Malignant mixed Müllerian tumor with heterologous component arising in the fallopian tube - a case report

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Summary

Primary malignant mixed Müllerian tumors (MMMTs) of the fallopian tube are rarities in gynecologic oncology with only 26 cases of MMMTs with a heterologous component reported thus far. We report a case of FIGO Stage II primary MMMT of the fallopian tube with a heterologous tumor portion in an 80-year-old woman presenting with abdominal discomfort at the time of primary diagnosis. After performance of total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy follow-up examination three months postoperatively did not show signs of disease recurrence. The patient finally presented six months after the initial diagnosis with extensive intraabdominal metastasis and died several days thereafter. The present report supports the aggressive nature of these neoplasms. The efficacy of chemotherapy and radiation remains to be defined in future studies.

Key words: Malignant mixed Muellerian tumor; Fallopian tube; Histogenesis.

Introduction

Primary neoplasms of the fallopian tube are uncommon tumor entities and account for less than one percent of all primary cancers of the female genital tract [1-3]. Compared to tubal adenocarcinomas, primary malignant mixed Müllerian tumors (MMMTs) arising in the fallopian tube are exceedingly rare malignancies with only 72 cases reported in the medical literature to date [4, 5]. MMMTs consist of both carcinomatous components with predominantly glandular differentiation assuming an endometrioid, clear cell, papillary serous or rarely squamous pattern and sarcomatous tumor elements [1, 6]. 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 fibres, cartilage and their polymorphic precursor cells lead to the classification of a heterologous component of the sarcomatous portion of MMMTs. To our knowledge, only 26 cases of primary tubal MMMTs with heterologous components have been reported thus far [4, 7]. We present a case of Stage II primary MMMT of the fallopian tube with extensive dedifferentiation of the sarcomatous portion resembling a heterologous component of the tumor.

Case Report

An 81-year-old (gravida 2 para 0) female of Caucasian origin presented with lower abdominal discomfort and bloating. She had a known history of stage I breast cancer with breast conserving surgery following whole breast irradiation and four years of anti-hormonal therapy with tamoxifen and NYHA grade II heart insufficiency. Regular follow-up examinations such as mammograms, pelvic ultrasound examinations, cervical smears and routine laboratory tests had been normal in recent years. At presentation in July 2005, vaginal ultrasound and computer tomography (CT) of the abdomen revealed an inhomogenous 10 x 8 x 6 cm solid right adnexal mass without signs of infiltration in surrounding pelvic structures (Figures 1A and B). CEA and CA-125 ranged within normal limits. At the time of operation, the tumor appeared as a solid, livid-grey mass originating from the right fallopian tube with loose adherence to the terminal ileum (Figure 2). There was no sign of peritoneal metastasis, gross infiltration of surrounding anatomical structures or ascites or peritoneal fluid in the pouch of Douglas. A frozen section was performed with the preliminary diagnosis of carcinosarcoma of unknown origin. The patient then underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy and infracolic omentectomy. Her postoperative course was normal and she was discharged seven days after surgery. The patient did not receive further adjuvant therapies due the advanced age and concomitant internal diseases. Follow-up examinations three months later did not show any signs of disease recurrence. However, six months postoperatively, the patient returned due to abdominal discomfort and dyspnea. CT revealed marked disease recurrence with a complex multicystic, partially solid mass (14 x 9 x 13 cm) in her middle and upper abdomen as well as a solitary hepatic nodule, multinodular-multicystic peritoneal structures and a collection of ascites resembling peritoneal carcinosis. The patient was treated with analgetic medication and died six days later, six months after the primary diagnosis.

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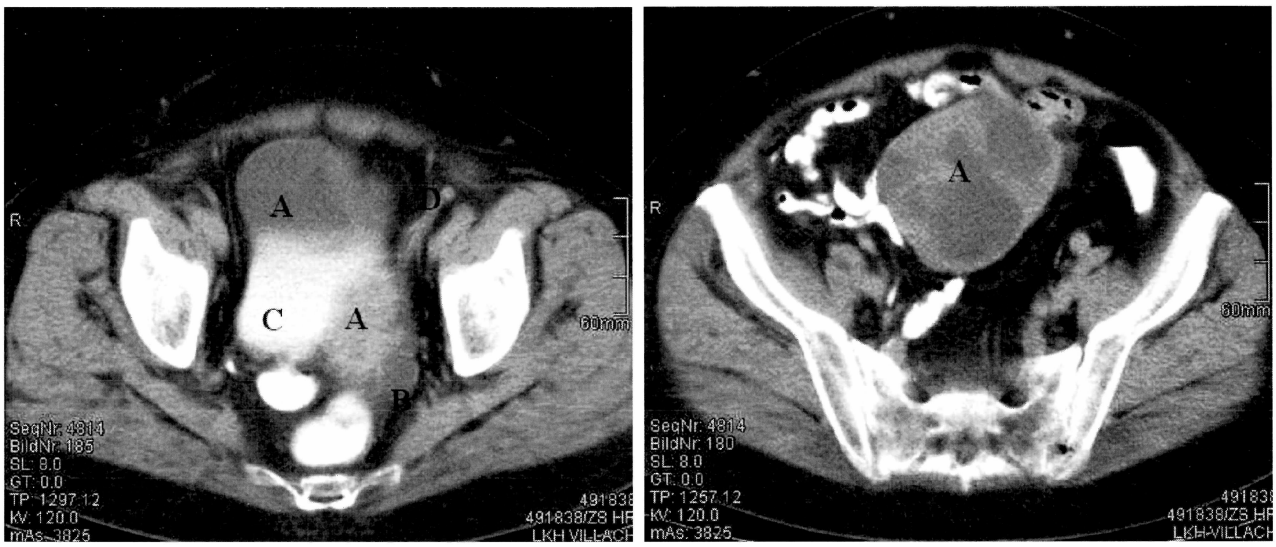
Fig. 1A



