Published in final edited form as:

Ann Diagn Pathol. 2011 August ; 15(4): 273–277. doi:10.1016/j.anndiagpath.2010.03.004.

Malignant mixed müllerian tumor of primary peritoneal origin*

Margaux Kanis, MD^a, Joshua P. Kesterson, MD^{b,*}, Stuti Shroff, MD, PhD^c, Shashikant Lele, MD^b, and Paulette Mhawech-Fauceglia, MD^c

^aSchool of Medicine, University at Buffalo, Buffalo, NY 14214, USA

^bDivision of Gynecologic Oncology, Roswell Park Cancer Institute, Buffalo, NY 14263, USA

^cDepartment of Pathology, Roswell Park Cancer Institute, Buffalo, NY 14263, USA

Abstract

The aim of this study was to describe 2 cases of primary peritoneal malignant mixed müllerian tumor (MMMT). Two patients with primary peritoneal MMMT were examined for their clinical and pathologic features. We describe 2 cases of primary peritoneal MMMT in which the carcinomatous and mesenchymal components were readily identifiable, predominantly involving the peritoneum, with no ovarian involvement. The peritoneum and ovaries, with their common embryologic origin, likely account for the peritoneum's ability to undergo a similar malignant transformation, with the resultant genesis of an MMMT of peritoneal origin.

Keywords

Malignant mixed müllerian tumor; Primary peritoneal

1. Introduction

Malignant mixed müllerian tumor (MMMT) is a rare neoplasm, consisting of carcinomatous (epithelial) and sarcomatous (mesenchymal) components. Malignant mixed müllerian tumors most commonly arise in the endometrium [1] and more infrequently in the ovaries [2,3], fallopian tube [4,5], cervix [6], and vagina [7]. Malignant mixed müllerian tumor arising from the extragenital structures is an exceptionally rare occurrence, with only about 2 dozen reported cases in the literature, primarily in the form of case reports [8,9]. Herein, we report 2 cases of primary peritoneal MMMT, including their clinical and pathologic features.

2. Case report

2.1. Case 1

An 80-year-old woman was referred to our institution for a pelvic mass and elevated cancer antigen-125 (CA-125). She initially presented with complaint of increased abdominal girth

*Conflict of Interest Statement: The authors have no conflicts of interest to declare.

*Corresponding author. Tel.: +1 716 845 8376; fax: +1 716 845 7608. mjkanis@gmail.com (M. Kanis), joshua.kesterson@roswellpark.org (J.P. Kesterson), sgshroff@buffalo.edu (S. Shroff), shashi.lele@roswellpark.org (S. Lele), paulette.mhawech-fauceglia@roswellpark.org (P. Mhawech-Fauceglia).

and left lower extremity swelling. A pelvic ultrasound showed an $8 \times 5 \times 5$ -cm pelvic mass as well as ascites. Her CA-125 was elevated at 253 U/mL. Ovarian cancer was suspected, and surgical therapy was initiated. At exploratory laparotomy, she had bloody ascites, omental caking, and a 15×10 -cm mass located in the cul-de-sac and involving the rectosigmoid colon. Both ovaries appeared normal. She underwent a hysterectomy, bilateral salpingo-oophorectomy, omentectomy, ureterolysis, and rectosigmoid resection with end colostomy formation. She recovered from her surgery and was discharged home 7 days after surgery. Postoperatively, she was offered platinum-based chemotherapy consisting of carboplatin, paclitaxel, and gemcitabine but declined and died of disease 4 months later.

2.2. Case 2

A 57-year-old woman presented with abdominal distension and early satiety. Her examination was consistent with ascites and omental caking. A CA-125 level was elevated at 193 U/mL. Ovarian malignancy was suspected, and she was taken to surgery for a planned cytoreduction. Intraoperatively, she had 6 L of bloody ascites and a $15 \times 20 \times 15$ -cm necrotic, fleshy mass in the pelvis, in addition to extensive peritoneal tumor implants. She underwent an exploratory laparotomy, hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and resection of peritoneal tumor, with optimal tumor debulking. The patient's postoperative course was uneventful, and she was discharged home 5 days after surgery. Postoperatively, she was started on adjuvant chemotherapy consisting of carboplatin (area under the curve of 6), paclitaxel (175 mg/m^2), and gemcitabine (800 mg/m^2) administered every 3 weeks. Besides requiring a change from paclitaxel to docetaxel (75 mg/m^2) after her second cycle due to paclitaxel side effects, she has tolerated therapy well. She is alive without evidence of disease at 4 months of follow-up and at present has completed 5 of a planned 6 cycles with a decrease in her CA-125 from 193 U/mL preoperatively to 15 U/mL.

