


CASE REPORT

A rare and distinct bilateral ovarian tumor: Carcinosarcoma

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Abstract

Carcinosarcomas are aggressive biphasic neoplasms composed of high-grade, malignant, epithelial, and mesenchymal elements. They usually occur in the uterus and rarely involve the ovaries. Only 10% of them are bilateral. Their diagnosis relies on histological examination coupled with immunohistochemistry.

KEYWORDS

carcinosarcoma, immunohistochemistry, ovary, pathology, tumor

1 | INTRODUCTION

Carcinosarcoma is a malignant mixed mesodermal neoplasm accounting for less than 1% of all ovarian tumors. It is an aggressive tumor, composed of both carcinomatous and mesenchymal components. Ovarian carcinosarcomas are about three times less prevalent than those of the uterus.¹ To the best of our knowledge, less than 400 cases of ovarian carcinosarcomas have been reported in the literature and only 10% of them are bilateral.^{2,3} In this paper, we report a new case of bilateral ovarian carcinosarcoma in a 52-year-old woman. In order to improve the awareness of this rare and distinct ovarian neoplasm, this study aimed to analyze its clinical and pathological features.

2 | CLINICAL HISTORY

A 52-year-old postmenopausal and nulliparous woman with a familial past medical history of gynecological cancer, presented with a four-month history of progressive diffuse abdominal pain, and distension. Physical examination revealed an abdominal swelling with perception of pelvic masses. Contrast-enhanced computed tomography

scan of the abdomen revealed bilateral variegated ovarian masses with heterogeneous enhancement (Figure 1A). The right ovarian mass measured 43 × 53 × 60 mm and the left ovarian mass measured 75 × 76 × 89 mm. The pre-operative serum level of cancer antigen 125 (CA125) was elevated to 67 U/ml (normal range: <35.0), whereas the carcinoembryonic antigen (CEA) and cancer antigen 19–9 (CA19-9) values were within the respective normal ranges. At laparotomy, the surgeon found bilateral ovarian masses and massive ascites. The left ovarian mass was adherent to the uterus. Intraoperative frozen section analysis of both ovarian masses concluded to a malignant neoplasm. The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection, para-aortic lymph nodal sampling, peritoneal biopsies, and total omentectomy. Grossly, both ovarian masses were ill defined, lobulated and friable with capsular rupture. The external surface showed numerous fragmented pieces, which were soft, encephaloid, gray, glistening with areas of hemorrhage (Figure 1B). On cut section, the tumors were solid, gray white showing variegated appearance with areas of hemorrhage and necrosis (Figure 1C). We did not notice residual ovarian tissue. Moreover, there was tumor invasion on the left side of the

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uterine corpus (Figure 1D). Histological examination of both ovarian masses showed a malignant biphasic tumor proliferation. The major part of the tumor was sarcomatous (Figure 2A) with the carcinomatous part well differentiated serous adenocarcinoma (Figure 2C). Heterologous elements including cartilage (Figure 2B) and adipose tissue (Figure 2D) were found in the tumor. Mitotic activity was frequent (8-9/10 high power field). We also noted the presence of tumor necrosis. Immunohistochemical study showed positive immunostaining of the sarcomatous component with desmin, smooth muscle actin and

calponin. Cytokeratin highlighted the epithelial component. Tumor cells did not show positive immunostaining with myogenin. Omentum, lymph nodes and peritoneal biopsy were negative for malignant cells. Cytological examination of the ascitic fluid did not reveal the presence of malignant cells. Based on the histopathological and immunohistochemical findings, the final diagnosis was that of bilateral ovarian carcinosarcoma classified as stage IIA according to the International Federation of Gynecology and Obstetrics (FIGO) 2014. The postoperative course was uneventful. The patient was planned for adjuvant

