Ovarian carcinosarcoma associated with serous tubal intraepithelial carcinoma

Carcinosarcoma ovárico asociado a carcinoma seroso intraepitelial tubárico

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ABSTRACT

Primary ovarian carcinosarcoma is a low incidence neoplasm that is usually diagnosed in advanced stages and has a poor prognosis. We report the case of a 64-year-old female patient with a 15 cm abdominopelvic tumor. Histological examination revealed a malignant ovarian biphasic malignancy associated with a serous tubal intraepithelial carcinoma, a finding that would be related to the pathogenesis of this neoplasm.

Key words: Carcinosarcoma, Mullerian Mixed Tumor, Mixed tumor, malignant, Ovarian cancer

INTRODUCTION

Carcinosarcoma is a mixed malignant neoplasm consisting of a high-grade carcinoma and a sarcoma. It represents approximately 2% of malignant ovarian neoplasms and usually occurs in postmenopausal women[1].

The diagnosis is usually made in advanced stages and the prognosis of patients is unfavorable. The origin of this neoplasm is not completely known, as well as its clinical and surgical management. We present a case of ovarian carcinosarcoma associated with serous tubal intraepithelial carcinoma (STICs) whose origin would be related to the epithelial-mesenchymal transition theory of the neoplasm.

CASE REPORT

A 64-year-old female patient, multiparous, with controlled arterial hypertension, with no other medical history of importance, with a one-month history of pelvic pain and vaginal bleeding. Physical examination revealed an abdominopelvic tumor of 15 cm in diameter, non-mobile. Pelvic ultrasound showed a 15 x 13 cm pelvic tumor that appeared to correspond to the uterus body, predominantly solid with anechogenic areas. No endometrium or right adnexa could be visualized. The lesion was classified as probable uterine sarcoma. The CT scan showed a mixed tumor mass that appeared to correspond to the right adnexa (Figure 1), and bilateral hydronephrosis. In the laboratory tests, the outstanding findings were a hemoglobin of 8 g/dL and decreased renal function.
A CT-guided percutaneous biopsy of the tumor was performed and the anatomopathologic result was reported as undifferentiated sarcoma, suspected to correspond to mesenchymal component of carcinosarcoma. With these findings the patient was scheduled for cytoreductive surgery. This surgery was performed during the time of the COVID-19 pandemic, so a freeze biopsy was not available. Cytoreduction was reported as optimal. Macroscopic examination of the uterus and adnexa revealed a solid, irregular, right adnexal tumor measuring 15 x 13 x 8 cm, which formed a body with the right lateral aspect of the uterus. Laminations showed that this tumor infiltrated the serosa and myometrium without compromising the uterine cavity. Histology showed mixed epithelial-mesenchymal malignant neoplastic proliferation consistent with carcinosarcoma and serous intraepithelial carcinoma was found in the tubal mucosa (Figure 2). The immunohistochemistry of this intraepithelial carcinoma was positive for p16 and p53 with a pattern of positivity similar to that found in ovarian carcinosarcoma. Other markers were also performed such as Ki67 which showed a proliferation index of 80%, WT1 positive; S100 was focal positive in the chondromatous component and CD10 in the endometrial stromal sarcoma component of the carcinosarcoma. Other markers such as ER and PR were negative.

The endometrium was atrophic and the cervix showed no histological alterations.

The patient presented with postoperative complications consisting of acute renal failure, multisystem failure, and death two months after surgery.

**Discussion**

Ovarian cancer is the fifth leading cause of cancer deaths among women and represents the most lethal neoplasm of the female reproductive system (2). This cancer originates mainly in older women. About half of the women diagnosed with ovarian cancer are over 60 years of age, as in the case presented.

Carcinosarcoma is a mixed neoplasm that usually presents a high-grade serous carcinoma as the epithelial component, although other epithelial strains such as endometrioid carcinoma or clear cell carcinoma can also be observed. Likewise, in the sarcomatous component an endometrioid stromal sarcoma, a leiomyosarcoma or other sarcomatous differentiation can be found, which can even be heterologous (coming from a tissue that is not usually present in the uterus), such as a chondrosarcoma or liposarcoma (3). The histology of the present case showed a carcinosarcoma with an epithelial component of high-grade serous carcinoma and a mixed mesenchymal component consisting of endometrial stromal sarcoma and chondrosarcoma (Figure 2B).

Molecular studies suggest that carcinosarcomas are predominantly monoclonal, i.e., the two...
types of neoplasm observed originate from the same cell. This theory is the most widely accepted because mutation of the tumor suppressor gene p53 has been found in both carcinoma and sarcoma components, which supports the theory of an epithelial-mesenchymal transition as the origin of this neoplasm. On the other hand, it is widely accepted that STICs is a precursor lesion of the high-grade serous carcinoma observed in the ovary. Therefore, the tubal mucosa would be the site of origin of this carcinoma⁴,⁵. The finding of serous intraepithelial carcinoma in the tubal mucosa of our case leads us to propose that the starting point of this neoplasm was the tubal epithelium with an serous intraepithelial carcinoma, which subsequently gave rise to a high-grade serous carcinoma in the ovary and underwent a mesenchymal epithelial transition. Finally, it gave rise to the carcinosarcoma observed in this patient, which overcame the ovarian capsule and infiltrated the uterine body, giving an image suggestive of a uterine tumor. This approach was supported in our case by the immunohistochemical study with p53 and p16.

Figure 2. HE microscopy, 40X. A) In the upper and right side of the image there is a biphasic neoplastic proliferation invading the myometrium located below and to the left. B) Heterologous zone of the sarcomatous component corresponding to chondrosarcoma. C) and D) Serous tubal intraepithelial carcinoma at 40X and 400X, respectively. E) P16 positive. F) P53 positive.
antibodies applied to both the intraepithelial tubal carcinoma and the ovarian carcinosarcoma. A similar pattern of labeling was observed, suggesting that there was a clonal relationship between both neoplasms, as has been found by other investigators.\(^6,7\)

Symptomatology and imaging findings are similar to other ovarian carcinomas, the most frequent symptoms being weight loss, pelvic pain and abdominal distension, among others.\(^8\). Due to the aggressive nature of this neoplasm, the average survival time is less than 24 months, and 5-year survival is only 15-30% of patients. Survival of women with this disease is worse than those with other histological subtypes of ovarian carcinoma, such as endometrioid and high-grade serous.\(^9\)

As a consequence of its low incidence, knowledge of its clinical and surgical treatment is limited, so it currently receives the same management as other ovarian carcinomas.\(^10\), with the combination of cytoreductive surgery and chemotherapy based on platinum and taxanes generally being offered to these patients.\(^11,12\). In the case of this patient, adjuvant chemotherapy could not be administered due to post-surgical complications.

In conclusion, ovarian carcinosarcoma is a malignant neoplasm of rare presentation and poor prognosis, whose treatment has not been established due to its low incidence. Therefore, it would be advisable to carry out research aimed at elucidating the specific characteristics of this neoplasm in order to provide a more adequate treatment.

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