Malignant mixed Müllerian tumor of the fallopian tube: a case report

T. Watanabe[1], T. Sugino[2], S. Furukawa[1], S. Soeda[1], H. Nishiyama[1], K. Fujimori[1]

[1]Department of Obstetrics and Gynecology, [2]Department of Pathology, Fukushima Medical University School of Medicine, Fukushima (Japan)

Summary

Malignant mixed Müllerian tumor (MMMT) of the female genital tract is uncommon and extremely rare in the Fallopian tube. We describe a case of primary MMMT of the Fallopian tube with carcinomatous and heterologous mesenchymal components in a 60-year-old woman. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic and paraaortic lymph node dissection, and resection of intrapelvic metastases. The tumor formed a large polypoid mass within the right Fallopian tube and had penetrated the wall to the paraovarian space. Microscopic examination revealed two components of poorly differentiated adenocarcinoma and high-grade sarcoma with chondromatous differentiation. The patient received six courses of adjuvant chemotherapy with ifomide and cisplatin and is currently in remission. Although MMMT in the Fallopian tube shows poor prognosis, primary cytoreductive surgery with platinum-based combination chemotherapy may improve survival.

Key words: Malignant mixed Müllerian tumor; Fallopian tube; Heterologous element.

Introduction

Primary carcinomas of the Fallopian tube are rare, accounting for less than 2% of gynecological malignancies [1]. Adenocarcinoma is the most common histology in Fallopian tube malignancies [2], whereas sarcoma, particularly malignant mixed Müllerian tumor (MMMT), is extremely uncommon, with only about 70 cases reported in the English literature to date [3, 4]. Of these cases, approximately 30 cases displayed heterologous sarcomatous elements, such as rhabdomyosarcoma, chondrosarcoma and osteosarcoma [3, 5]. We report herein a case of MMMT in the Fallopian tube with heterologous chondrosarcomatous elements.

Case Report

A 60-year-old woman (gravida 2, para 2) presented complaining of abdominal enlargement and pain. She had a history of breast cancer with total mastectomy and axillary lymph node dissection at 36 years of age. Family history included the deaths of her mother and younger sister from ovarian cancer. Echography and computed tomography suggested the presence of a large mass in the right adnexal region. Serum levels of CA72-4 were mildly elevated. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic and paraaortic lymph node dissection, and resection of the intrapelvic metastasis.

Macroscopically, an 8 × 6 cm tumor was observed in the right adnexal region involving the Fallopian tube. The tumor was completely separated from the right ovary (Figure 1). The cut surface revealed a solid, polypoid mass with focal hemorrhage and necrosis within the lumen, penetrating the luminal wall to form a tumor mass (Figure 1). A peritoneal metastasis in the pouch of Douglas and small amount of ascites were observed.

Microscopically, the tumor comprised two elements (Figure 2a): adenocarcinoma forming irregular papillary and tubular structures, and spindle cell sarcoma resembling fibrosarcoma and focal heterologous mesenchymal malignancy with cartilaginous differentiation. Tumor within the lumen mostly comprised adenocarcinoma (Figure 2b), whereas the extraluminal tumor included sarcomatous elements with chondrosarcoma in addition to the epithelial tumor (Figure 2c, d). Transitional features from carcinoma to sarcoma were observed (Figure 2e). The final clinicopathological diagnosis was MMMT with heterologous chondrosarcoma arising in the Fallopian tube. The tumor was staged as FIGO IIc.

Postoperatively, serum levels of CA72-4 fell within normal ranges. The patient received six courses of adjuvant chemotherapy with ifomide and cisplatin, and as of the time of writing remains in remission.

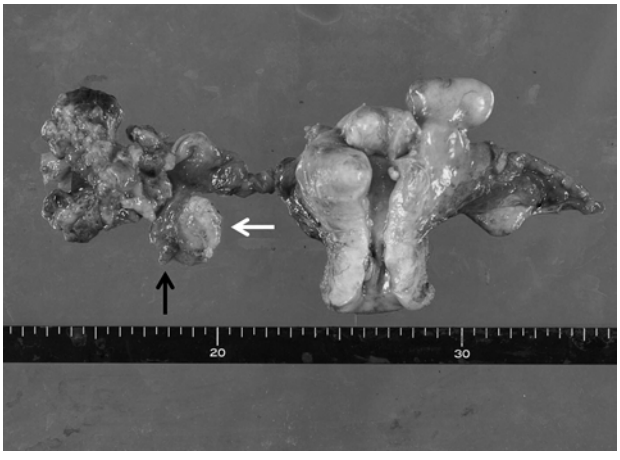

Figure 1. — Gross finding of the MMMT and uterus. The black arrow indicates the fimbriated end of the Fallopian tube. The white arrow shows the atrophic right ovary.

