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Pallister-Killian syndrome: A chromosomal abnormality with great variability of the fetal phenotype

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The first prenatal diagnosis of Pallister-Killian syndrome (PKS) was reported by Gilgenkrantz et al in 1985. This report was referring to about 60 prenatal cases, but both sonographic and cytogenetic diagnosis were difficult. Although ultrasound anomalies such as congenital diaphragmatic hernia, polyhydramnios and rhizomelic micromelia in association with fetal overgrowth are very suggestive of the syndrome, they are inconstant and they may even be absent. The mosaic distribution of the supernumerary isochromosome 12p greatly increases these difficulties. No prenatal cytogenetic technique is sensitive enough to ensure prenatal diagnosis and false-negative results have been described on fetal blood, chorionic villi and amniocentesis. In this study we report a prenatal case of PKS which illustrates great variability of the fetal phenotype. A pregnant woman of 25 years old was referred to our hospital at the 22 week of gestation with the symptoms of polyhydramnios and suspected rhizomelic micromelia in routine ultrasound examination. Fetal chromosome analysis was performed using fibroblasts obtained by amniocentesis and mosaicism of 47XY and isochromosome of 12p were diagnosed . The mother vaginally delivered a male fetus who died just after the delivery. Autopsy findings included rhizomelic micromelia, narrow and angulated palate and skin fibroblastic polyp at the left small finger of 0.5 cm in diameter. Micrognathia, flattened nose and low-set ears were also noted. Pallister-Killian syndrome is a clinically recognized syndrome, usually due to a tissue-limited mosaicism for a supernumerary 12p isochromosome (i12p). Premeiotic mitotic error may be the most likely mechanism for i(12p) formation which is maternally inherited. A quite wide spectrum of associated congenital malformations including diaphragmatic hernia, rhizomelic micromelia, mental retardation, cleft palate, pigmentary skin changes and physiognomy alterations have been reported in Pallister-Killian syndrome. Since diaphragmatic hernia and acral hypoplasia can be also found in Fryns syndrome, the differential diagnosis between the two conditions depends on the demonstration of the 12p isochromosome by FISH. Our case did not appear diaphragmatic hernia which is the most common skeletal malformation. Instead of cleft palate, our patient had narrow and angulated palate with minor facial signs and there was an additional minor feature: a skin fibroblastic polyp of the left small finger. Primary cultures of skin fibroblasts obtained by amniocentesis revealed an extra metacentric chromosome i(12p). In reviewing the 63 reported cases of PKS, Doray et al attempt to determine ultrasound indicators of the syndrome and to define a cytogenetic strategy. In cases where ultrasound indicators are present, they proposed first to perform chorionic villus of placental sampling and then amniocentesis when the first cytogenetic result is normal. Fetal blood sampling is the least indicated method because of the low frequency of the isochromosome in lymphocytes. In this cytogenetic strategy fluorescent in situ hybridization (FISH) and especially interphase FISH on non-cultured cells increases the propability of identifying the isochromosome. The analysis of cord blood lymphocytes revealed only 0.5% incidence of tetrasomy of 12p. The incidence of tetrasomy was 8.0% for the placental chorionic villi, 48.0% for the fibroblasts obtained from the umbilical cord and 70.0% for the skin fibroblasts. Thus the diagnosis of PKS is confirmed by mosaicism of i(12p) with the abnormal karyotype expression limited in lymphocytes but marked in skin fibroblasts.

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Immunohistochemical expression and prognostic signifficance of the biological markers bcl-2, p53, mdm-2 and Ki-67 in early stages of invasive cervical carcinomas

