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Neuroendocrine Carcinoma of the Cervix: Clinical and Immunohistochemical Aspects of a Case Report

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Abstract **Case Report**

Gynecologic small cell neuroendocrine carcinomas are unusual, representing only 2% of cervical tumors. Given their rarity and the absence of randomized trials, the diagnostic and therapeutic management of these tumors is difficult and is essentially modeled on that of pulmonary neuroendocrine tumors. Like the latter, and despite multimodal treatment, their prognosis remains poor. We report a case in an 86-year-old patient, discovered at an advanced stage.

Keywords: Neuroendocrine Carcinoma, cervix, rare tumor.

INTRODUCTION

Gynecologic small cell neuroendocrine carcinomas are unusual, accounting for only 2% of cervical tumors [1]. They tend to be aggressive and are associated with a poorer prognosis, even when diagnosed at an early stage.

PATIENT AND OBSERVATION

This is Mrs. NA, a patient aged 86, 7 children all delivered vaginally, menopausal, without significant medical and surgical history. Admitted to the hospital for postmenopausal metrorrhagia evolving for 6 months.

The clinical examination finds a patient on the hemodynamic level.

The gynecological examination:

Speculm: presence of a large ulcerative budding mass taking up the entire cervix, measuring approximately 6 cm, bleeding on contact.

Vaginal examination: palpation of a large ulcerative budding mass, necrotic taking up the entire cervix, bleeding on contact.

Rectal examination: uterus of normal size, the parameters appear to be invaded bilaterally.

Breast examination: B-cup breasts, symmetrical, no skin changes, no palpable nodule. Free lymph node areas.

A cervical biopsy was performed, the pathological result of which returned in favor of a malignant tumor proliferation of a carcinomatous nature consisting of small or medium-sized cells, with moderately abundant eosinophilic cytoplasms with highly anisokaryotic nuclei strongly in mitosis. These cells are arranged in diffuse masses or sheets often centered by necrosis without notable glandular or malpighian differentiation. These carcinomatous masses are arranged within a moderately abundant fibrocollagenous stroma.

Immunohistochemical study was compatible with a differentiated and infiltrating small cell neurocarcinoma of the cervix.

Thoracic, abdominal and pelvic CT scan:

Bulky tumor mass of the cervix invading the vagina, the parametrium and the ureters, iliac, lumboaortic and supra and subclavicular lymphadenopathy left.

DISCUSSION

These tumors occur at a median age of 42 years (20-87) [2, 3] the age of our patient is 87 years, higher than the median age and equal to the upper age limit.

Neuroendocrine tumors develop mainly in the digestive tract and lungs, at the level of the cervix, they represent only 0.9 to 1.5% of cervical tumors which are generally predominated by squamous cell carcinoma [4]. They manifest clinically by menometrorrhagia and leukorrhea, exceptionally by a paraneoplastic syndrome (Cushing's syndrome, carcinoid syndrome, hypoglycemia, syndrome of inappropriate secretion of antidiuretic hormone, hypercalcemia) [5].

The diagnosis is based mainly on histological data and immunohistochemical study. Four types of neuroendocrine carcinoma are distinguished: typical carcinoid tumors, atypical carcinoid tumors, small cell carcinomas and so-called high-grade large cell carcinomas. Endocrine cells have a considerable diversity of size, argyrophilia, immunohistochemical staining and ultrastructure. They can be identified histochemically using Grimelius staining by highlighting argyrophilic or neurosecretory granules, immunohistochemically by positivity to NSE, chromogranin, synaptophysin and antibodies for gastrin, insulin or by ectopic production of adrenocorticotropic hormone (ACTH), ßMSH, serotonin, histamine and amyloidosis [6]. Small cell neuroendocrine carcinomas are the tumors with the worst prognosis. They have similarities with small cell carcinomas of the lung, as they have a high mitotic index, extensive necrosis, and massive lymphatic and vascular invasion [7].

They are distinguished from squamous cell carcinomas by their higher recurrence rates and the delay in their diagnosis due to the ineffectiveness of screening for this type of tumor by cervical smear. On the other hand, the association with "human papillomavirus (HPV)" 16 and 18 constitutes a common risk factor between the two carcinomas. Moreover, according to a study carried out in 2018 concerning the contribution of HPV on the formation of neuroendocrine tumors of the cervix on a series of 10,575 cases of invasive cervical tumors; HPV DNA was detected in 85.7% of cases of neuroendocrine tumor (HPV16 54.8% and HPV18 40.5%) [8].

In general, according to the recommendations published by Chan et al. in 2003 [9], surgical treatment is indicated mainly for NETs classified as I-IIA, measuring less than 4 cm, sometimes followed by adjuvant chemotherapy or radio-chemotherapy, while for I-IIA tumors measuring more than 4 cm, neoadjuvant chemotherapy is recommended before surgery. For neuroendocrine tumors of the cervix classified as IIb-IV, radiochemotherapy using the Hoskins protocol is desirable.

In case of metastatic disease or recurrence, chemotherapy, comprising either cisplatin and etoposide alone or alternating with VAC (vincristine, adriamycin and cyclophosphamide) chemotherapy is indicated. Prognostic factors are clinical stage, tumor size, presence and number of metastatic adenopathies, small cell histology and smoking. Clinical stage was the only predictive factor for survival, 80% in stage I/II, and 38% in stage III/IV. The most common sites of distant relapse are bone and lung (28%) rather than local relapse (13%) [10].

CONCLUSION

Despite the rarity of neuroendocrine carcinoma of the cervix, randomized trials are needed to facilitate diagnostic and therapeutic management.

Conflict of Interest: The authors declare no conflict of interest

Authors Contributions: All authors have read and approved the final version of the manuscript

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