and p=0.0001, respectively). Conclusion: Lymphatic invasion determined by D2-40 staining could be much more accurate predictive factor for lymph node metastasis.

PP4-17
ENDOMETRIAL CYTOLOGY IN DIAGNOSIS OF ENDOMETRIAL CARCINOMA

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Cytodiagnosis of the precancerous lesions of the endometrium has remained unclear compared to that for cervical lesions. Endometrial cytology and biopsy have been performed for patients with atypical genital bleeding, who were over fifty, postmenopausal or nulliparous. The cytologic diagnosis of endometrial cancer using material obtained with the Inocurette endometrial sampler was assessed for 64 patients.The cytologic findings for benign and malignant samples are described and illustrated in detail. Relative to other endometrial sampling devices, the Inocurette is inexpensive and was easily used by the gynecologist and well tolerated by the patients, with no complications and minimal discomfort.

PP4-18
EVALUATION OF COMBINED BCL-2/MDM-2 IMMUNOHISTOCHEMICAL EXPRESSION AS A PROGNOSTIC FACTOR IN EARLY STAGES OF INVASIVE CERVICAL CARCINOMAS

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BACKGROUND: The present study was designed to evaluate the immunohistochemical expression of apoptosis regulating proteins (bcl-2, mdm-2 and p53) in correlation with proliferation (Ki-67), human papillomavirus (HPV) infection and other histopathological and clinical parameters in early stage cervical carcinomas and the estimation of their prognostic significance. Special attention was given to combined bcl-2/mdm-2 immunophenotypes in predicting the recurrence of the disease. METHOD: The subject of this study was a series of 83 surgically treated patients with cervical carcinoma confined to the uterine cervix (pT1b1/1b2), who subsequently received complete radiotherapy. The presence of HPV DNA was determined by the conventional method of in situ hybridization (ISH) and catalyzed reporter deposition signal amplification ISH. The immunostaining was performed using avidin-biotin-peroxidase complex method and the expression of the biological markers was semiquantitatively evaluated as the percentage of immunostained cells. RESULTS: During the clinical follow-up (mean 120.7, range 4.4-181 months) a relapse was diagnosed in 9 (10.8%) patients and the expected 5-, 10- and 15- year disease-free survival was 92.7%, 90.8% and 86.6%, respectively. The results of the univariate analysis indicate that significant predictive indicators for recurrence are: lymphonodal status, maximal tumor diameter, depth of stromal invasion, histological type and HPV DNA presence and type. Immunohistochemical markers showed the following correlations: increased expression of Ki-67 (P=0.031) and bcl-2 negativity (P=0.047) correlated with poor disease-free survival, while mdm-2 positivity showed borderline significance (P=0.051) and p53 expression had no influence on disease-free survival. Additional evaluation of combined bcl-2/mdm-2 expression showed that cases with bcl-2+/mdm-2- and bcl-2-/mdm-2+ immunophenotype had better survival (P=0.048) compared to bcl-2+/mdm-2+ and bcl-2-/mdm-2- phenotype. In the multivariate analysis, histological type, HPV DNA presence and the expression of Ki-67 have been selected as

the most significant independent prognostic parameters (P=0.0024). CONCLUSION: The evaluation of combined bcl-2/mdm-2 immunohistochemical expression provides more relevant information for the prediction of the recurrence of the disease than their individual expression. However, neither individual expression of bcl-2 and mdm-2 nor their combined immunohistochemical expressions are independent predictors of prognosis in early stages of invasive cervical carcinomas.

PP4-19
SCLEROSING STROMAL TUMOR OF THE OVARY WITH SEX CORD ELEMENTS

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Screrosing stromal tumor of the ovary is a distinctive type of benign stromal tumor characterized by a cellular pseudolobular pattern. The tumor cell population is composed of fibroblasts and round cells separated by hypocellular, oedematous or collagenous tissue. In the recent literature there have been very rare reports of the coexistence of sex cord elements in, otherwise typical, sclerosing stromal tumors of the ovary. We present a case of a seventeen-year-old girl with a sclerosing stromal tumor in which sex cord elements were observed. Multiple histological sections were studied and immunohistochemistry was performed with a wide spectrum of antibodies. Morphological and immunohistochemical findings led to the diagnosis of sclerosing stromal tumor with sex cord elements. The tumor cells stained positive for desmin, vimentin and SMA. Sclerosing stromal tumors comprise a very distinct type of ovarian stromal tumors with very characteristic histology, which is presented in detail.