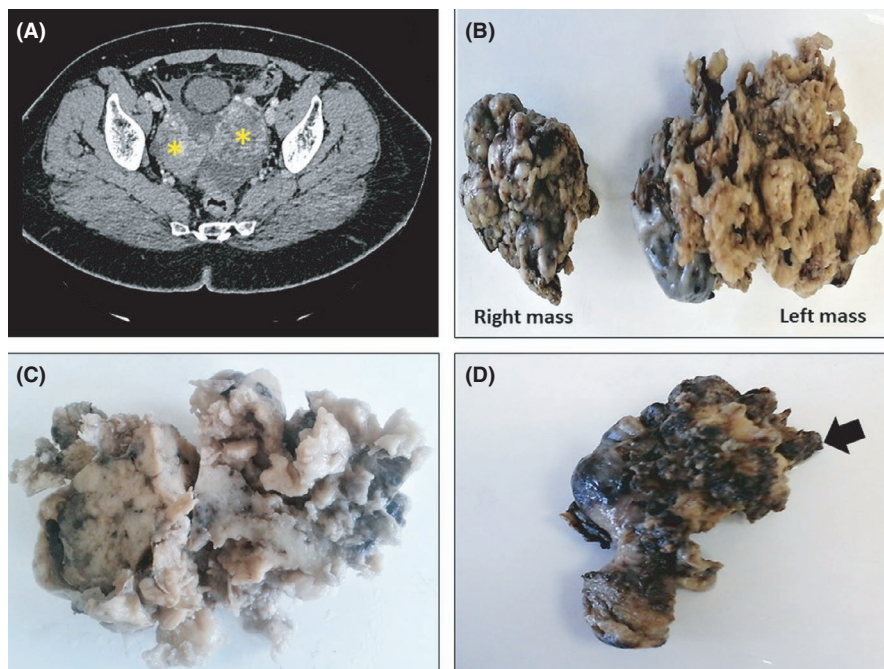


FIGURE 1 (A) Contrast-enhanced CT scan axial image showing bilateral variegated ovarian masses with heterogeneous enhancement. (B) Grossly, both ovarian masses were ill defined, lobulated and friable with capsular rupture. The external surface showed numerous fragmented pieces, which were soft, encephaloid, gray, glistening with areas of hemorrhage. (C) On cut section of the resected ovarian mass, the tumor was friable, whitish with foci of hemorrhage. (D) Total hysterectomy specimen showing tumor invasion of the uterine corpus (black arrow)

