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Research Letter

A successfully treated primary peritoneal carcinosarcoma and serous carcinoma of stage IIIC rescued from hypovolemic shock due to tumor rupture

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Dear Editor,

A 63-year-old, para 2, menopausal woman presented with abdominal swelling, dizziness, constipation, nausea and vomiting of three weeks' duration. Her past history revealed fairly controlled type 2 diabetes mellitus, mild hypertension, and hyperlipidemia. She had an emergency right salpingo-oophorectomy for ovarian torsion in the first trimester of pregnancy 30 years ago and an appendectomy the following year.

During the clinical visit, an abdominal tumor was found. Ultrasonography showed small uterine myomas and a complex tumor. Computerized tomography also identified an irregular peritoneal tumor (10 cm) ruptured with hemoperitoneum (Fig. 1A). She then fainted and went into hypovolemic shock because of massive intra-abdominal bleeding. The patient underwent emergency laparotomy, and enlarged right external iliac and inguinal lymph nodes were confirmed. Intraoperatively, blood loss of about 4700 mL, a friable metastatic omental cake, peritoneal seeding, and left pelvic metastatic lymph nodes (3/16) were recorded. Her mildly enlarged uterus contained small uterine myomas of about 1–2 cm each. Examination of the left adnexa was normal without gross tumors. Optimal debulking surgery (total abdominal hysterectomy and left salpingo-oophorectomy with pelvic lymphadenectomy and omentectomy) was carried out. The result of serum tumor marker testing reported a CA-125 level of 1660 U/mL later. A small section of the fimbriated end of the left fallopian tube (1 mm) was microscopically interpreted as high-grade metastatic serous carcinoma. The "pelvic tumor" was identified as carcinosarcoma, primary or secondary, and the peritoneal tumors were found to be high-grade metastatic serous carcinoma (pT3 pN1 M0, Stage IIIC). Immunohistochemical staining of the tumor for CK7 (focal +), WT-1 (+), CK5/6 (focally weak +), calretinin (−), and desmin (−) was performed, and results indicating high-grade serous carcinoma 60% and high-grade non-specific sarcoma 40% including the heterologous element, chondrosarcoma <1% were obtained (Fig. 1B).

We carried out targeted high-throughput next-generation sequencing (NGS) for selected genes of the peritoneal carcinosarcoma formalin-fixed paraffin-embedded (FFPE) specimen [1]. DNA was extracted from the archival FFPE carcinosarcoma specimen which was processed with the NextSeq next-generation sequencing platform (Illumina Inc, San Diego, California) and achieved with an average of 10,000x deep sequencing coverage (or read depth). If ever a mutation is detected, it will be independently validated by Sanger sequencing.

The patient was subsequently treated with standard adjuvant chemotherapy [2] including paclitaxel (175 mg per square meter of body-surface area) and carboplatin (mg in a dose equivalent to an area under the curve of 6) and angiogenesis inhibition with bevacizumab (9 mg per kg of body weight) administered intravenously every 21 days for 6 cycles under dosage adjustment. On follow-up computerized tomography, a mass in the upper lobe of the left lung, 15 mm, was found and later proven to be caseating granulomatous inflammation of tuberculosis; this infection was treated appropriately. The patient remained asymptomatic and relatively well in remission at the time of this report, 24 months after initial management.

The pathogenetic mechanism of peritoneal carcinosarcoma has not been entirely clarified [3]. Primary peritoneal carcinosarcomas are rare, with the majority of the tumors occurring in the pelvic peritoneum; on fewer occasions, these tumors occur on the serosal (peritoneal) surface of the colon, retroperitoneal, anterolateral abdominal peritoneum, and omentum [4]. Patients with disease arising mostly from the pelvic peritoneum and cul-de-sac have