2.3. Pathologic findings

2.3.1. Case 1—The specimen consisted of a hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and sigmoidectomy. Grossly, the omentum measured 21×17 cm and was completely involved by tumor. The cut surface of the tumor was pink, fleshy, and necrotic. The uterus weighed 360 g, and the uterine serosa revealed a necrotic mass measuring 15×6 cm that also involved the myometrium. The endometrial cavity was unremarkable. The left ovary measured 2.2×1 cm, and the right ovary was 2×1.5 cm. Both ovaries and fallopian tubes were unremarkable. The sigmoid colon measured 5.8×3.5 cm, and the attached mesenteric adipose tissue showed a firm 6.5-cm mass that involved the colonic wall. Microscopically, the omental tumor was composed of endometrioid adenocarcinoma admixed with heterologous sarcomatous stroma that included rhabdomyosarcoma (Fig. 1A, B). These rhabdomyoblasts are characterized by round cells with abundant eosinophilic cytoplasm, and they were highlighted by myogenin and myoD1 immunomarkers (Fig. 2A, B). Microscopically, the primary tumor was composed of a 70% carcinomatous component and a 30% sarcomatous component, with the metastases also having both components. In addition, tumor cells involved the uterine serosa, the colonic serosa, and the muscularis propria. Both ovaries and fallopian tubes were negative for tumor.

The diagnosis was carcinosarcoma (MMMT), heterologous type, and the tumor was staged as International Federation of Gynecology and Obstetrics stage IIIC.

2.3.2. Case 2—The specimen consisted of a hysterectomy with bilateral salpingo-oophorectomy, and omentectomy. Grossly, the omentum measured 23 × 5 cm, and it was completely occupied by a tumoral mass. The mass was partially cystic and partially solid. The cysts ranged in size from 0.2 to 2 cm, and they were filled by a mucinous-serous material. The solid areas were white, friable, and necrotic. The uterus was unremarkable. The ovaries measured 2.2 × 2 cm each, and they were unremarkable (Fig. 3A, B). Microscopically, the omentum was infiltrated by a tumor exhibiting 2 components, an epithelial component and a mesenchymal component. The epithelial component consisted of endometrioid adenocarcinoma. The sarcomatous component consisted of heterologous sarcomatous stroma including chondrosarcoma (Fig. 4A, B). The tumor was predominantly composed of the carcinoma component (90%) with only a small sarcomatous (10%) component. The metastases, however, had only a carcinoma component. The ovaries and fallopian tubes were unremarkable with no evidence of tumor. The histologic diagnosis was MMMT with heterologous elements, and it was staged as International Federation of Gynecology and Obstetrics stage IIIC.

3. Discussion

Extragenital MMMTs are extremely rare, with descriptions limited to case reports. They have been described to arise within the peritoneum and, less commonly, the omentum. The first reported case of MMMT arising from the peritoneum was by Ober and Black [10] more than 50 years ago. In the 40 years that followed, fewer than 20 well-documented cases have been reported [8].

Primary peritoneal MMMT affects elderly, postmenopausal women with a mean age of 68 years [11]. Patients most frequently present with nonspecific clinical symptoms including abdominal distention, pain, and/or a palpable mass [11], a similar presentation to that of patients with epithelial ovarian cancer and thus, most patients initially undergo an exploratory laparotomy. The diagnosis, then, is confirmed at time of pathologic examination. Most tumors are found in the pelvic peritoneum followed in frequency by the serosal surface of the colon, parietal posterior peritoneum, and omentum. To distinguish the tumor's origin as being from the peritoneum rather than the ovary, the Gynecologic Oncology Group has developed a list of criteria [12] such as follows:

1. both ovaries must be physiologically normal in size and appearance upon laparotomy,
2. involvement in the extraovarian sites must be greater than that on the surface of either ovary, and
3. microscopically, there is minimal ovarian involvement by the tumor.

Our 2 cases fulfilled these 3 criteria as mentioned above, and in both of our cases, despite extensive pelvic and abdominal tumor involvement, the ovaries were not involved by tumor. The exact pathogenesis of peritoneal MMMT is unknown. Originally, Ober and Black [10]

hypothesized that peritoneal MMMT may have its origins in endometriotic implants. The presence of extragenital müllerian duct remnants, serving as the site of origin in primary peritoneal MMMT, has also been proposed [13]. Recently, pathologic and murine studies have served to elucidate the potential genesis of MMMT. Although the exact pathogenesis of MMMT is unknown, the most readily accepted etiology describes MMMT as a carcinoma with sarcomatous differentiation [14,15]. Furthermore, the immunohistochemical profile of MMMT is similar to endometrial carcinoma, suggesting that the epithelial cell component is the “parent” of MMMT [16]. This theory is supported by in vivo studies in which MMMT cell lines, transplanted into nude mice, have shown mesenchymal differentiation of the epithelial cell component. Given the close embryological relationship to the müllerian ducts, the mesothelium of the pelvis and lower abdomen is considered a secondary müllerian system, thus, explaining the potential for peritoneal tissue to develop a carcinosarcoma.