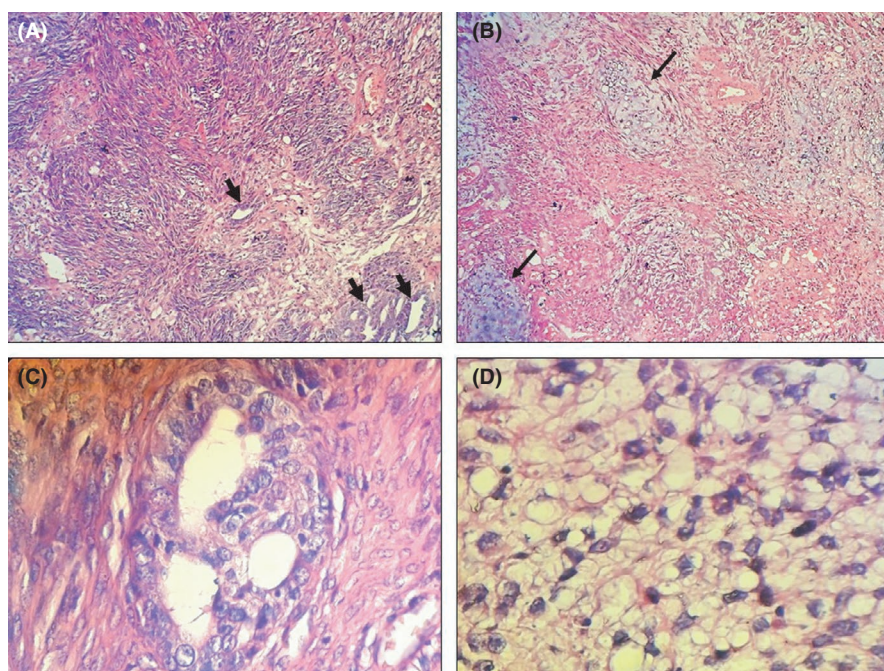


FIGURE 2 (A) Microscopically the ovarian tumor shows the presence of both epithelial (arrow) and stromal components, (Hematoxylin and eosin, magnification $\times 40$). (B) Heterologous elements including neoplastic cartilage (arrows) within a sarcomatous component, (Hematoxylin and eosin, magnification $\times 40$). (C) Epithelial component of the tumor (endometrioid carcinoma): glandular structures within a sarcomatous background. (Hematoxylin and eosin, magnification $\times 400$). (D) Heterologous elements including lipoblasts within the tumor proliferation, (Hematoxylin and eosin, magnification $\times 400$)

chemotherapy: six cycles of combination with paclitaxel and carboplatin. Currently, the patient is systematically monitored on an outpatient basis.

3 | DISCUSSION

Carcinosarcomas also called malignant mixed Mullerian tumors are highly aggressive biphasic neoplasms composed of high-grade, malignant, epithelial, and mesenchymal elements. They usually occur in the uterus and rarely involve the ovaries. Most patients with ovarian carcinosarcomas are postmenopausal of low parity and older than 60 years. Our patient was a 52-year-old, nulliparous, and postmenopausal woman. Only 10% of carcinosarcomas are bilateral as it was the case in our patient. Some studies reported that metastatic ovarian tumors were usually bilateral, and the bilaterality was a useful feature to differentiate primary from metastatic ovarian tumors.⁴ However, other authors reported that some common primary tumors such as serous and undifferentiated carcinomas are also known to involve bilateral ovaries in a high proportion of cases.⁵ In another study, most bilateral ovarian tumors on MR imaging were defined as serous carcinoma, mature teratoma, or metastasis. CA 125 serum level and maximum tumor diameter are useful indicators for the differentiation between metastasis and serous carcinoma or primary malignant ovarian tumors.⁶ The mechanisms behind bilaterality of ovarian carcinomas are not fully understood, as the two tumors could possibly represent two primary tumors, a primary tumor and a metastasis, or two metastases.⁷ Genomic studies of bilateral carcinomas have revealed a clonal association between the two tumors in each patient, including similarities in karyotype and copy number aberrations.⁸ Carcinosarcomas frequently present with widespread metastases at the time of diagnosis.⁹ The most common symptoms include abdominal pain, distension, nausea, vomiting, and weight loss.¹⁰ Our patient presented with a 4-month history of abdominal pain and distension. The pathogenesis of ovarian carcinosarcoma is still debated. The collision theory stipulates that the two components of the tumor are of different origin, whereas the combination theory suggests that the two components of the tumor derive from a common epithelial stem cell.¹¹ Some authors have reported an association between ovarian carcinosarcoma and pelvic irradiation.¹² Approximately 74%–90% of patients with ovarian carcinosarcoma will have an elevated CA-125 as it was the case of our patient.⁹ In one study, 80% of patients had elevated CA153 levels.¹³ The radiological features of ovarian carcinosarcomas are non-specific and are similar to ovarian epithelial neoplasms.¹³ There have been only scattered case studies that have described the imaging findings. Daimon