Fig

Figure 1A, B. — Computer tomography sequences showing a 10 x 8 x 6 cm solid right adnexal mass without signs of infiltration in surrounding pelvic structures (1B) primarily originating from the right fallopian tube (1A, see arrow; A = tumor, B = uterus, C = bladder, D = left round ligament).

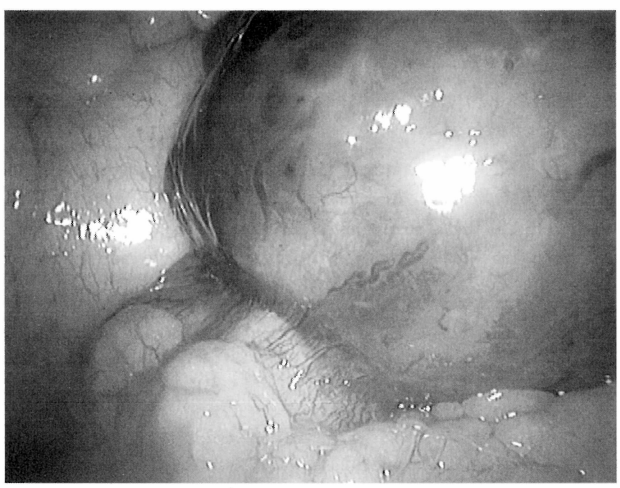


Figure 2. — Primary MMMT of the fallopian tube found as an adnexal mass with areas of necrosis.

Pathological Findings

Macroscopic findings

On gross examination the tumor presented as a 11 x 9 x 6 cm solid, livid-grey mass with a smooth serosa which showed small adhesions to the serosal surface of the terminal ileum. The tumor was completely separated from the ovary which appeared normal. The cut surface showed a pink-colored, mostly solid tumor with partial necrosis and areas of hemorrhage.

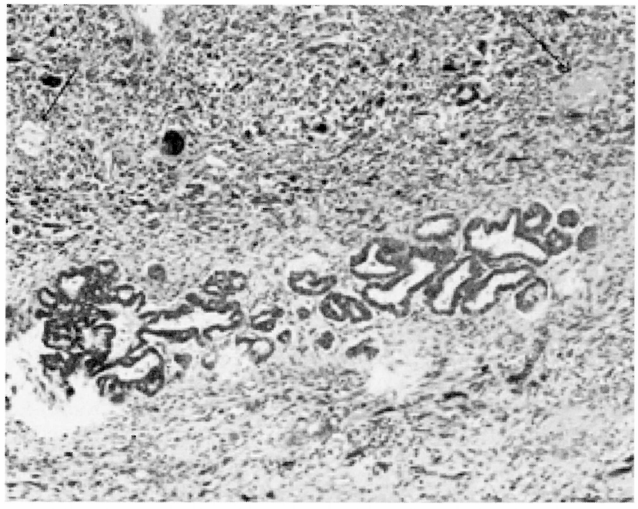
Microscopic findings and immunohistochemical analysis