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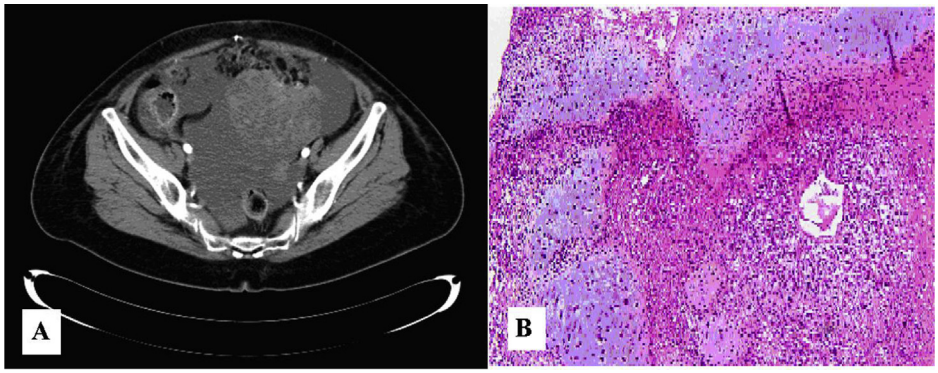

Fig. 1. (A) Computerized tomography showing an irregularly shaped 7.6 cm × 9.5 cm × 12.7 cm heterogeneous peritoneal tumor. (B) A high-grade serous carcinoma containing high-grade non-specific sarcomas including the heterologous element, chondrosarcoma, was microscopically determined. (H&E, X100).

Table 1
Results of the targeted next-generation sequencing (NGS) for selected genes of the peritoneal carcinosarcoma formalin-fixed paraffin-embedded specimen; in contrast to the frequency of mutations in endometrial carcinosarcoma from the literature.

Gene of interest	Frequency of mutations in the literature	Whole exome next-generation sequencing for selected genes of the peritoneal carcinosarcoma
TP53	Up to 91%[a]	Wild-type (831 hotspots)
PTEN	33.3%[b]	Wild-type (141 hotspots)
PIK3CA	28.6%[b]	Wild-type (86 hotspots)
ARID1A	23.8%[b]	Not checked
KRAS	16.7%[b]	Wild-type (47 hotspots)
CTNNB1	4.8%[b]	Wild-type (61 hotspots)
PPP2R1A	21.4%[b]	Not checked
BRAF	2.4%[b]	Wild-type (63 hotspots)
MET	Unknown	Wild-type (15 hotspots)
KIT	Unknown	Wild-type (123 hotspots)
RB1	11%[b]	Wild-type (17 hotspots)
PDGFRA	Unknown	Wild-type (24 hotspots)
ATM	44%–100% in ovarian cancer	Wild-type (23 hotspots)

[a] Reference 1.
[b] Found in endometrial carcinosarcoma (N = 42).

been found to have an average survival of 21.5 months [5]. Patients with a heterologous sarcomatous component have a poorer prognosis than those with a homologous component, although this difference is not statistically significant [3]. “Primary peritoneal high-grade serous carcinoma is very likely metastatic from serous tubal intraepithelial carcinoma (STIC)” [6]. Our patient had a microscopic lesion at the fimbriated end of her left fallopian tube, but it was approbated as metastatic, not primary, nor STIC. The uterus was normal and the endometrium was atrophic. The primary site of the tumor is thus unlikely to be the uterus, the right ovary or tube, which was removed 30 years ago. Because all of the peritoneal tumors identified were of high-grade metastatic serous carcinoma, the pelvic tumor was most likely a primary carcinosarcoma. In this patient's tumor, all of the thirteen relevant gynecologic cancer genes are all wild-type. The frequency of mutations in Table 1 was retrieved from the literature [1], and they were derived from the uterine carcinosarcoma testing. Currently, there is no NGS data for peritoneal carcinosarcoma in the literature. The purpose of NGS for this patient as stated above acts as both diagnostic to make a differential diagnosis of the origin of cancer and looking for actionable targets for possible molecular drug therapy in the future. The tumor contained less than 1% of a heterologous element (chondrosarcoma), indicating improved prognosis.

In conclusion, in cases of separate tumors at different locations, even in the case of emergency laparotomy as of our hypovolemic shock cancer patient, meticulous histological examination with serial sectioning may be necessary to identify the actual origin of the tumors.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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