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Objectives: The objectives of this study were the evaluation of the immunohistochemical expression of apoptosis regulating proteins (bcl-2, mdm-2 and p53 protein) in correlation with proliferation (Ki-67), human papillomavirus (HPV) infection and other histopathological and clinical parameters in early stage cervical carcinomas and estimation of their prognostic significance.
Methods: The subject of this study was a series of 83 surgically treated patients with cervical carcinoma confined to the uterine cervix, who subsequently received complete radiotherapy. The presence of HPV DNA in the neoplasm was determined by the conventional method of in situ hybridization (ISH) and catalyzed reporter deposition signal amplification ISH using mixed biotinylated probes to identify types 6/11, 16/18 and 31/33 or 31/33/51. The immunohistochemical expression of the biological markers was semiquantitatively evaluated as the percentage of immunostained cells in the three compartments of the neoplasm: the surface, the middle layer and the invasive front.
Results: 73 patients had a tumor confined to the uterine cervix less than 4 cm in diameter (pT1b1) and the other 10 had larger neoplasms that belong to the pT1b2 category. Regional lymph node involvement was found in 20 (24%) of the patients. During the clinical followup (mean, 120.7, range 4.4-181 months) a relapse was diagnosed in 9 (10.8%) patients, 6 of which (7.2%) died of the disease. The expected 5-, 10- and 15- year overall survival was 94.4%, 92.7% and 92.7%, and 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, HPV DNA presence and type, and the immunohistochemical expression of bcl-2, mdm-2 and Ki-67 in the invasive front of the neoplasm. In the multivariate analysis, histological type, HPV DNA presence and the expression of Ki-67 in the invasive front have been selected as the most significant independent prognostic parameters (P=0.0024). The value of the prognostic index (PI), calculated using the Cox regression model, provided the basis on which the patients were classified into two distinct risk groups with significantly different disease-free survival period (P=0.0009).
Conclusions: The results indicate that the invasive front of the neoplasms proved to be the most important area for the evaluation of immunohistochemical expression of biological markers. The prognostic index as an indicator of the patient's place in the prognostic spectrum enables the identification of the risk group of patients in whom, due to a higher risk of relapse, better results are to be expected with the application of more aggressive therapy.

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Female genital actinomycosis: a review of 24 cases

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Objectives: The aim of this retrospective study was to present the clinical characteristics of the patients with female genital actinomycosis in correlation with the histopathological findings. Actinomycosis is a relatively rare chronic granulomatous inflammatory disease caused by the bacteria Actinomyces israelii, a normal comensal of the gastrointestinal and genital tract. The abdominal form of the disease is rare, however the incidence of the female genital and pelvic actinomycosis is rising, especially among the intrauterine device (IUD) users (8-20%).

Methods: According to the computer database at our department, 965 cases of endometritis, 6,313 cases of cervicitis and 584 cases of pelvic inflammatory disease (PID) were diagnosed in a 15 year period (1991-2005). However, only 21 (2.2%) cases of endometrial, 1 (0.02%) cervical actinomycosis and 2 (0.3%) cases of pelvic actinomycosis were identified in this period. Explorative curettage was performed in 21 patients due to prolonged uterine bleeding and extirpation of an IUD was done in 19 of them. One patient had a biopsy taken for a suspicion of cervical neoplasm, consecutively diagnosed as endometrial adenocarcoma. In the PID group, one patient with a previous history of tubal pregnancy underwent a transabdominal biopsy for a paravesical tumor, two weeks after extirpation of an IUD. The last patient had no IUD and was surgically treated with hysterectomy and bilateral adnexectomy for a suspicion of malignant ovarian tumor. The biopsy, curettage and operative materials were formalin fixed, routinely processed and paraffin embedded. 4_ thin sections were cut and slides were stained using standard hematoxyllin–eosin staining procedure.
Results: The mean age of the patients was 52.3 ranging from 41 to 68. Macroscopically visible sulfur granules were not identified in any of the cases of disease confined to the uterus. However microscopically, in all the 22 biopsy and curettage materials, elements of chronic granulomatous endometritis and/or cervicitis were seen, together with branching filaments of Actinomyces. In the paravesical tumor, abscesses filled with necrotic debris and scattered Actinomyces colonies were found. Macroscopically visible sulfur granules were identified only in the operative material, where a rough necrotic grayish-yellow area was seen on the serosal surface on the left side and posterior wall of the uterine corpus, measuring 4 × 3 cm. A left tubo-ovarian abscess measuring 4 × 3 × 3 cm was also found. On sectioning, several small and large abscesses filled with puss were present. The histological examination confirmed multiple actinomycotic abscesses in the ovary, paraovarian region and the external third of the left lateral uterine wall.
Conclusions: Female genital actinomycosis is a rare and obscure granulomatous disease. It is most prevalent in IUD carriers and easily diagnosed when confined to the uterus. However, the pelvic actinomycosis is often misdiagnosed, simulating malignant pelvic or ovarian tumor. Therefore, unnecessary surgical interventions can be avoided with a careful examination of these patients and a timely identification of the disease.