Histological analysis of paraffin-embedded tissue revealed a tumor with carcinomatous and sarcomatous elements. The carcinomatous areas exhibited glandular structures with cubic neoplastic cells showing prominent nucleoli and cytological atypia. The predominant sarcomatous portion consisted of plump, poorly differentiated cells with intermingled spindle cells with elongated nucleoli and marked cytological atypia (Figure 3A). Between these neoplastic cells, plump giant cells with eosinophilic cytoplasm and prominent nucleoli were seen suggesting possible areas of precursor states of cartilaginous differentiation (Figure 3A, see arrow) exhibiting immunoreactivity for S100. The peritumoral matrix gave a myxoid appearance with infiltration of lymphocytes. Immunohistochemical features are depicted in Table 1. Sarcomatous portions exhibited positive staining for vimentin, MIB1 (Figure 3B), showed partial positivity for desmin, and p53 but stained negative for actin, CK AE1/AE3, estrogen and progesterone receptor (ER, PR), S100, HHF35, SMA and EMA. Intermediate staining for estrogen and progesterone (Figures 3C and D) receptors as well as for HHF35 and SMA was partially observed in spindle cells, therefore possibly resembling immature smooth muscle cells intermingled with sarcomatous tumor components. In contrast, epithelial components demonstrated strong immunoreactivity for EMA, CK AE1/AE3, MIB1 (Figure 3B) and actin but stained negative for ER, PR, S100, HHF35 and SMA. Spatial immunoreactivity for S100 was observed in plump giant cells with eosinophilic cytoplasm, therefore suggesting precursor cells of cartilaginous differentiation (Figure 3E). The extratumoral portion of the fallopian tube showed signs of salpingitis. Interestingly, uterine endometrial glands exhibited simple hyperplasia without atypia.

Table 1.

Antigen	Carcinomatous component	Sarcomatous component	Eosinophilic giant cells	Spindle cells (sarcomatous)
Actin (1A4)	++	–	–	+
CK AE1/AE3	+++	–	–	–
EMA	+++	–	–	–
Desmin	–	+	–	–
Vimentin	–	+	–	–
ER	–	–	–	++
PR	–	–	–	++
p53	–	+	–	–
SMA	–	–	–	–
S100	–	–	+	–
MIB1	++	+++	–	–

– negative; +/++/+++ weak; moderate; strong positivity.



3A

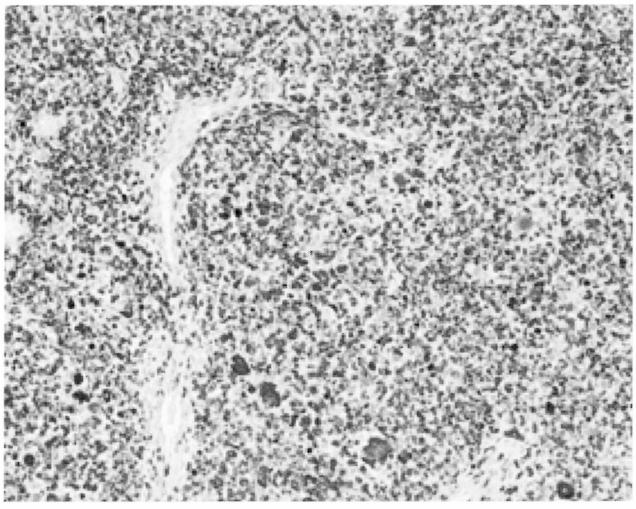
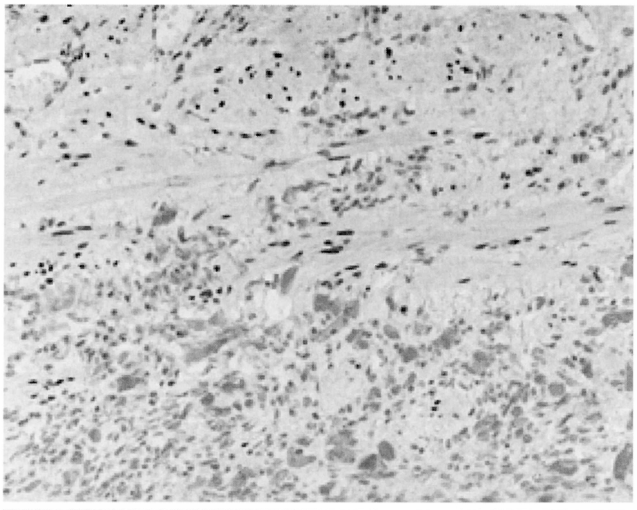