et al.¹⁴ reported a case of this tumor showing a multilocular mixed cystic-solid masses with a diameter of 27 cm, and the solid part of the tumor was hemorrhage. Uçar et al.¹⁵ reported a large solid, well-circumscribed mass of ovarian carcinosarcoma measuring 18 cm in the largest transverse diameter. Pankaj et al.¹⁶ showed a case of ovarian carcinosarcoma with multiloculated mixed cystic-solid mass and the size was 10 × 6.8 cm. One case reported by Vernadakis et al.¹⁷ showed a giant mass of 33 × 22 × 10 cm in size containing both solid and cystic elements. In the present case, ultrasonography and contrast-enhanced computed tomography scan of the abdomen revealed bilateral variegated ovarian masses with heterogeneous enhancement. Grossly, these tumors are large (mean size, 14 cm) and predominantly solid with frequent cystic degeneration and extensive hemorrhage and necrosis.¹⁸ Histologically, carcinosarcomas are composed of high-grade carcinoma and sarcoma. One or the other may predominate. In our case, the sarcomatous component predominated. Both components are distinct but are typically intermingled with one another. The carcinomatous component is most often a high-grade serous, endometrioid, or undifferentiated adenocarcinoma and rarely clear cell adenocarcinoma or squamous cell carcinoma.¹⁸ The sarcomatous elements are classified as homologous when the stromal component has a non-specific appearance or heterologous when rhabdomyosarcoma, chondrosarcoma (these being the most common), osteosarcoma, rarely liposarcoma or angiosarcoma are present. The presence of heterologous components can be confirmed by immunohistochemistry including desmin, myogenin and Myo D1 for rhabdomyosarcoma or S100 for chondrosarcoma.¹⁸ There is no existing consensus for the treatment of ovarian carcinosarcomas. However, the mainstay of treatment relies on optimal surgical cytoreduction followed by platinum-based chemotherapy. Combination chemotherapy with ifosfamide and cisplatin or taxol and carboplatin is favored. This results in improved progression-free survival according to large retrospective series.^{19,20} The prognosis of ovarian carcinosarcoma is poor with a median survival reported in the majority of the studies around 11 months.²¹ Patients with ovarian carcinosarcoma usually have advanced disease at the time of diagnosis, and about 75% of the cases present with widespread metastatic disease [stages III-IV] at the initial surgery. Ovarian carcinosarcoma is more aggressive than serous ovarian carcinoma with worse overall outcomes at any stage. The adverse prognostic factors of carcinosarcomas include the presence of extra-ovarian sarcomatous elements, the advanced stage and age, the suboptimal cytoreduction, the stromal predominant tumors and tumors with serous epithelial component.¹⁸

In conclusion, ovarian carcinosarcoma is a rare and distinct ovarian neoplasm with no specific clinical and imaging

features. Due to the rarity of this entity, determination of the best adjuvant therapy remains difficult and management recommendations have been made largely based on the experience collected from retrospective studies. The optimal management of this rare disease needs further studies with collaborative, prospective multi-institutional trials. Patients with carcinosarcomas often develop a recurrence quickly and have a poor prognosis. These results emphasize the need to recognize carcinosarcoma as a distinct entity that requires a different strategy in its management from other ovarian carcinomas, such as high-grade serous carcinoma. The present case is significant owing to the extreme rarity of this ovarian neoplasm which is also bilateral. Given their aggressive nature and poor prognosis, ovarian carcinosarcomas require careful follow-up after treatment. We must record such cases for future reference with regard to the treatment provided and the outcome achieved.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Dr Faten LIMAIEM prepared, organized, wrote, and edited all aspects of the manuscript. She performed the gross and microscopic evaluation of the pathology specimen. She prepared all of the histology figures in the manuscript. She read, edited, and approved the final version of the manuscript. All authors should have made substantial contributions to the manuscript. Dr Ahmed HALOUANI and Dr Khalil SAFFAR, participated in the conception and design of the study and the acquisition of data, analysis and interpretation of the data, Pr Saadia BOURAOUI participated in the drafting of the article and revising it critically for important intellectual content, the gross and microscopic evaluation of the pathology specimen. All authors participated in the final approval of the manuscript before its submission.

ETHICAL APPROVAL

All procedures performed were in accordance with the ethics standards. The examination was made in accordance with the approved principles.

CONSENT

Published with written consent of the patient.

DATA AVAILABILITY STATEMENT

In accordance with the DFG Guidelines on the Handling of Research Data, we will make all data available upon request.

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