

Primary peritoneal carcinosarcoma arising from the secondary Müllerian system: case report and literature review

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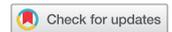
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Carcinosarcomas, also known as malignant mixed Müllerian tumours (MMMT), are aggressive neoplasms that are biphasic as they contain both carcinomatous and sarcomatous elements. Most commonly arising from the endometrium, extragenital carcinosarcomas are extremely rare and most cases develop from the peritoneum. The case is reported of a 70-year-old female who presented with abdominal pain and distention. On evaluation a large abdomino-pelvic mass with ascites was noted. She underwent complete cytoreductive surgery and the histopathology reported carcinosarcoma of primary peritoneal origin, of heterologous type arising *de novo* from the secondary Müllerian system with no synchronous or metachronous carcinomas or endometriosis. She declined adjuvant treatment and re-presented with disseminated abdominal disease and unfortunately succumbed to the disease within four months. Carcinosarcomas of the extragenital sites have been postulated to arise from pre-existing foci of endometriosis, Müllerian duct remnants, or the secondary Müllerian system, all of which are derivatives of the coelomic epithelium. They are extremely aggressive, and there is little knowledge concerning their natural history and scant data regarding their management.

Keywords: carcinosarcoma, malignant mixed Müllerian tumour, primary peritoneal

Introduction

Carcinosarcomas, also known as malignant mixed Müllerian tumours (MMMT), are aggressive neoplasms that are biphasic as they contain both carcinomatous and sarcomatous elements and can arise in almost every organ in the body. In the pelvis they usually arise from the uterus and ovaries. Extragenital carcinosarcomas are extremely rare and most cases develop from the peritoneum. Carcinosarcomas of the extragenital sites have been postulated to arise from pre-existing foci of endometriosis, Müllerian duct remnants, or the secondary Müllerian system, all of which are derivatives of coelomic epithelium.¹ These highly aggressive tumours are generally diagnosed in postmenopausal women, at late stages and carry a dismal prognosis.

Case report

A 70-year-old female was admitted with abdominal pain and distention of two months' duration. Abdominal examination revealed a 30 cm mass occupying all quadrants of the abdomen. The serum CA-125 level was 130 IU/ml and CEA was < 0.5 ng/ml. Radiologically, positron emission tomography/computerised tomography (PET/CT) revealed a 30 cm solid mass in the right anterior peritoneal cavity extending from pelvic to sub-hepatic region with a standardised uptake value (SUV) of 23.5. Mild ascites with nodular thickening of the omentum and peritoneum was noted with a few discrete sub-diaphragmatic lymph nodes.

Exploratory laparotomy disclosed loculated ascites with a cystic and solid mass 20 x 20 cm, which was adherent to the anterior abdominal, distal ileum, ascending colon, transverse colon and omentum (Figure 1). The uterus, bilateral tubes, ovaries and cervix were grossly normal. The tumour was resected, and a total

abdominal hysterectomy, bilateral salpingo-oophorectomy, right hemicolectomy, small bowel resection and anastomosis with ileostomy was performed. She had complete cytoreductive surgery.

Histologically, the tumour showed a picture of carcinosarcoma characterised by a mixture of malignant epithelial and sarcomatous elements (Figure 2). The section studied showed infiltrating malignant glands, which represented the epithelial component in a cellular stroma. The stroma in turn was composed of cells showing marked atypia and nuclear pleomorphism representing the mesenchymal component. Tumour infiltration was seen in the small and large intestines, omentum and appendix. There was minimal surface involvement of both ovaries. There was neither primary carcinosarcoma in the endometrium nor any foci of endometriosis in the resected specimens. On immunohistochemistry (IHC), the carcinoma component was positive for CK, vimentin, Pax-8, CK-7, ER and PR and negative for CK 20. The sarcoma component was positive for vimentin and CD 10 and negative for CK, SMA, Myf-4, S-100, DOG -1 and CD-34. Hence, a final diagnosis of primary peritoneal carcinosarcoma of heterologous type was made.

The patient declined adjuvant chemotherapy and re-presented to us two months following surgery with abdominal pain and generalised weakness. A computerised tomography (CT) scan revealed interval development of a large solid cystic mass extending from the perihepatic space to the right paracolic gutter; splenic surface, suprapancreatic, gastrocolic and colonic serosal deposits were also noted. She declined chemotherapy and opted for palliative care. She succumbed to the disease four months from the date of diagnosis.

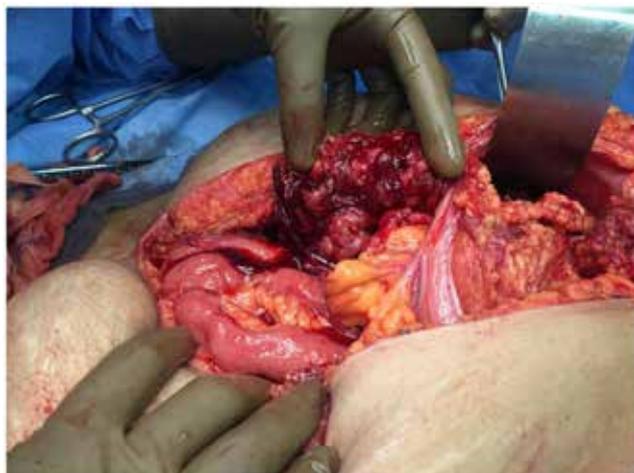


Figure 1: Intraoperative image showing a tumour adherent to the abdominal wall, omentum and intestines.

