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Research Letter

Stage III malignant mixed Müllerian tumor of the fallopian tube: A case of 5-year survival after optimal debulking and adjuvant chemotherapy with paclitaxel plus carboplatin

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Fallopian tube cancer is the least common gynecologic malignancy. The most common histology is high-grade serous adenocarcinoma. Sarcomas occur infrequently, and malignant mixed Müllerian tumors (MMMTs) are extremely rare [1]. Because of the rarity of MMMTs of the fallopian tube, information on optimal management is limited.

A number of studies suggest that cytoreductive surgery followed by platinum-based chemotherapy may be an effective treatment, but related data are quite limited [2–7].

Herein, we report a case who responded well after an optimal debulking operation and postoperative chemotherapy with paclitaxel and carboplatin. The diagnosis, prognosis, and treatment are discussed.

The patient was a 53-year-old, gravida 2, para 0, married Chinese woman with no history of hormone therapy or major systemic disease. She visited our clinic with the complaint of postmenopausal vaginal spotting for several months. Bimanual examination revealed a normal-sized uterus and a left adnexal mass of about 5 cm in size. Ultrasonography showed a left adnexal solid tumor measuring $6 \times 4 \times 3$ cm^3, with prominent central flow (resistance index was 0.4) (Fig. 1).

Laboratory tests, including a blood cell count, biochemistry, tumor marker (CA-125), and chest X-ray, were all within normal limits. Malignancy was highly suspected; an abdominopelvic computed tomography (CT) scan revealed a low-density lesion over the left adnexa (Fig. 2) with a small amount of ascites, as well as omental cake. There was no significant retroperitoneal lymphadenopathy.

The patient then underwent an exploratory laparotomy. Bilateral ovaries and left fallopian tube were grossly normal. The right-side tube was swollen like a sausage, about $8 \times 4 \times 4$ cm^3 in size. On cutting, a solid tumor arising from the tubal lumen and protruding outside the fimbriae was observed, which was apparently causing some adhesion to the posterior uterine wall. Confluent superficial tumor seeding over the pelvic peritoneum was noted, which was causing adhesion of the sigmoid colon to the peritoneum. Omental cake up to $17 \times 3 \times 2$ cm^3 was noted over the right-side omentum and low border. There were no enlarged para-aortic or pelvic lymph nodes. Subdiaphragm and liver surface were smooth by palpation. The patient underwent a total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph node dissection, para-aortic lymph node sampling, appendectomy, omentectomy, and maximum resection of intra-abdominal metastasis. Since there was no gross residual tumor, the procedure was designated as optimal debulking. The final pathological diagnosis was MMMT [mixed with endometrioid adenocarcinoma (50%) and undifferentiated high grade sarcoma] of the fimbriae (Figs. 3 and 4).

The patient's stage was assessed as FIGO (Federation of Gynecology and Obstetrics) stage IIIc. After the first postoperative week, the patient received six consecutive courses of chemotherapy, consisting of 175 mg/m^2 paclitaxel and AUC 5 carboplatin, administered at 3-week intervals. After the patient had completed this therapy, we followed up with pelvic examinations, CA-125 monitoring, periodic pelvic ultrasonographs, chest X-rays, and abdominopelvic CT scans. She is

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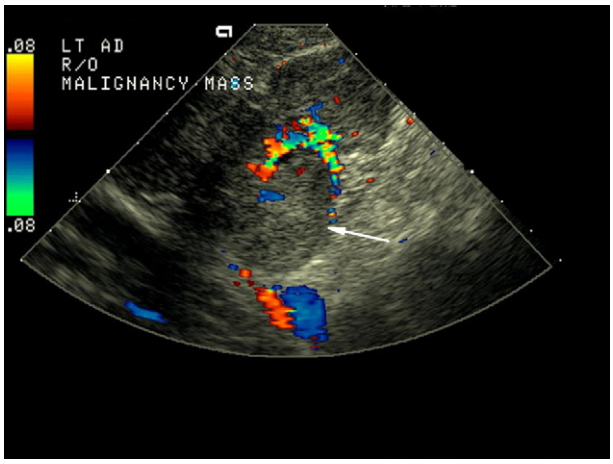

Fig. 1. Ultrasonography. The left adnexa was enlarged due to a tumor with a sausage-like appearance, approximately 6 × 4 × 3 cm^3 in size (white arrow). Prominent central flow was noted.

alive and disease free 5 years after receiving the debulking surgery and related treatment.

MMMTs, by definition, contain malignant epithelial and stromal elements. Endometrium is generally reported as the most common site of mixed Müllerian tumors, whereas the tube is the least common site [8–10]. MMMTs of the fallopian tube are extremely rare (0.1–0.5% of all gynecologic malignancies), with fewer than 54 cases reported in the related literature [11].

Because cancer of the fallopian tube is very uncommon, a high index of suspicion is necessary for its diagnosis. Most cases are postmenopausal women with nonspecific abdominal symptoms of pain or distension and/or vaginal spotting or bleeding. Usually, the diagnosis is not made until the time of surgery, with the most common preoperative diagnosis being ovarian malignancy. Staging procedures at laparotomy should include collection of ascites or washing cytology, thorough exploration of all peritoneal surfaces, hysterectomy, bilateral salpingo-oophorectomy, omentectomy, lymph node sampling,

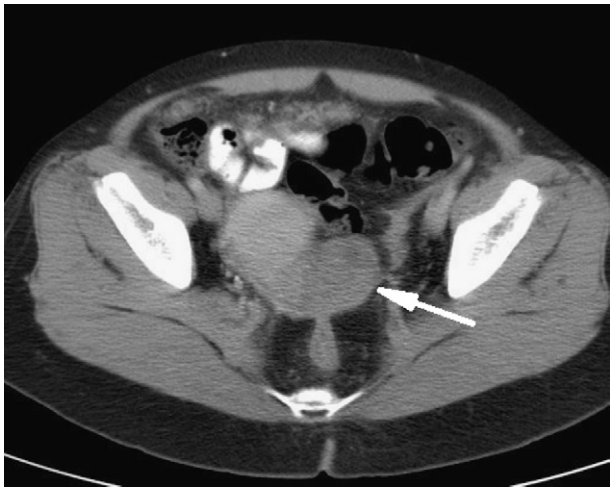

Fig. 2. Computed tomography: axial view. A low-density lesion can be seen at the left adnexa (white arrow), with a small amount of pelvic ascites.

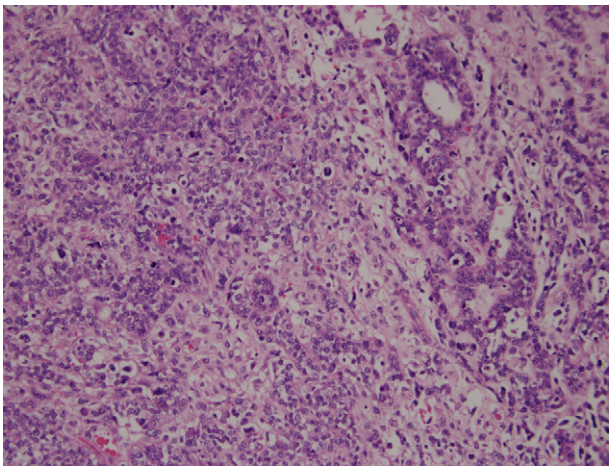

Fig. 3. Hematoxylin and eosin stain (200×). At the right upper part of the picture, poorly differentiated carcinoma was composed of highly atypical cells in a ribbon-like pattern. The undifferentiated sarcoma was predominantly in the center and lower portion of the picture.

and peritoneal biopsies, as necessary. As with ovarian cancer, a maximal cytoreductive effort should be emphasized [1]. The biology of the spreading of tubal cancer seems to resemble that of ovarian cancer closely, with intra-abdominal peritoneal surface spread. The most common metastatic sites are the ovaries, uterus, contralateral tube, and other peritoneal surfaces; pelvic and para-aortic lymph nodes are not as frequently involved, and distant metastasis is rare [12].

