

LARGE CELL NEUROENDOCRINE CARCINOMA OF THE UTERINE CERVIX: A CLINICOPATHOLOGIC STUDY OF FIVE CASES.

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Background: Cervical carcinoma in not developed countries is the first cause of death for woman's cancer, in Mexico 9,913 new cases were reported on 2000 whit 4,620 deaths in the same year. The large cell neuroendocrine carcinoma (LCNC) of the uterine cervix is a rare entity and few cases have been reported in the international literature. The LCNC have been described as aggressive tumor with "organoid" growth patterns (trabecular, insular and solid). The neoplastic cells are large whit vesicular nuclei, prominent nucleoli, atypical mitosis (3-12 per high power field) and necrosis.

Design: All the cases identified as small cell neuroendocrine or undifferentiated cervical carcinoma from a period from 1991 to 2003 were revised separately by three pathologist using the criteria described in the background. Immunohistochemical staining with cromogranin and synaptophysin were done. Clinical information was obtained from patient's charts.

Results: Five patients were selected using the previous mentioned criteria from a pool of 103 cases; the tumors where no consensus in the diagnosis were obtained were excluded. Patients age ranged in 43-61 years. One patient was stage IIA and four patients were stage IIB. Maximal dimensions were 8 cm. Two patients were treated with surgery, chemotherapy and radiotherapy, two patients with chemotherapy and radiotherapy without surgery and one patient was lost, this patient was associated whit adenocarcinoma of the colon treated whit surgery and chemotherapy. Immunohistochemistry study was done, all the cases were positive for cromogranin and synaptophysin. Disease progression was documented in three patients; two with cerebral metastasis, one with node metastasis; one patient had persistent disease. Two patients are alive whit disease 17 and 18 months after diagnosis and two die with disease 6 and 8 months after diagnosis.

Conclusions: large cell neuroendocrine carcinoma is a rare neoplasia frequently confused with small cell neuroendocrine carcinoma or undifferentiated carcinoma. The patients had a high grade tumors whit advanced disease, and despite aggressive treatment, the patients have had progression and early recurrence.

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SMALL AND LARGE CELL NEUROENDOCRINE CARCINOMAS OF THE UTERINE CERVIX. A REPORT OF 10 CASES

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BACKGROUND: Small (SCC) and large cell (LCC) neuroendocrine carcinomas of the uterine cervix are rare and highly aggressive neoplasms. Their association with the integration of human papilloma virus (HPV) DNA of the types 16 or 18 has been documented in many studies.

AIMS: The purpose of this study is to present the clinical, histopathological, immunohistochemical characteristics and

the presence of HPV DNA in ten cases of SCCs and LCCs of the uterine cervix.

METHODS: Seven patients with primary SCCs and three patients with LCCs of the uterine cervix were diagnosed at our department between 1989 and 2004. Clinical data were retrieved from the patients' files and included age, recurrence and survival. Routinely processed operative and/or biopsy specimens were used for immunohistochemical stains and hybridization procedures. Primary antibodies against several epithelial, neuroendocrine, mesenchymal and proliferative markers were included. The presence of HPV DNA was assessed by conventional in situ hybridization (ISH) using probes for HPV 16/18 and 31/33/51 and polymerase chain reaction (PCR), using three primers (MY09/11, GP5+/GP6+, E6). Six of the patients were surgically treated. Postoperatively, four received chemo and/or radiotherapy, two rejected further treatment and one patient was lost to follow-up. The other four patients underwent conservative treatment due to advanced disease.

RESULTS: The patients' age ranged from 25 to 71 years. Histologically, the tumors showed trabecular, nesting or a sheet-like pattern, with areas of necrosis and frequent mitoses. Their neuroendocrine nature was confirmed by diffuse positive immunostaining for neuron-specific enolase and low molecular weight cytokeratins. Focal positivity for chromogranin, synaptophysin and S100, together with pancytokeratin and EMA, was evident in the majority of the tumors. Their aggressive potential was confirmed by high Ki-67 proliferative index (50-90%). HPV types 16/18 were found in 4 tumors using ISH, and HPV 16 in additional 3, using PCR (type 16). 3 of the patients developed distant metastases and died 7-48 months after receiving partial or full treatment, while 6 are alive and without evidence of disease after 4-38 months.

CONCLUSIONS: SCCs and LCCs are highly aggressive neoplasms. However, early diagnosis and combined therapy may improve survival in some patients. Although mainly a morphologic diagnosis, immunohistochemistry may help in the diagnosis of SCC and LCC.

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EVALUATION OF TUMOUR NECROSIS FACTOR (TNF ALPHA) IN EUTOPIC & ECTOPIC ENDOMETRIA OF WOMEN WITH ENDOMETRIOSIS & ENDOMETRIUM OF HEALTHY WOMEN

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To achieve a successful implantation, in addition to adequate embryonic quality, an appropriate endometrium is mandatory. Some alterations have been found in the eutopic endometrium of women with endometriosis that could be responsible, at least in part, for the subfertility in these women.

The aim of this study is to compare eutopic & ectopic endometrium of women with endometriosis with that of healthy controls, regarding expression of TNF alpha using immunohistochemical staining. Also, to gain more information about the possible role of cytokine TNF alpha in autocrine & paracrine growth regulation of endometriosis.

The study included 30 patients having endometriosis & endometriotic cysts in the ovary (study group). Those patients were subjected to laparoscopy to confirm the diagnosis & obtain a biopsy of the endometriotic cyst, besides an endometrial biopsy. The control group included 30 healthy fertile women without endometriosis, they did laparoscopy for tubal ligation followed by endometrial biopsy. For both groups the biopsies obtained were immunohistochemically stained & examined for TNF alpha expression.