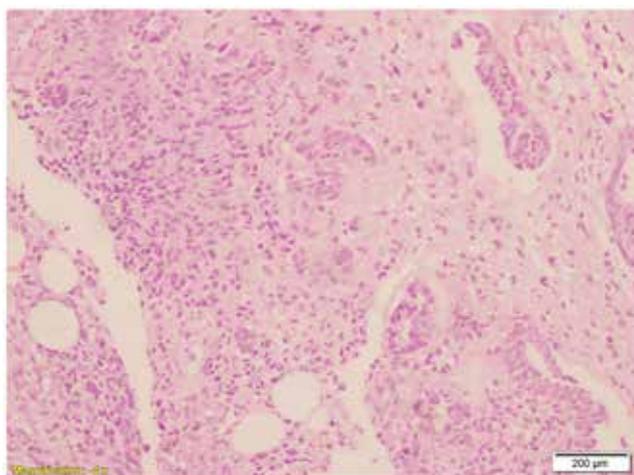


Figure 2: Histopathological image of primary peritoneal carcinosarcoma.

Discussion

Extragenital carcinosarcomas are rare, highly aggressive neoplasms that may arise from the pelvic or abdominal peritoneum as a part of the so-called secondary Müllerian system. Ober and Black in 1955² reported the first case of peritoneal carcinosarcoma occurring in the rectovaginal peritoneum. Carcinosarcomas comprise both carcinomatous and sarcomatous components and may be categorised as of homologous or heterologous type. Homologous elements are commonly endometrial stromal sarcoma or fibrosarcoma, while heterologous elements most frequently are rhabdomyosarcoma, chondrosarcoma, osteosarcoma or liposarcoma in order of frequency.³ They generally present in postmenopausal women, and usually with symptoms of abdominal pain and distention.

The aetiology and pathogenesis of primary peritoneal carcinosarcoma is unknown. There are a few theories postulated in the literature concerning the origin of this mysterious cancer. Its association with endometriosis has been suggested.¹ The occurrence of carcinosarcoma with previous radiation treatment exposure has also been proposed by Garamvoelgyi.⁴ Another

explanation is that poorly differentiated epithelial neoplasms such as ovarian or colonic carcinomas undergo secondary mesenchymal differentiation to give rise to the sarcomatous component of carcinosarcomas. This mirrors the conversion theory proposed by Sternberg *et al.*,⁵ which states that carcinosarcoma could be a consequence of metaplastic transformation of one neoplastic population to another. Extragenital carcinosarcomas can also arise *de novo* from the secondary Müllerian system, consisting of the abdominal and pelvic peritoneum as stated by Lauchlan in 1972.⁶ According to this theory, the secondary Müllerian components, due to their shared ancestry with the coelomic epithelium and the primary Müllerian system, have the potential to spontaneously differentiate into Müllerian components and thus give rise to Müllerian malignancies.⁷ There are two possibilities of genesis of carcinosarcoma from the secondary Müllerian system. The first is collision theory, which supports a biclonal origin. The other is combination theory, which postulates that a common stem cell precursor is the origin of both populations of cells. Molecular data published by Wada *et al.*⁸ suggest that most are combination tumours. Our case as described earlier fits into this category.

Due to the rarity of the disease, limited data regarding the management of peritoneal carcinosarcoma exist. The treatment options for carcinosarcoma include surgery combined with chemotherapy and/or radiotherapy. The mainstay of treatment is cytoreductive surgery; achieving complete cytoreduction at times can be difficult due to widespread metastatic disease at the time of presentation. Various chemotherapeutic agents have been tried, such as ifosfamide, paclitaxel, doxorubicin and carboplatin. Until we have clear guidelines regarding adjuvant treatment these tumours should be managed along the lines of high-grade serous carcinoma of the ovary.⁹ Currently prognostic factors for peritoneal carcinosarcoma are not well defined. Since these tumours are managed along similar lines to that of ovarian carcinosarcoma, the literature has shown that patients who had only homologous stromal elements fared better than those with the heterologous type.¹⁰

After a search of literature in English for similar cases with no coexistent carcinoma or endometriosis, we found 30 cases including ours, reviewed the literature and summarised it as follows. The mean age of this cohort was 61.2 (22–87) years. Lower abdominal pain and distention were the most common symptoms of presentation, noted in 60% of patients. Three patients underwent only diagnostic biopsy followed by chemotherapy while the rest had cytoreductive surgery as a part of their treatment. It was noted that the origin of the disease in 33.3% of patients was the abdominal peritoneum, 26.6% the pelvic peritoneum, 10% the omentum and 30% patients had multiple sites of involvement. Fifteen patients had chemotherapy and two had radiotherapy as their adjuvant treatment. Mean survival was 5.89 (0–21) months in this group. Of the 30 patients, 23 (76.6%) of the tumours were of heterologous type with chondrosarcoma and rhabdomyosarcoma as the common heterologous elements. The mean survival among patients who had homologous vs. heterologous components was 9.1 months (5–20) and 4.8 months (0–21) respectively, reflecting that those patients with homologous elements fared better than those with heterologous components, in agreement with the findings of Barakat *et al.*¹⁰

Conclusion

Carcinosarcomas of primary peritoneal origin are rare aggressive tumours with a poor prognosis. There is little knowledge about their natural history or behaviour and sparse data regarding their management. Synchronous or metachronous gynaecological tumours can often exist, hence a detailed examination of the genital tract must be made. Until more evidence is available, primary peritoneal carcinosarcomas should be managed similarly to high-grade epithelial ovarian cancer.

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