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Synchronous endometrioid carcinoma of the uterine corpus and ovary: A case report

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Synchronous endometrioid carcinoma of the uterine corpus and ovary is an uncommon but well recognized event. Diagnosis as either separate independent primary or as metastatic tumors requires careful consideration of a number of gross and histological features. These features illustrate the criteria helpful in distinguishing independent primaries from metastatic carcinomas which have a different therapeutic implication. The possible link between fertility drugs and carcinogenesis still remains controversial. We report a case of a 52 year old woman who came to our hospital with cystic left ovarian mass (8cm). Hysterectomy and bilateral salpingo-oophorectomy were carried out. Histological examination showed well differentiated endometrioid endometrial cancer. Endometrial tumor was intra-mucosal without myometrial or vascular invasion and was associated with atypical complex hyperplasia. The woman had not been previously treated with ovulation induction drugs. She was free of recurrence 20 months after surgery. Patients with synchronous endometrioid tumors of the endometrium and ovary are generally younger than reported for either endometrial adenocarcinomas or ovarian epithelial adenocarcinomas. They tend to be low grade and early stage and are frequently associated with endometriosis. The prognosis of endometrioid type carcinomas is better than other histological types of carcinoma.

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Clinicopathological study of Bcl-2 immunohistochemical expression in endometrioid adenocarcinoma

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Objective: The Bcl-2, an anti-apoptotic protein, plays a central role in apoptosis, acting as an inhibitor of the apoptotic process. The aim of our study was to evaluate the expression of Bcl-2 in endometrioid adenocarcinoma and its clinocopathological significance.
Methods: 78 patients with endometrioid adenocarcinoma were included in the study. The median follow-up time was 43 months. Immunohistochemical analysis for Bcl-2 antigen was performed on formalin-fixed, paraffin embedded tissues of 74 patients.
Results: The median age of the women was 65 years. The cancer related survival was significant correlated with advanced FIGO stage (P=0.0025) and metastatic disease (P=0.0005). Disease free survival was closely associated with tumor diameter (P=0.04), risk factor (P=0.035) and tumor depth (P<0.013), while the most important correlations were associated with metastatic status (P=0.007), FIGO stage (P<0.001) and tumor differentiation (P<0.001). Bcl-2 immunoreactivity was detected in 24/74 (32%) cases of histologic grade 1 and 2, P=0.028. Lack of Bcl-2 expression was directly correlated with high risk patients (9/38), P=0.001.
Conclusions: Bcl-2 is an early event in endometrioid adenocarcinoma. The anti-apoptotic effect of the Bcl-2 is limited in advance stage carcinomas as well in high risk patients.

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P53 overexpression and prognostic impact in endometrial carcinoma of endometrioid subtype

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Objective: Overexpression of p53 in endometrial carcinoma has been reported to correlate with the unfavourable clinicopathologic features and poor prognosis. The aim of the study was to investigate the p53 overexpression and its prognostic significance in patients with endometrial cancer.
Methods: Immunohistochemistry for p53 expression was performed on paraffin embedded material of 71 surgically treated patients with endometrial carcinoma of endometrioid histologic subtype. The evaluation of staining was performed using a relative rank scale from 0 to 2. The 2+ was considered as overexpression. The median follow-up time was 43 months.
Results: The median age of the women was 65 years (range 35-80). Thirty seven of the 71 cases (52%) stained positive for p53, while overexpression of p53 was detected in 20/71 cases (28%). p53 overexpression was significant correlated with unfavourable tumor differentiation (P=0.028) and positive nodal status (P=0.032), while with the overall survival and disease free survival was insignificant (P=NS).