Revised manuscript accepted for publication September 2, 2011

Fig. 2a

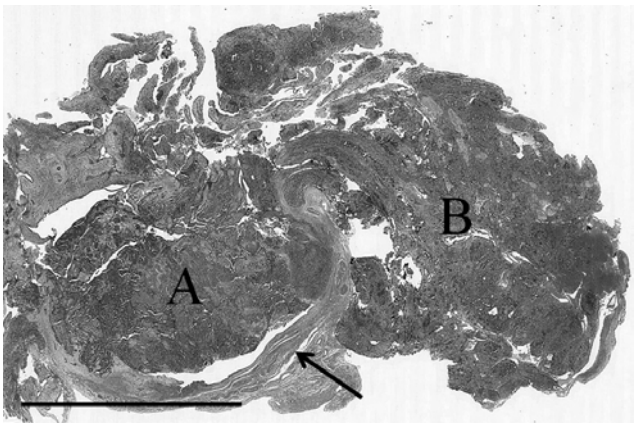

Fig. 2b

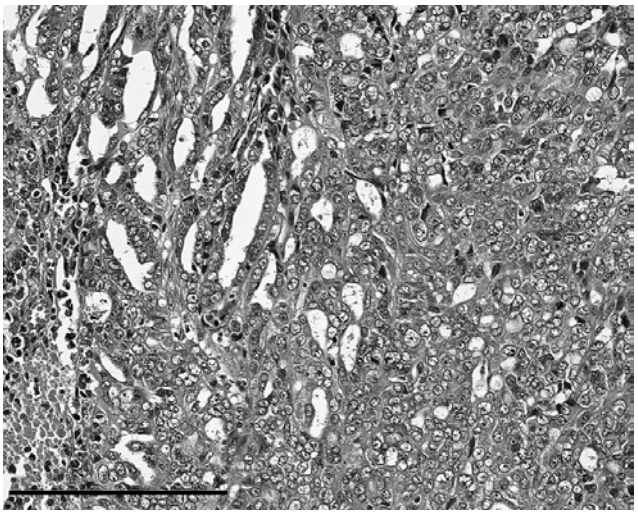

Fig. 2c

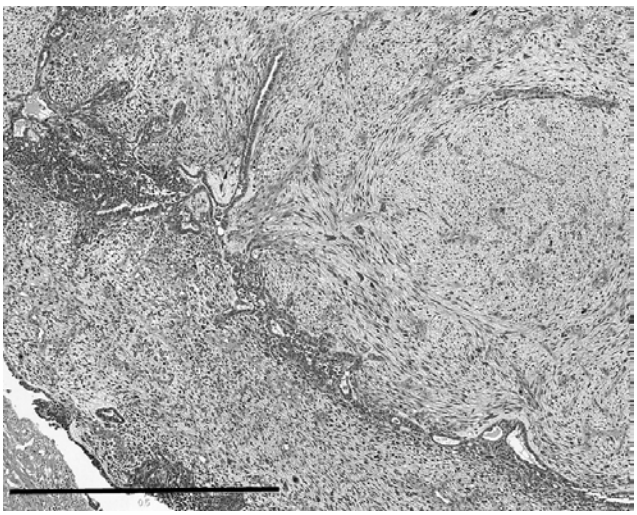

Fig. 2d

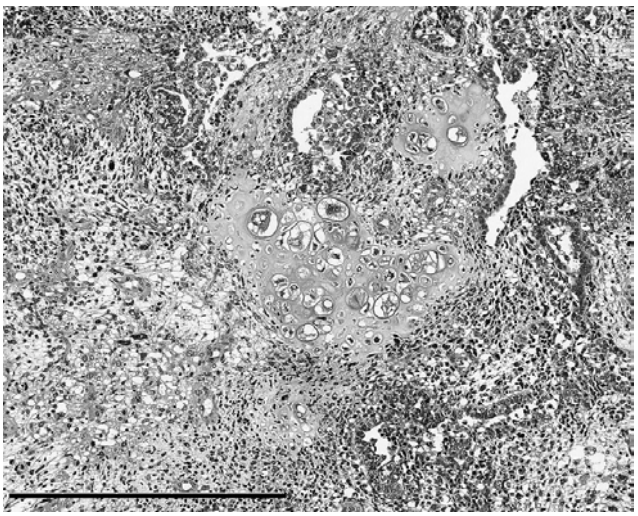

Fig. 2e

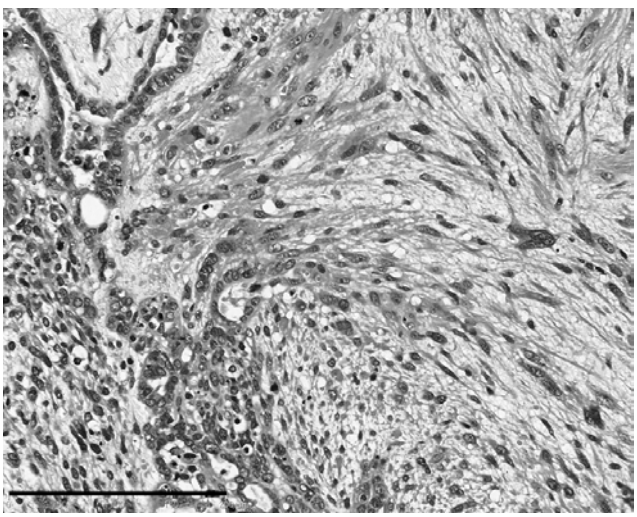

Figure 2. — Microscopic findings of the tumor. a) The tumor in the right Fallopian tube (A) has penetrated the wall (arrow) to the paraovarian region (B). b) The main component of tumor A is poorly differentiated adenocarcinoma. c) Tumor B comprises epithelial and mesenchymal components. d) The tumor has a heterologous element with chondromatous differentiation (*). e) Transition from carcinoma to sarcoma is seen. Bars: a, 10 mm; b, 0.2 mm; c, 1 mm; d, 0.5 mm. e, 0.2 mm. a-e: hematoxylin and eosin staining.

Discussion

The great majority of Fallopian tube tumors are diagnosed after surgery by anatomopathological evaluation based on the criteria established by Hu *et al*. and modified by Sedlis as follows: 1) main tumor in the tube and arising from the endosalpinx; 2) histological pattern reproducing the epithelium of the mucosa and usually showing a papillary pattern; 3) if the Fallopian tube wall is found to be totally invaded, a transition zone between benign and malignant epithelium should be able to be

demonstrated; and 4) the ovary and endometrium are either normal or contain less tumor than the tube [6, 7]. MMMT of the Fallopian tube grossly resembles Fallopian tube carcinoma, with a dilated tube that contains an intraluminal papillary mass.

The Fallopian tube is the least common site for MMMT in the female genital system, accounting for less than 4% of reported cases [8]. To date, only about 70 cases of primary MMMT of the Fallopian tube have been reported, including about 30 reports describing tumors with heterologous mesenchymal elements. Patients were in the fifth or sixth decade of life, with a mean age of 58 years [9]. Symptoms of MMMT in the Fallopian tube resemble those of Fallopian tube carcinoma. Patients present with abdominal pain, atypical genital bleeding or abdominal distension [8, 9]. A discrepancy between cytological abnormalities in cervical or endometrial smears and negative findings on colposcopy, cervical biopsy, and endometrial curettage or hysteroscopy could prompt further diagnostic exploration, but diagnosis is not usually made until the time of surgery [10].

