Malignant mixed müllerian tumor of primary mesenteric origin associated with a synchronous ovarian cancer: case report and literature review

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Summary

Malignant mixed müllerian tumor (MMMT) is a rare tumor in females and extragenital MMMT is even more so. We report a patient with MMMT primarily in the mesentery with synchronous ovarian cancer. In the English literature, 42 cases of extragenital MMMT have been reported other than the presented case, and this is only the second MMMT arising from the mesentery. Furthermore, among the cases reviewed, MMMTs tend to be associated with synchronous or metachronous colonic cancer or gynecologic tumors originating from the müllerian duct, including ovarian tumors, fallopian tube cancer, endometrial cancer, cervical cancer, and serous carcinoma of the peritoneum (14 out of 43 patients; 32.6%). The risk factors for MMMT include obesity, nulliparity, exogenous estrogen, and long-term tamoxifen use. The prognosis of MMMT is catastrophic and the treatment is based on the experience of those of uterine sarcomas, which is composed of operation, radiotherapy and chemotherapy.

Key words: Malignant mixed müllerian tumor; Mesentery; Ovarian cancer.

Introduction

Malignant mixed müllerian tumor (MMMT) is a rare tumor with both epithelial (carcinoma) and mesenchymal (sarcoma) components. MMMT is further classified into homologous or heterologous type according to the sarcomatous component. MMMTs generally originate in the organs of the müllerian duct: uterus, ovaries, fallopian tubes, cervix, and vagina in descending order of frequency and rarely occur in the extragenital area. To the best of our knowledge, 42 cases have been reported in the English literature with extragenital MMMTs and only one case is of primary mesenteric origin. Here, we reported a patient with MMMT arising from the mesentery along with synchronous right ovarian cancer.

Case Report

A 62-year-old, gravida 4, para 2, abortion 4, postmenopausal female presented with abdominal fullness and lower abdominal pain of more than two weeks duration. She was not on hormonal replacement therapy. Physical examination revealed a large, firm, nontender mass in the right lower abdomen and pelvis. Ultrasonography revealed a solid tumor with mixed internal components in the right side of the pelvis, measuring 11 cm in the largest diameter. Computed tomography confirmed a large tumor in the right side of the pelvis with compression and displacement of the uterus and the bladder to the left with ascites in the peritoneum (Figure 1). The serum CA125 level was 24.7 U/ml while lactate dehydrogenase (LDH) and CA 19-9 were high at 1041 IU/l and 48 U/ml, respectively. She was admitted to the Department of Obstetrics and Gynecology with the suspicion of right ovarian cancer.

At laparotomy, the uterus and the left adnexa were intact. There was a tumor measuring 11.5 × 10 × 7.5 cm arising from the mesentery involving the terminal ileum, the greater omentum, the right fallopian tube and the right ovary. Therefore, a right salpingo-oophorectomy, excision of the mesenteric tumor, and segmental resection of the ileum with end-to-end anastomosis were performed after consulting the Department of Surgery. Gross findings showed a well-capsulated tumor in the mesentery and the cut surfaces were yellow to white in color and soft in consistency on macroscopic observation. Areas of hemorrhage and necrosis were observed (Figure 2).

Histopathologic examination revealed sheets of spindle cells, which demonstrated positive reaction to vimentin (BioGenex, San Ramon, CA) and scattered islets of epithelial cells forming solid nests, which showed positive reaction to cytokeratin AE1/AE3 (Dako, Glostrup, Denmark) (Figure 3). Marked nuclear pleomorphism with frequent bizarre tumor giant cells and geographic tumor necrosis were also noted. A diagnosis of MMMT with homologous type was confirmed. Furthermore, there was a small nodular lesion composed of malignant glandular structures in bland-looking fibrous stroma in the right ovary and adenocarcinoma was ultimately diagnosed (Figure 4). The right fallopian tube was also invaded by the ovarian adenocarcinoma.

Unfortunately, tumor recurrence developed three months after the first operation. The patient received adjuvant chemotherapy with regimens composed of ifosfamide, carboplatin and etoposide. She is currently able to carry on normal activity six months after chemotherapy, though the best response condition is only stabilization of the disease.