PP4-20
THE IMPORTANCE OF THE TUMOR SUPPRESSOR GENE DESIGNATED PTEN AND OF THE PROLIFERATION MARKERS Ki-67 AND PCNA IN THE EVALUATION OF THE MALIGNANCY POTENTIAL IN ENDOMETRIAL HYPERPLASIA

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Introduction: Endometrial Hyperplasia (increase in gland/stroma ratio, disorder number and shape of the glands like modifications of the glandular epithelium: exhibits loss of nuclear polarity, stratification, etc) is a lesion frequently associated with the uterine leiomyomas Purpose: The Study was realized at the Universitary Emergency Hospital Bucharest, Romania on 210 endometrium biopsies taken in the period 2004-2005 from women with ages between 45 and 55. Material and methods: Hematoxylin –eosin stained slides of endometrial formalin fixed, paraffin embedded tissue has emphasized in 105 cases the simple hyperplasia (SH), in 75 cases the complex hyperplasia (CH), in 11 cases the simple atypical hyperplasia (SAH) and in 23 cases the complex atypical hyperplasia (CAH). We performed the indirect tristadial ABC method of IHC for 3 antibodies: PTEN, Ki-67 and PCNA on formalin fixed embedded tissue taken by biopsies from 50 cases (8 SH, 8 CH, 34 SAH and CAH). Results: PTEN was focal positive for SAH, diffuse for CAH and for 1-2 cases of SH and CH. Ki-67 and PCNA were also very frequent in group SAH and CAH. Conclusion: PTEN, Ki-67 and PCNA take part in the process of endometrial carcinogenesis following probably molecular pathways and determine the malignity potential of atypical hyperplasia of endometrium.

PP4-21
EGFR AND HER2/NEU EXPRESSION IN ENDOMETRIAL CARCINOMA. CORRELATION WITH TYPE AND STAGE

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BACKGROUND: Epidermal Growth Factor Receptor (EGFR - Her1) and Human epidermal growth factor type II (Her2/neu) are members of the subfamily of tyrosine kinase transmembrane receptors. The expression of EGFR and Her2/neu has been documented in a variety of malignant neoplasms of epithelial origin as breast, ovary and lung. The expression of these markers correlates with advanced stage, poor prognosis and metastasis. The status of these oncoproteins in endometrial carcinoma, however, is not entirely clear. Aim of this study was the evaluation of EGFR and Her2/neu in endometrial carcinoma (endometrioid and serous –type I and II), the relation to other prognostic factors and the possible therapeutic implications. MATERIAL and METHODS: Forty one cases of endometrial carcinoma were selected, 22 endometrioid (type I) and 19 serous (type II). Formalin fixed-paraffin embedded tissues were immunohistostained with EGFR (clone 31G7, Zymed, CA, USA) and Her2/neu (clone CB11, Bio Genex, CA,USA). Over-expression of Her2/neu was defined as moderate or strong membranous staining (≥2+ staining) in more than 10% of the cells. EGFR's expression was interpreted as positive (any membranous staining) or negative. Tumors were subdivided into two stage groups, 1 and ≥2. RESULTS: Patients ranged in age from 27-84 years, mean age 59,81 in endometrioid and 68,26 in serous carcinomas. Her2/neu was over-expressed in 9,9% of type I and 41,1% of type II (P< 0,001) and in stage ≥2 in comparison to stage 1 (54,5% vs 25%). EGFR's expression was demonstrated in 40,9% and 31,6% of type I and II carcinomas, respectively. Stage 1 type I carcinomas expressed EGFR in statistically significant percentage, compared to stage ≥2 (77,8% vs 15,4% , P<0,05). CONCLUSIONS: Her2/neu usually is over-expressed in serous type of endometrial carcinoma. Moreover, the expression increases with stage. EGFR especially is expressed in endometrioid type carcinoma and mainly in low stage. Newly developed drugs that target these receptors may have a role in the treatment of endometrial cancer. These results, obtained by immunohistochemistry, have to be confirmed using molecular methods (CISH or FISH).

PP4-22
EXPRESSION OF MASPIN IN TYPE I AND II ENDOMETRIAL CARCINOMA, ITS CORRELATION WITH VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) AND CLINICAL PARAMETERS

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BACKGROUND: Maspin (mammary–specific serpin) is a tumor suppressor gene that inhibits the invasion and angiogenesis. Maspin is expressed in normal human mammary and prostate epithelial cells but is down –regulated during cancer progression. Interestingly, the protein's prognostic significance in various cancers is highly impact by its cellular localization (nuclear vs cytoplasmic).Vascular endothelial growth factor (VEGF) plays important role in angiogenesis. The aim of this study is to determine the maspin's pattern expression in endometrioid (EC) and serous uterine carcinomas (SC), its correlation with VEGF and the clinicopathologic variables. MATERIAL AND METHODS: We examined maspin and VEGF expression in 22 endometrioid and 19 serous uterine carcinomas. Paraffin blocks