Histologically, MMMT consists of both carcinomatous elements with predominantly glandular differentiation assuming an endometrioid, clear cell, papillary serous or rarely squamous pattern and sarcomatous elements. About half of the reported patients had well differentiated adenocarcinoma and the remaining half had poorly differentiated adenocarcinoma. The sarcomatous portions can exhibit differentiation towards mesenchymal tubal tissue layers such as smooth muscle or stroma and are therefore designated as consisting of homologous components. In contrast, the predominant presence of structures that are foreign to the Fallopian tube such as bone or non-smooth muscle fibers, cartilage and their polymorphic precursor cells lead to the classification of the heterologous component of the sarcomatous portion of MMMT.

Treatment for this disease is identical to that for epithelial ovarian cancer. Exploratory laparotomy is necessary to remove the primary tumor, stage the disease, and resect metastases. The overall 5-year survival rate for patients with tubal carcinoma is 44% [11]. However, the survival rate of MMMT is very poor, and most patients die of the disease within two years [9]. Extratubal spread is the most important prognostic factor for survival in adenocarcinoma of the Fallopian tube. The presence or absence of heterologous elements does not appear related to outcome. A single positive observation is the markedly better probability of survival for women with tumors confined to the muscularis [12].

Postoperatively, platinum-based combination chemotherapy has been performed for patients with MMMT of the Fallopian tube. VAC or CYVADIC therapy was also administered in several cases [9]. In a prospective phase II GOG study, overall 5-year survival was 62% for patients with Stage I or II uterine MMMT who received ifosfamide and cisplatin [13]. Complete response rate for paclitaxel and carboplatin therapy was 4/5 (80%) in patients with advanced or recurrent MMMT of the uterus [14]. Some papers have indicated that adjuvant radiation therapy can improve survival for patients with uterine MMMT [13]. Although some reports have described beneficial effects of platinum-based chemotherapy and radiotherapy for tubal MMMT, no standard adjuvant therapy has been devised due to the very small number of cases encountered.

Although the pathogenesis of MMMT is somewhat unclear, three main theories to explain the histological features found in this type of tumor have received strong support. First, the collision theory suggests that the carcinoma and sarcoma represent two independent neoplasms. Second, the combination theory suggests that both components are derived from a single stem cell that undergoes divergent differentiation early in the evolution of the tumor. Third, the composition theory suggests that the stromal component of MMMT is not truly neoplastic, but actually a reactive response to the presence of the malignant epithelial component. Recently, several lines of evidence have supported a monoclonal origin of MMMT with subsequent divergent differentiation. Immunohistochemical studies of MMMT have suggested a common epithelial origin [15]. Furthermore, the epithelial and mesenchymal components frequently share patterns of X-inactivation, allelic loss, and TP53 mutation [16-18] Clinically, the carcinoma component is more frequently found in metastatic deposits, leading most clinicians to approach this tumor as a poorly differentiated carcinoma rather than a sarcoma [15, 19] In the present case, a transition area from carcinoma to sarcoma was histologically observed in this tumor and may add weight to the combination theory.

In conclusion, the present report underlines a case of advanced Fallopian tube MMMT with heterologous chondrosarcoma elements. We performed optimal debulking surgery and ifosfamide and cisplatin therapy in this case, and the patient has remained free of disease as of more than one year after diagnosis. Although MMMT of the Fallopian tube is extremely aggressive and historically shows very poor prognosis, complete surgical resection with platinum-based combination chemotherapy may improve survival.

References

[1] Schink J.C., Lurain J.R.: "Rare gynecologic malignancies". *Curr. Opin. Obstet. Gynecol*., 1991, *3*, 78.

[2] Schneider C., Wight E., Perucchini D., Haller U., Fink D.: "Primary carcinoma of the fallopian tube. A report of 19 cases with literature review". *Eur. J. Gynaecol Oncol*., 2000, *21*, 578.

[3] Maitra R.N., Lee J., McConnell D.T., Kenwright D.N., Dady P.: "Malignant mixed mullerian tumour of the fallopian tube occurring in a patient with Peutz-Jegher's syndrome". *Aust. N.Z.J. Obstet. Gynaecol.,* 2004, *44,* 77.

[4] Kuroda N., Moriki T., Oguri H., Maeda N., Toi M., Miyazaki E. *et al*.: "Malignant müllerian mixed tumor (carcinosarcoma) of the fallopian tube: an immunohistochemical study of neoplastic cells". *APMIS,* 2005, *113,* 643.