Malignant mixed müllerian tumors of peritoneal origin are highly aggressive with associated poor outcomes in spite of initial surgery and cytotoxic therapy [8,11]. This may be in part explained by their advanced stage at presentation. Garamvoelgyi et al [8], in their review of 18 patients with peritoneal MMMT, reported a 14-month median postoperative survival time, with most patients dead of disease within 1 year. Long-term survivors are the exception. Ko et al [9] reported a case of primary peritoneal MMMT with a 60-month disease-free survival after cytoreductive surgery and ifosfamide (5 mg/m²) with cisplatin (75 mg/m² initially then 40 mg/m²) for 6 cycles followed by pelvic radiation. Ohno [17] reported an excellent tumor response with cyclophosphamide as evidenced by a prolonged disease-free interval.

Because of the rarity of peritoneal MMMT, there is no standardized treatment. Extrapolating data from ovarian carcinosarcoma would support platinum-based therapy [18]. Investigators have achieved median survival in excess of 2 years with platinum and taxane combination chemotherapy [3,19,20]. In an attempt to improve outcomes, we added gemcitabine to our patients’ regimens, as it has proven activity against sarcomas [21–23] and can be given in combination with carboplatin and paclitaxel [24].

We have reported 2 cases of an extremely rare entity in primary peritoneal MMMT. Both cases involved postmenopausal females, diagnosed at an advanced stage. The carcinomatous and mesenchymal components were readily identifiable, predominantly involving the peritoneum, with no ovarian involvement. The peritoneum and ovaries, with their common embryologic origin, likely account for the peritoneum’s ability to undergo a similar malignant transformation, with the resultant genesis of an MMMT of peritoneal origin.

References

1. Dictor M. Malignant mixed mesodermal tumor of the ovary: a report of 22 cases. *Obstet Gynecol.* 1985; 65:720–4. [PubMed: 2984621]
2. Rutledge TL, Gold MA, McMeekin DS, Huh WK, Powell MA, Lewin SN, et al. Carcinosarcoma of the ovary-a case series. *Gynecol Oncol.* 2006; 100:128–32. [PubMed: 16213011]
3. Silasi DA, Illuzzi JL, Kelly MG, Rutherford TJ, Mor G, Azodi M, et al. Carcinosarcoma of the ovary. *Int J Gynecol Cancer.* 2008; 18:22–9. [PubMed: 17451459]

