Ovarian carcinosarcoma: Five histopathological features in one patient

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ABSTRACT

Introduction: Ovarian carcinosarcomas are rare gynecological cancers, accounting for less than 1% of all ovarian tumors. They are characterized by containing both high grade, malignant, epithelial and mesenchymal components. This unusual histology can represent a challenge both in terms of diagnosis and treatment. In previously reported cases and small series, patients were submitted to optimal cytoreductive surgery followed by platinum-based chemotherapy. Case Report: We report a clinical case describing a 71-year-old Caucasian woman diagnosed with an ovarian carcinosarcoma with uncommon histopathological features. She was submitted to surgery and systemic chemotherapy. Conclusion: Prospective studies are necessary to further clarify the best approach regarding the treatment of carcinosarcoma.

Keywords: Carcinosarcoma, Malignant mixed Müllerian tumors, Ovary

INTRODUCTION

Ovarian carcinosarcomas, also known as malignant mixed Müllerian tumors, are exceptionally rare gynecological cancers, accounting for less than 1% of all ovarian neoplasms [1]. Histologically, they are characterized by containing both high grade, malignant, epithelial and mesenchymal components [2]. The latter can be further divided into homologous (composed of tissue normally found in the ovary) or heterologous (composed of tissue normally found in extra-ovarian sites) [3].

Ovarian carcinosarcomas occur more frequently in postmenopausal women and generally have a highly aggressive behavior and an overall poor prognosis [4]. This unusual histology can represent a challenge both in terms of diagnosis and treatment.

Herein, we present a clinical case of a woman with an ovarian carcinosarcoma with uncommon histologic features and its subsequent management.

CASE REPORT

A 71-year-old Caucasian female, with prior history of arterial hypertension, presented at our hospital in October 2016, with diffuse abdominal pain with two months of evolution, increase in abdominal circumference, bilateral
leg oedema and a weight loss of 7.7%. During the physical examination, we found a hypogastric well-defined, round-shaped, regular and hard mass, with 4 cm in diameter; ascites; and bilateral leg edema extending knees. There were no abnormal gynecological findings. Workup, including an abdominopelvic computed tomography (CT) scan and magnetic resonance imaging (MRI) scan, documented a large and heterogenic retrouterine mass, with 15x12 cm in size, with extension to both adnexa, mesenteric fat thickness and ascites. The thoracic CT scan was normal. The patient’s pre-surgical CA-125 levels were 574 UI/L.

In November 2016, she was submitted to an exploratory midline laparotomy with close inspection of the pelvic and abdominal organs, hysterectomy, bilateral oophorectomy and omentectomy, without evidence of residual macroscopic disease.

Para-aortic biopsies and diaphragmatic cupola cytology were also performed. Pathological assessment described an ovarian carcinosarcoma containing five distinctive histologic patterns: high-grade serous carcinoma (Figure 1), squamous cell carcinoma (Figure 2), high grade undifferentiated sarcoma (Figure 3), pleomorphic rhabdomyosarcoma (Figure 4) and chondroblastic osteosarcoma (Figure 5). The tumor was staged according to the International Federation of Gynecology and Obstetrics (FIGO) as stage IIIB tumor. The cytology was positive for neoplastic cells. Post-surgical CA-125 levels were 8.5 UI/L.

The patient was treated with cisplatin 50 mg/m² and doxorubicin 50 mg/m² on D1, and ifosfamide 1.5 mg/m² on D1-D3, every three weeks, for six cycles, without significant toxicity. She has recently completed chemotherapy and is currently on follow-up. Her last laboratory results showed a CA-125 of 4.90 UI/L.

**DISCUSSION**

Since ovarian carcinosarcomas are rare, there is seldom literature regarding this entity. This case is even more uncommon, given the five different histological elements found within the same tumor.

Two components constitute a malignant epithelial differentiation: High-grade serous carcinoma, normally arising from the serous epithelial layer of the ovary, and frequently associated to TP53 mutations [5] and squamous cell carcinoma, a rare type of epithelial ovarian neoplasm with squamous differentiation.

The other three distinct histological components constitute a sarcomatous differentiation: high grade undifferentiated sarcoma, showing nuclear pleomorphism, high grade mitotic activity and tumor cell proliferation with atypical nuclear features and no identifiable line of differentiation (morphologically or immunohistochemically) (low power view H&E stain).
necrosis, without smooth muscle or endometrial stromal differentiation; chondroblastic osteosarcoma, referring to tissue of mesenchymal origin, characterized by atypical bone cell and chondroblastic cell proliferation; and pleomorphic rhabdomyosarcoma, a rare subtype of skeletal muscle phenotype.

Limited available evidence supports the role of maximal cytoreductive surgery in the prognostic improvement of these patients. The procedure should be similar to that of patients diagnosed with epithelial ovarian cancer and satisfy two goals: the removal of the entire visible tumor, ideally with an operatory specimen with tumor-free margins (R0), and tumor staging, with a careful inspection of the abdominal cavity to exclude peritoneal metastases.

The patient was submitted to optimal cytoreductive surgery followed by adjuvant chemotherapy. Regarding the treatment of ovarian carcinosarcomas, the American Society of Clinical Oncology recommends following the guidelines for the group of epithelial ovarian cancer, fallopian tube cancer and primary peritoneal cancer (briefly ovarian cancer, version 2.2017) [6]. However, the superiority of a chemotherapy regimen has not been established to date.

The management of said patients is mainly based on data from case reports, small prospective and retrospective series and extrapolation from ovarian cancers with different histological profiles. These tumors may present variable amounts of carcinomatous and sarcomatous components, which can occasionally be helpful with chemotherapy treatment decisions [7].

The rationale for using platinum-based regimens is based on their well-known effectiveness on epithelial ovarian tumors.

A literature review reports a higher overall response rate with the use of platinum-based chemotherapy regimens, compared with the non-platinum containing regimens (68% versus 23%, respectively) [8, 9].

Rauh-Haind et al. reported a response rate of 66% in patients with documented metastases treated with carboplatin and paclitaxel [10].

Other platinum-based regimens have shown different levels of efficacy. The activity of chemotherapeutic agents normally used to treat sarcomas, like doxorubicin or ifosfamide, can also be inferred, given the presence of a sarcomatous component in these neoplasms.

Crotzer et al. prospectively studied the combination of ifosfamide and cisplatin in the treatment of patients with metastatic carcinosarcoma. A complete response was achieved in seven out of eight patients [11].

Doxorubicin showed activity against metastatic carcinosarcoma, on a study by Plaxe et al., wherein the use of this drug in combination with cisplatin resulted in a complete response in 10 out of 13 patients [12].

Since our patient had a good performance status, based on the aforementioned data, she was treated with a platinum-based triplet combination: cisplatin, ifosfamide and doxorubicin, with no major toxicity observed.

**CONCLUSION**

Prospective studies are necessary to further clarify the best approach regarding the adjuvant treatment of ovarian carcinosarcoma. A more thorough comprehension of the underlying molecular basis and mechanisms of this heterogeneous disease could help us find more effective treatment strategies.

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Simão Pinto Torres – Substantial contributions to conception and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Marta Vaz Batista – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published
António Alves – Substantial contributions to conception and design, Revising it critically for important intellectual content, Final approval of the version to be published
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Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES