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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%).