[5] Costa M.J., Guinee D. Jr.: "CD34 immunohistochemistry in female genital tract carcinosarcoma (malignant mixed müllerian tumors) supports a dominant role of the carcinomatous component". *Appl. Immunohistochem. Mol. Morphol.,* 2000, *8,* 293.

[6] Hu C.Y., Taymor M.L., Hertig A.T.: "Primary carcinoma of the fallopian tube". *Am. J. Obstet. Gynecol*., 1950, *59,* 58.

[7] Sedilis A.: "Primary carcinoma of the fallopian tube". *Obstet. Gynecol. Surv*., 1961, *16,* 209.
[8] Hanjani P., Petersen R.O., Bonnell S.A.: "Malignant mixed Mullerian tumor of the fallopian tube. Report of a case and review of literature". *Gynecol. Oncol*., 1980, *9,* 381.
[9] Imachi M., Tsukamoto N., Shigematsu T., Vatanabe T., Uehira K., Amada S. *et al*.: "Malignant mixed Müllerian tumor of the fallopian tube: report of two cases and review of literature". *Gynecol. Oncol*., 1992, *47,* 114.
[10] Kinoshita M., Asano S., Yamashita M., Matsuda T.: "Mesodermal mixed tumor primary in the fallopian tube". *Gynecol. Oncol*., 1989, *32,* 331.
[11] Baekelandt M., Jorunn Nesbakken A., Kristensen G.B., Tropé C.G., Abeler V.M.: "Carcinoma of the fallopian tube". *Cancer,* 2000, *89,* 2076.
[12] Muntz H.G., Rutgers J.L., Tarraza H.M., Fuller A.F. Jr.: "Carcinosarcomas and mixed Müllerian tumors of the fallopian tube". *Gynecol. Oncol*., 1989, *34,* 109.
[13] Sutton G., Kauderer J., Carson L.F., Lentz S.S., Whitney C.W., Gallion H., Gynecologic Oncology Group: "Adjuvant ifosfamide and cisplatin in patients with completely resected Stage I or II carcinosarcomas (mixed mesodermal tumors) of the uterus: a Gynecologic Oncology Group study". *Gynecol. Oncol*., 2005, *96,* 630.
[14] Toyoshima M., Akahira J., Matsunaga G., Niikura H., Ito K., Yaegashi N., Tase T.: "Clinical experience with combination paclitaxel and carboplatin therapy for advanced or recurrent carcinosarcoma of the uterus". *Gynecol. Oncol*., 2004, *94*, 774.
[15] Bitterman P., Chun B., Kurman R.J.: "The significance of epithelial differentiation in mixed mesodermal tumors of the uterus. A clinicopathologic and immunohistochemical study". *Am. J. Surg. Pathol*., 1990, *14,* 317.
[16] Wada H., Enomoto T., Fujita M., Yoshino K. *et al*.: "Molecular evidence that most but not all carcinosarcomas of the uterus are combination tumors". *Cancer Res*., 1997, *57*, 5379.
[17] Kounelis S., Jones M.W., Papadaki H., Bakker A., Swalsky P., Finkelstein S.D.: "Carcinosarcomas (malignant mixed mullerian tumors) of the female genital tract: comparative molecular analysis of epithelial and mesenchymal components". *Hum. Pathol*., 1998, *29*, 82.
[18] Fujii H., Yoshida M., Gong Z.X., Matzumoto T., Hamano Y., Fukunaga M. *et al*.: "Frequent genetic heterogeneity in the clonal evolution of gynecological carcinosarcoma and its influence on phenotypic diversity". *Cancer Res*., 2000, *60,* 114.
[19] Silverberg S.G., Major F.J., Blessing J.A., Fetter B., Askin F.B., Liao S.Y. Miller A. *et al*.: "Carcinosarcoma (malignant mixed mesodermal tumor) of the uterus. A Gynecologic Oncology Group pathologic study of 203 cases". *Int. J. Gynecol. Pathol*., 1990, *9,* 1.

Address reprint requests to:
T. WATANABE, M.D., Ph.D.
Department of Obstetrics and Gynecology
Fukushima Medical University
School of Medicine
Fukushima 960-1295 (Japan)
e-mail: t-wata@fmu.ac.jp