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Table 1. — *Extragenital MMMTs in the English literature.*

Case	Year	Author	Age	Primary site	Tissue type	Associated tumor	Treatment	Prognosis
1	1955	Ober and Black	74	Pelvic peritoneum	Homologous	None	Operation RT	Death at 5 months
2	1967	Ferrie and Ross	47	Abdominal retroperitoneum	Homologous	Hydatidiform mole	Operation	Unknown
3	1977	Weisz-Carrington *et al.*	77	Cecal peritoneum	Heterologous	None	Operation	Death at 1 week, from pulmonary membolism
4	1982	Marchevsky *et al.*	40	Pelvic retroperitoneum	Homologous	None	Operation CT (adriamycin, cisplatin)	Death at 12 months
5	1983	Hermann and Tessler	72	Abdominal retroperitoneum	Heterologous	Ovarian serous papillary carcinoma, metachronous	Operation CT (adriamycin, cytoxan, DTIC, vincristine)	Deatg at 6 months
6	1984	Hasiuk *et al.*	77	Abdominal retroperitoneum	Heterologous	None	Biopsy	Death at 20 days
7	1986	Campins *et al.*	58	Pelvic peritoneum	Homologous	None	Operation	Unknown
8	1986	Chumas *et al.*	67	Rectosigmoid peritoneum	Homologous	Mucinous cystadenoma, metachronous	Operation CT	Death at 24 months
9	1986	Nguyen and Berendt	58	Greater omentum	Heterologous	None	Operation RT	Death at 6 months
10	1988	Chen and Wolk	58	Pelvic peritoneum	Homologous	Ovarian serous papillary adenocarcinoma, metachronous	Operation RT	Death at 11 months
11	1989	El-Jabbour *et al.*	76	Ascending colon peritoneum	Heterologous	Colonic adenocarcinoma, synchronous	Operation	Death at 14 days
12	1989	Ohno *et al.*	66	Descending, sigmoid colon peritoneum	Heterologous	None	Operation CT (cyclophosphamide)	Death at 21 months, from MI
13	1991	Garde and Jonesaza	65	Diaphragmatic peritoneum	Heterologous	Ovarian endometrioid adenocarcinoma, metachronous	Operation CT (cisplatin, adriamycin, ifosfamide)	Death at 6 months
14	1991	Solis *et al.*	54	Pelvic peritoneum	Heterologous	Serous carcinoma of the peritoneum, synchronous	Operation	Unknown
15	1993	Nimaroff *et al.*	82	Sigmoid colon peritoneum	Homologous	None	Operation CT (cisplatin, adriamycin, cytoxan)	Death at 5 months
16	1994	Choong *et al.*	63	Sigmoid colon peritoneum	Heterologous	None	Operation	Unknown
17	1994	Garamvoelgyi *et al.*	59	Pelvic peritoneum	Heterologous	Endometrial adenocarcinoma, metachronous	Operation CT (cisplatin, doxorubicin, ifosfamide)	Death at 24 months
18	1994	Garamvoelgyi *et al.*	64	Pelvic peritoneum	Homologous	Fallopian tube carcinoma in situ, synchronous	Operation CT (ifosfamide)	Death at 8 months
19	1994	Garamvoelgyi *et al.*	84	Retrouterine peritoneum	Heterologous	Colonic adenocarcinoma, synchronous	Operation	Death at 2 months, from heart disease
20	1994	Westra *et al.*	55	Spleen	Homologous	None	Operation	Unknown
21	1995	Mira *et al.*	62	Pelvic peritoneum	Heterologous	Ovarian endometrioid adenocarcinoma, synchronous	Operation	Survival for 28 months
22	1995	Mira *et al.*	83	Cecal peritoneum	Heterologous	None	Operation	Death at 6 months
23	1997	Rose *et al.*	57	Peritoneum	Homologous	None	Operation CT (cisplatin, ifosfamide)	Survival for 42 months
24	1997	Rose *et al.*	71	Peritoneum	Homologous	Uterine cervical adenocarcinoma, synchronous	Operation CT (cisplatin, ifosfamide)	Death at 6 months
25	1997	Rose *et al.*	67	Peritoneum	Homologous	None	Operation CT (cisplatin, ifosfamide)	Death at 3 months
26	1997	Ibanez-Manlapaz *et al.*	58	Abdominal peritoneum	Homologous	None	Operation CT (adriamycin, cisplatin)	Death at 20 months
27	1997	Ibanez-Manlapaz *et al.*	75	Pelvic peritoneum	Heterologous	None	Operation CT (ifosfamide)	Death at 6 months
28	1999	Arai *et al.*	56	Pelvic peritoneum	Heterologous	None	Operation	Unknown
29	2001	Shen *et al.*	67	Greater omentum	Heterologous	None	Operation	Survival for 8 months
30	2001	Shen *et al.*	33	Pelvic peritoneum	Heterologous	Endometrial adenocarcinoma, synchronous	Operation	Death at 12 months
31	2001	Shen *et al.*	66	Pelvic peritoneum	Heterologous	None	Operation	Death at 12 months
32	2001	Shen *et al.*	53	Retroperitoneum	Heterologous	None	Operation	Death at 1 month
33	2001	Shen *et al.*	40	Pelvis	Heterologous	Fallopian tube carcinoma, metachronous	Operation	Unknown
34	2001	Shintaku and Matsumoto	51	Pelvic peritoneum	Homologous	None	Operation CT (epirubicin, carboplatin)	Survival for 42 months
35	2002	Wei *et al.*	67	Omentum	Heterologous	None	Operation CT (cisplatin, pirarubicin, etoposide)	Liver metastasis after 8 months
36	2002	Sumathi *et al.*	77	Pelvic peritoneum	Heterologous	Benign endometrial polyp, synchronous	Operation	Death at 2 hours
37	2002	Sumathi *et al.*	87	Pelvic peritoneum	Heterologous	None	Operation	Unknown
38	2002	Dincer *et al.*	50	Pelvic peritoneum	Heterologous	None	Operation CT (anthracycline)	Unknown
39	2004	Booth *et al.*	71	Retroperitoneum	Homologous	None	Operation RT	Survival for 8 months
40	2005	Ko *et al.*	45	Pelvic peritoneum	Homologous	none	Operation RT CT (cisplatin, ifosfamide)	Disease free for 60 months
41	2005	Mikami *et al.*	53	Mesentery	Heterologous	Fallopian tube carcinoma, synchronous	Operation CT	Survival for 6 months
42	2005	Shaco-Levy	85	Omentum	Heterologous	Colonic adenocarcinoma, metachronous	Operation	Survival for 3 months
43	2006	Current case	62	Mesentery	Homologous	Ovarian adenocarcinofibroma, synchronous	Operation CT (ifosfamide, carboplatin, etoposide)	Survival for 6 months (still alive)

CT, Chemotherapy; RT, Radiotherapy; MI, Myocardial infarction.

Fig. 1

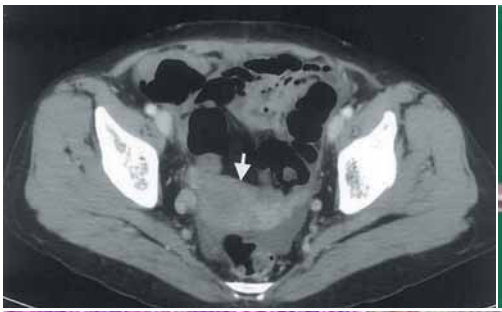

Fig. 2

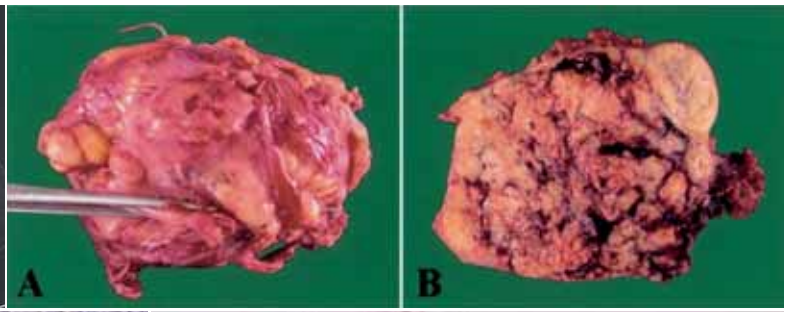

Fig. 3

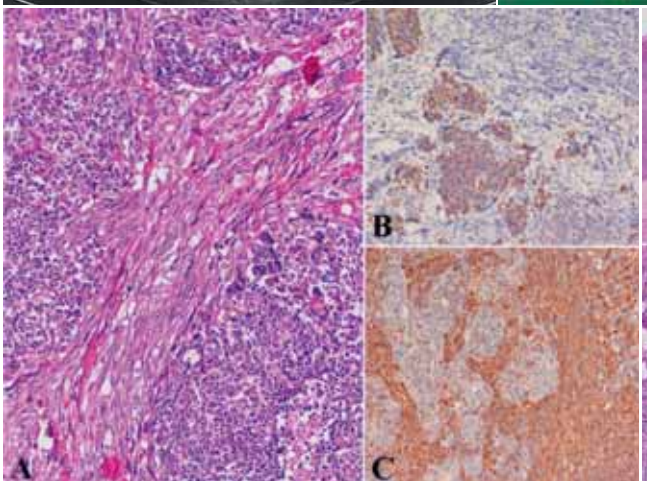

Fig. 4

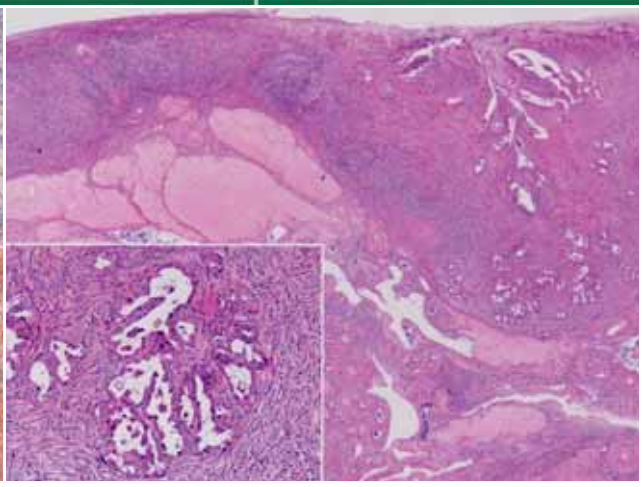

Figure 1. — Computed tomography revealed a large tumor in the right side of the pelvis (arrow head).
Figure 2A) — Gross examination shows a well-encapsulated tumor in the mesentery; 2B) The cut surface is yellow to white in color and soft in consistency, with hemorrhage and necrosis.
Figure 3A) — The tumor demonstrates a distinctly biphasic pattern including epithelial and sarcomatous elements (H&E stain, 100 x); 3B) Immunohistochemical study confirms the presence of epithelial immunostain (cytokeratin AE1/AE3, 100 x); 3C) mesenchymal components vimentin immunostain (original magnification, 100 x).
Figure 4. — Ovarian stroma shows a small nodular lesion which is composed of malignant glandular structures in bland-looking fibrous stroma (original magnification, 20 x; Insert, 100 x).

Discussion

MMMT generally arises in the female reproductive organs of the müllerian system, including the uterine, ovaries, fallopian tubes, cervix and vagina consecutively in frequency. The incidence of MMMT is extremely low, accounting for about 2-5% of all tumors arising from the uterine area and about 1% of those arising from other female reproductive organs. Extragenital origin is even rarer, which was first described by Ober and Black in 1955 [1]. In the English literature, there have been only 42 other cases reported until now [1-31]. It was previously described as occurring on peritoneal surfaces, including visceral peritoneum of the cecum, the rectosigmoid colon, the parietal peritoneum of the abdomen, pelvis and diaphragm, and the retroperitoneum. This is the second patient with MMMT originating primarily in the mesentery, which was first reported by Mikami *et al*. in 2005 [30].

Among all the cases reported, the majority were postmenopausal with a median age of 64 years (range 33-87 years). There were 14 out of 43 patients (32.6%) with synchronous or metachronous colon cancer (3 cases) or tumors of müllerian duct origin, including ovarian tumors (4 cases of cancer, including the present case, and 1 case of benign tumor), fallopian tube cancer (3 cases), endometrial tumors (2 cases of cancer and 1 case of benign polyp) and cervical cancer (1 case). This may indicate that either MMMTs could be found incidentally when treating gynecological tumors or the female genital organ should be checked carefully when managing MMMTs, especially at the time of surgery.

The risk factors for MMMT include obesity, nulliparity, and exogenous estrogen, similar to those for endometrial carcinoma [32]. Long-term use of tamoxifen, a synthetic nonsteroidal triphenyl antiestrogen with partial estrogenic effects serving as hormone therapy for breast cancer, is another risk factor for MMMT [33-36]. Curtis *et al*. [33] determined that the relative risk was 4.62 for MMMT and increased 8-fold for breast cancer patients surviving five years or longer. McCluggage *et al*. [34] reported 19 patients who had used tamoxifen for one to 15 years (median: 7.1 years) developed MMMT, and Kloos *et al*. [35] reported five patients who had used tamoxifen for five to 20 years (median: 9 years). Seven out of 43 patients (16.3%) altogether had endometriosis,

and Dincer *et al*. [27] also suggested that MMMT seems to be associated with endometriosis. It was reported that MMMT could occur following irradiation [5, 13, 17, 23, 37, 38]. Callister *et al*. [38] analyzed 300 patients with MMMT of the uterus and 32 patients (11%) had a history of previous pelvic irradiation. The median interval from radiotherapy to development of MMMT was 14 years (range 1-43); however, the role that radiotherapy plays in MMMT is still unclear.

The treatment of MMMT is generally based on the experience of treating sarcomas of the uterus. The prognosis is poor and survival is usually several months to less than a year, however, some patients could survive till 21 to 42 months with aggressive treatment comprising surgery, chemotherapy, and radiotherapy. Ohno *et al*. [12] reported a complete response to cyclophosphamide with survival of 21 months and Rose *et al*. [20] reported a regimen of ifosfamide and cisplatin attained a complete response with a survival of 42 months in one patient. Ko *et al*. [29] demonstrated the best result of a case with five years of disease-free survival after surgery followed by ifosfamide and cisplatin and then radiotherapy.

Conclusion

Extragenital MMMTs are rare and usually associated with female reproductive tumors. The female reproductive area should be well investigated during surgery of MMMTs or of gynecologic tumors. Although the prognosis is poor, long-term survival can be achieved with treatment by surgery, chemotherapy and radiotherapy in some cases.

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