The prognosis for patients with MMMTs of the fallopian tube is usually poor. In one review, average survival was only 16.1 months [2]. To date, only three patients, who lived for more than 5 years without evidence of disease, have been reported [5]. However, all three of these patients were stage IA. Some reports in the literature indicate that the prognosis of MMMTs might be related to the sarcomatous components. Homologous MMMTs are thought to be associated with a better prognosis than heterologous MMMTs [5,13,14]. In our case, the sarcomatous component was undifferentiated, which was allocated to homologous MMMTs.

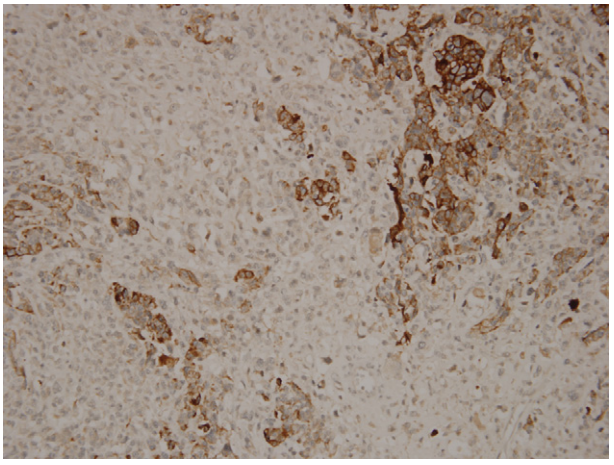

Fig. 4. IHC stain (200×) for cytokeratin AE1/AE3 antibodies. The carcinoma part is highlighted by the IHC stain for pancytokeratin. The sarcoma part is negative. IHC = immunohistochemical.

Due to the small number of cases, no definite conclusions regarding the best treatment strategies can be reached at this time. However, surgery is usually followed by postoperative adjuvant therapy. Platinum-based combination chemotherapy has been recommended on the basis of its effectiveness against gynecologic cancer, especially to mixed Müllerian tumors of the uterus and ovaries [2–7,15].

Studies in the related literature have shown that, for tubal MMMT, the most frequently used adjuvant chemotherapy is a combination of cyclophosphamide, doxorubicin, and cisplatin regimen [2–7]. Data on paclitaxel/platinum combination chemotherapy in patients with tubal MMMTs are limited. In one study, a patient with stage IV disease (malignant pleural effusion) underwent complete debulking surgery, followed by five courses of paclitaxel/platinum combination chemotherapy. Post-treatment CT showed no evidence of peritoneal implants. This proved that MMMTs of the fallopian tube show good response to a paclitaxel/platinum regimen. However, 8 months after the surgery, the patient was found to have a recurrent $15 \times 10\ cm^2$ cystic pelvic mass and died with the disease 12 months after the surgery [4]. Another case report confirmed that paclitaxel and carboplatin therapy reduced the size of a measurable tumor in a patient with MMMT of the fallopian tube effectively (shrunk by 60% after three courses of chemotherapy). This patient was classified as FIGO stage IIIc, and was alive/free of disease 28 months after the debulking surgery [16]. Our patient was also in stage IIIc. She has prolonged survival after an optimal debulking operation and six courses of paclitaxel/carboplatin combination chemotherapy. Our patient remains disease free after 5 years of regular follow-up at our outpatient department. To the best of our knowledge, she is the longest-surviving patient with advanced stage (stage III–IV) MMMT, as documented in the literature.

Although data about the best treatment strategies for MMMT are limited, our patient's excellent response to paclitaxel/platinum chemotherapy indicates that this regimen may be effective for the treatment of MMMT of the fallopian tube.

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