Fig. 3B



3C

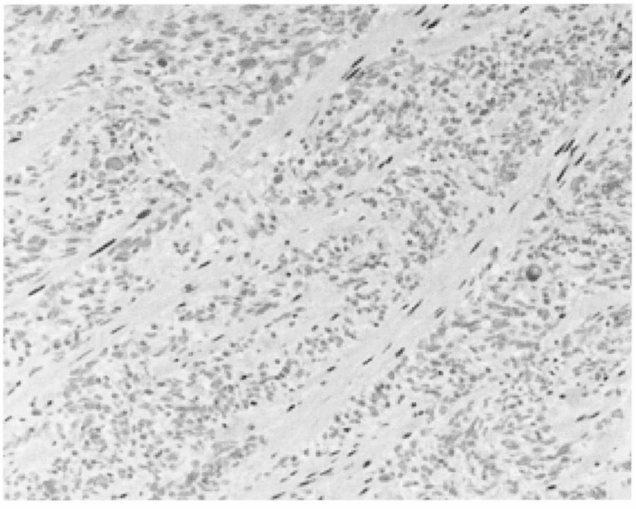
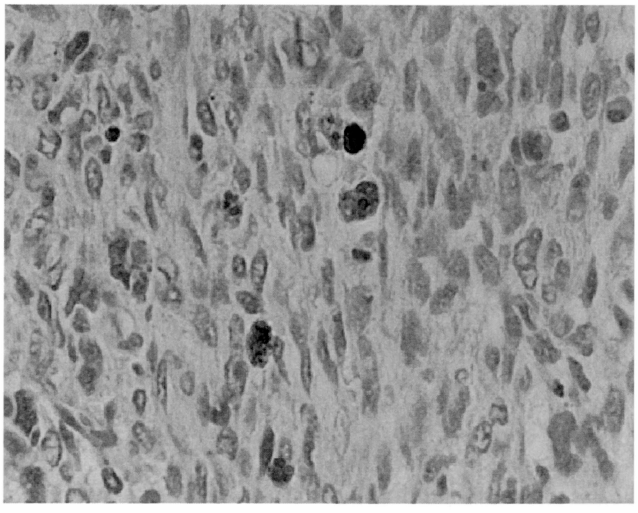


Fig. 3D



3E

Figure 3A. — Primary MMMT of the fallopian tube containing a mixture of poorly differentiated sarcomatous elements and a carcinomatous portion assuming a glandular growth pattern. Arrows indicate plump eosinophilic giant cells showing positive immunoreactivity for S100 (Figure 3E) suggesting chondroid precursor cells.

Figure 3B. — Carcinomatous and sarcomatous elements exhibiting strong immunoreactivity for MIB1 indicating high proliferation of both tumor compomemts.

Figure 3C, D. — Positive immunoreactivity for ER (Figure 3C) and PR (Figure 3D) observed in spindle cells possibly resembling immature smooth muscle cells intermingled with sarcomatous tumor cells staining negative for both receptors.

Figure 3E. — Positive immunostaining for s100 in plump cells possibly resembling chondroid precursor cells.

Discussion

MMMTs are highly aggressive neoplasms that arise in the uterus in one-third of the cases described in the English literature [8]. Extragenital locations are exceedingly rare and include the rectovaginal peritoneum, the serosal surface of the colon and the retroperitoneal space [8]. To date, only 72 cases of primary MMMTs of the fallopian tube have been reported including 26 reports on fallopian MMMTs with heterologous components. The biphasic pattern and therefore unclear histogenetic origin of these tumors is still discussed controversially. On one hand, several authors suggest a mechanism of conversion,

i.e., transformation of epithelial to mesenchymal tumor cells to cause the development and growth of MMMTs [8, 9]. Support for this hypothesis is given by reports on initially diagnosed epithelial tumors such as endometrial carcinoma that further metastasized as carcinosarcoma [8]. On the other hand, MMMTs have also been suggested to originate from one pluripotent stem cell deriving from the Müllerian duct that further differentiates into an epithelial and a sarcomatous component. Although some studies have given inconclusive results [8], several lines of evidence support a monoclonal origin of MMMT with subsequent divergent differentiation [10-12]. Due to the limited number of cases, data on possible risk factors of MMMTs of the fallopian tube are lacking. Nevertheless, a comparison of patients with uterine MMMTs and patients with endometrial carcinoma has revealed similar risk factor profiles including body weight, nulliparity and estrogen use [13]. The patient presented received tamoxifen over five years for hormone-responsive breast cancer. One could therefore hypothesize that the intake of a partial estrogen agonist could possibly promote the development of MMMTs. However, the majority of reports including ours were unable to detect the expression of ER or PR in tumoral tissue components.

Research on published works revealed that the vast majority of patients present with advanced stage disease (FIGO Stage II-IV) in 70%-90% [1] and unspecific symptoms such as abdominal discomfort and weight loss. As a consequence, prognosis of advanced stage MMMTs strongly depends on the stage of disease at the time of diagnosis but is generally poor with overall survival ranging between three to 16 months despite surgical interventions, chemotherapy and irradiation [2, 4]. Although there are some reports on the benefical effects of platinum-based therapy and irradiation in tubal MMMTs [2, 4, 6], the true efficacy of these regimens in patients with advanced stage disease remains controversial. The patient presented here exhibited disease progression within months after surgery and died six months after initial diagnosis without undergoing further chemotherapeutic or radiotherapeutic interventions. In conclusion, the present report underlines the aggressive nature of extragenital MMMTs. Further studies are needed to better define the molecular biology of fallopian MMMTs as well as the role of chemotherapy and radiation in the treatment of these rare but highly malignant tumor entities.

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