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TUMOR INFILTRATING LYMPHOCYTES AND ANTIGEN PRESENTING CELLS IN HUMAN PAPILLOMAVIRUS - ASSOCIATED SQUAMOUS EPITHELIAL NEOPLASMS OF THE CERVIX

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The human papillomavirus (HPV) infection is significantly linked with the producing and progression of the squamous cell benign and malignant neoplasms . A prolonged HPV infection acting as an oncogene is associated to a modified immune response of the host. The object of this work is an " in situ " analysis of the different cell populations participating in this response, as correlated with the morphological appearance of the squamous cell lesions and the presence of the viral proteic structures. For this aim, a retrospective study was accomplished using a formalin fixed, paraffin embedded material from 20 cervical condilomas and 10 squamous cell carcinomas from a files of V.Babes Institute and of Morphopathology Department,University of Medicine, Craiova . For typing immunohistochemically (IHC) the subpopulations of TIL ,the Langerhans' cells of the epithelium and the dendritic /macrophages cells of the stroma, anti - CD 20, UCHL 1, CD8, S 100, CD 68 - antibodies (Dako, Glostrup, Denmark) and CD4 antibody (Sigma, St.Louis,USA)were used; the visualisation of the proteic capside of the HPV was performed IHC, using a polyclonal anti-HPV serum. (Dako). The lymphocytes and the immunoassociated cells disposition was compared for the two lesional categories, trying to find a relationship between the tumoral form and the cellular immune response

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HUMAN PAPILLOMA VIRUS DNA PRESENCE IN EARLY STAGE CERVICAL CARCINOMAS: CORRELATION WITH OTHER PROGNOSTIC FACTORS AND RECURRENCE RATE

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BACKGROUND: Although the role of humanpapillomavirus (HPV) in cervical carcinogenesis is reasonably well established, the attempts to determine the prognostic value of presence or absence of detectable human papillomavirus DNA and HPV type in cervical carcinoma have yielded conflicting results.
OBJECTIVE: The objective of our study was to assess the prognostic significance of the presence of HPV DNA by exploring the relationship of HPV presence to the recurrence rate and clinical and histopathologic features of 92 patients with cervical carcinoma. In this report the preliminary results of a larger programme aimed to search for the prognostic factors in a fairly homogenous population of patients with early stage cervical carcinomas who underwent abdominal hysterectomy with pelvic lymphadenectomy as primary therapy, followed by postoperative adjuvant pelvic radiotherapy, are presented.
MATERIALS AND METHODS: Routinely processed formalin-fixed paraffin-embedded cervical carcinoma surgical specimens were examined for the presence of HPV DNA by in situ hybridization technique using mixed biotinylated probes to identify HPV types 6/11, 16/18 and 31/33/51 (Enzo Diagnostics, New York). Clinical data and histopathologic features of these patients were analyzed retrospectively to determine their relation to presence or absence of HPV DNA. All the patients were staged according to the postoperative TNM classification of UICC (1987) guidelines. In our case series the tumor was limited to cervix in 48 (52.5%) patients, while local extension to vagina and parametrial tissues was found in 10 (10.9%) and 34 (36.9%) patients, respectively. Pelvic lymph node involvement was found in 25 (27.2%) patients. During the follow up period (range, 2–87, mean, 35 months), recurrences were observed in 13 patients. Variables were compared by cross classification and statistical significance determined by χ^2 and Fisher's exact test.
RESULTS: HPV DNA was detected in 41 (44.6%) cervical carcinoma specimens. The prevalence rate of different HPV types was 37% (34) for HPV 16/18, 6.5% (6) for HPV 31/33/5, while HPV type 6/11 was detected only in one case of verrucous carcinoma. Recurrence rate was significantly higher in patients with HPV DNA negative cervical carcinomas (P = 0.02). Among the HPV DNA positive patients with cervical carcinoma the recurrence rate was 4.9% (2 cases), compared to 21.6% (11cases) for the HPV DNA negative group. Various clinical and histopathologic features of the patients with cervical carcinomas (tumor extent, grade, presence of regional lymph nodal metastases, number of positive lymph nodes, histologic subtype, maximum depth of cervical stromal invasion, maximal tumor diameter, longitudinal endocervical involvement, proportionate longitudinal endocervical involvement, tumor-cervix are quotient, maximal and minimal sagittal tumor area, parametrial involvement, vaginal involvement, lymph-vascular space invasion, peri- and intra-tumoral lymphocytic infiltration, surgical margins involvement, age) were also correlated with the presence of HPV DNA. No statistically significant association was found between the presence of HPV DNA and 18 other clinical and histopathologic variables. On the other hand recurrence rats were significantly related to tumor extent (P = 0.0001), presence of regional lymph nodal metastases (P = 0.0002), maximal tumor diameter(P = 0.014), proportionate longitudinal endocervical involvement (P = 0.007), maximal sagittal tumor area (P = 0.04), parametrial involvement (P = 0.0001), vaginal involvement (P = 0.03), and lympho-vascular space invasion (P = 0.0023).
CONCLUSIONS: The preliminary results of our study are consistent with the observations reported by several other authors. The presence of HPV DNA appeared to be related to recurrence rate and unrelated to various histopathologic characteristics of well-known prognostic significance. However, having in mind the limited number of cases studied, as well as a lower sensitivity of in situ hybridization technique, an analysis of larger series, as well as introducing a more sensitive technique like PCR assay, will be necessary to determine whether the presence of HPC DNA, status (presence, copy number and HPV type) should be considered when developing treatment strategies and assessing prognosis in patients with early stage cervical carcinomas.

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THE ROLE OF p53 AND HPV IN CERVICAL ADENOCARCINOMAS

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AIM: In this study, the role of HPV in the differantial diagnosis of cervical and endometrial adenocarcinomas was investigated. Furthermore, the presence of p53 protein in HPV positive cervical adenocarcinomas was searched to bring to ligth the relationship between HPV infections and p53 mutations.
METHOD:Sections from paraffin-embedded tissue blocks of 15 endometrial and 10 cervical adenocarcinoma cases were studied for the presence of HPV DNA sequences, using digoxygenin labelled HPV spesific DNA probes. Subtyping was performed on HPV-positive cases using type 16/18 and type 31/33 spesific DNA probes. In addition, mutant p53 protein was studied immunohistochemically in 10 cervical adenocarcinomas.
FINDINGS:HPV was not demostrated in any of endometrial adenocarcinomas. HPV DNA positivity was encountered in 30% (three cases) of cervical adenocarcinomas. These three cases were diagnosed as cervical mucinous adenocarcinomas and the histologic grades were II in all. The HPV type was 16/18 in one and 31/33 in the other two. Of the 10 cervical adenocarcinomas evaluated for p53 positivity the case with HPV type 16/18 sequence revealed a diffuse p53 positivity.

CONCLUSION:Because HPV was found to be negative in all cases of endometrial adenocarcinomas, it is thought to be a valuable factor in differential diagnosis. Of the cervical adenocarcinomas with HPV infection types 16,18,31, and 33 were identified as subtypes with high risk of oncogenic potential. The E6 protein of HPV type 16 disturbs the normal structure of the p53 gene of the host and causes malignant transformation of the cell.