4. Muntz HG, Rutgers JL, Tarraza HM, Fuller AF Jr. Carcinosarcomas and mixed mullerian tumors of the fallopian tube. *Gynecol Oncol.* 1989; 34:109–15. [PubMed: 2544489]
5. Weber AM, Hewett WF, Gajewski WH, Curry SL. Malignant mixed mullerian tumors of the fallopian tube. *Gynecol Oncol.* 1993; 50:239–43. [PubMed: 8397154]
6. Clement PB, Zubovits JT, Young RH, Scully RE. Malignant mullerian mixed tumors of the uterine cervix: a report of nine cases of a neoplasm with morphology often different from its counterpart in the corpus. *Int J Gynecol Pathol.* 1998; 17:211–22. [PubMed: 9656116]
7. Peters WA III, Kumar NB, Andersen WA, Morley GW. Primary sarcoma of the adult vagina: a clinicopathologic study. *Obstet Gynecol.* 1985; 65:699–704. [PubMed: 2984620]
8. Garamvoelgyi E, Guillou L, Gebhard S, Salmeron M, Seematter RJ, Hadji MH. Primary malignant mixed Mullerian tumor (metaplastic carcinoma) of the female peritoneum. A clinical, pathologic, and immunohistochemical study of three cases and a review of the literature. *Cancer.* 1994; 74:854–63. [PubMed: 7518735]
9. Ko ML, Jeng CJ, Huang SH, Shen J, Tzeng CR, Chen SC. Primary peritoneal carcinosarcoma (malignant mixed mullerian tumor): report of a case with five-year disease-free survival after surgery and chemoradiation and a review of literature. *Acta Oncol.* 2005; 44:756–60. [PubMed: 16227168]
10. Ober WB, Black MB. Neoplasms of the subcoelomic mesenchyme; report of two cases. *AMA Arch Pathol.* 1955; 59:698–705. [PubMed: 14375493]
11. Mikami M, Kuwabara Y, Tanaka K, Komiyama S, Ishikawa M, Hirose T. Malignant mixed mullerian tumor of primary mesenteric origin. *Int J Gynecol Cancer.* 2005; 15:1249–53. [PubMed: 16343225]
12. Bloss JD, Liao SY, Buller RE, Manetta A, Berman ML, McMeekin S, et al. Extraovarian peritoneal serous papillary carcinoma: a case-control retrospective comparison to papillary adenocarcinoma of the ovary. *Gynecol Oncol.* 1993; 50:347–51. [PubMed: 8406199]
13. Ferrie RK, Ross RC. Retroperitoneal mullerian carcinosarcoma. *Can Med Assoc J.* 1967; 97:1290–2. [PubMed: 6054929]
14. Costa MJ, Khan R, Judd R. Carcinoma (malignant mixed mullerian [mesodermal] tumor) of the uterus and ovary. Correlation of clinical, pathologic, and immunohistochemical features in 29 cases. *Arch Pathol Lab Med.* 1991; 115:583–90. [PubMed: 1710102]
15. de Brito PA, Silverberg SG, Orenstein JM. Carcinosarcoma (malignant mixed mullerian (mesodermal) tumor) of the female genital tract: immunohistochemical and ultrastructural analysis of 28 cases. *Hum Pathol.* 1993; 24:132–42. [PubMed: 7679366]
16. Meis JM, Lawrence WD. The immunohistochemical profile of malignant mixed mullerian tumor. Overlap with endometrial adeno-carcinoma. *Am J Clin Pathol.* 1990; 94:1–7. [PubMed: 1694389]
17. Ohno S, Kuwano H, Mori M, Sakata H, Mori A, Shinohara K. Malignant mixed mesodermal tumour of the peritoneum with a complete response to cyclophosphamide. *Eur J Surg Oncol.* 1989; 15:287–91. [PubMed: 2544465]
18. Tate Thigpen J, Blessing JA, DeGeest K, Look KY, Homesley HD. Cisplatin as initial chemotherapy in ovarian carcinosarcomas: a Gynecologic Oncology Group study. *Gynecol Oncol.* 2004; 93:336–9. [PubMed: 15099942]
19. Duska LR, Garrett A, Eltabbakh GH, Oliva E, Penson R, Fuller AF. Paclitaxel and platinum chemotherapy for malignant mixed mullerian tumors of the ovary. *Gynecol Oncol.* 2002; 85:459–63. [PubMed: 12051874]
20. Leiser AL, Chi DS, Ishill NM, Tew WP. Carcinosarcoma of the ovary treated with platinum and taxane: the memorial Sloan-Kettering Cancer Center experience. *Gynecol Oncol.* 2007; 105:657–61. [PubMed: 17395252]
21. Hensley ML, Blessing JA, Degeest K, Abulafia O, Rose PG, Homesley HD. Fixed-dose rate gemcitabine plus docetaxel as second-line therapy for metastatic uterine leiomyosarcoma: a Gynecologic Oncology Group phase II study. *Gynecol Oncol.* 2008; 109:323–8. [PubMed: 18394689]
22. Maki RG. Gemcitabine and docetaxel in metastatic sarcoma: past, present, and future. *Oncologist.* 2007; 12:999–1006. [PubMed: 17766660]

23. Maki RG, Wathen JK, Patel SR, Priebe DA, Okuno SH, Samuels B, et al. Randomized phase II study of gemcitabine and docetaxel compared with gemcitabine alone in patients with metastatic soft tissue sarcomas: results of sarcoma alliance for research through collaboration study 002 [corrected]. *J Clin Oncol*. 2007; 25:2755–63. [PubMed: 17602081]
24. du Bois A, Belau A, Wagner U, Pfisterer J, Schmalfeldt B, Richter B, et al. A phase II study of paclitaxel, carboplatin, and gemcitabine in previously untreated patients with epithelial ovarian cancer FIGO stage IC-IV (AGO-OVAR protocol OVAR-8). *Gynecol Oncol*. 2005; 96:444–51. [PubMed: 15661234]

Fig. 1.
(A) Microscopic examination. The first component consisted of a proliferation of neoplastic cribriform glands. (B) The second component is composed of sarcomatous stroma with a proliferation of rhabdomyoblasts that are characterized by round cells with ample eosinophilic cytoplasm and round nuclei and prominent nucleoli.

Fig. 2.
(A) Immunohistochemistry staining for MyoD1. (B) Immunohistochemistry staining for desmin antibodies highlights the rhabdomyoblasts which were strongly and diffusely positive for desmin with a cytoplasmic pattern.

Fig. 3.
 (A) Grossly, the omentum was completely replaced by a partially cystic and partially solid mass measuring 23×5 cm. (B) The uterus, bilateral ovaries, and fallopian tubes were normal, with no evidence of tumor.

Fig. 4. (A) At microscopic examination, the first component was that of endometrioid adenocarcinoma. (B) The second component was a sarcomatous stroma with heterologous elements including chondrosarcoma.