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Primary Metastatic Leiomyosarcoma of the Fallopian Tube: A Rare Case Report

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Key Words
Leiomyosarcoma · Fallopian tube carcinoma · Gynecologic cancer · Histology · Therapy options

Schlüsselwörter
Leiomyosarkom · Tubenkarzinom · Gynäkologischer Tumor · Histologie · Therapieoptionen

Summary

Background: Leiomyosarcoma of the fallopian tube is an extremely unusual gynecologic neoplasm. Since 1886, only 19 of about 35 sarcomas of the fallopian tube have been identified as leiomyosarcomas. As such, clinical diagnosis and therapy management are difficult. **Case Report:** We report on the case of a 59-year-old woman with leiomyosarcoma of the fallopian tube and liver metastases at the time of diagnosis. After initial tumor debulking, she received palliative chemotherapy with gemcitabine 900 mg/m^2 (d1+8) and docetaxel 100 mg/m^2 (d8) (q21). For additional bone metastases, she started local radiation plus bisphosphonates (q28). After 2 cycles of chemotherapy, the disease progressed, and the patient died within 8 months of diagnosis. A review of the literature is given. **Conclusions:** Primary metastatic leiomyosarcoma of the fallopian tube is a progressive disease with limited therapy options. For better prognostic evaluation and disease management in such rare cases, it is important to report and compare more cases regarding course of disease and outcome.

Zusammenfassung

Hintergrund: Leiomyosarkome der Tuben sind extrem seltene gynäkologische Neubildungen. Seit 1886 sind nur 19 von rund 35 Sarkomen der Tube als Leiomyosarkome eingeordnet worden. Deshalb sind klinische Diagnose wie auch Therapiemanagement schwierig. **Fallbericht:** Wir berichten über eine 59-jährige Frau mit Leiomyosarkom der Tube und Lebermetastasierung zum Zeitpunkt der Diagnose. Nach initialer Tumordebulking-Operation erhielt sie eine palliative Chemotherapie mit Gemcitabin 900 mg/m^2 (d1+8) und Docetaxel 100 mg/m^2 (d8) (q21). Für die zusätzliche Knochenmetastasierung erhielt sie Bestrahlungstherapie und Bisphosphonate (q28). Nach 2 Zyklen der Chemotherapie zeigte die Erkrankung einen massiven Progress, und die Patientin verstarb 8 Monate nach Diagnosestellung. Außerdem wird eine Literaturübersicht gegeben. **Schlussfolgerungen:** Primär metastasiertes Leiomyosarkom der Tube ist eine rasch fortschreitende Erkrankung mit begrenzten Therapieoptionen. Zur besseren prognostischen Bewertung und für das Behandlungsmanagement derartig seltener Fälle ist es wichtig, diese zu publizieren sowie mit anderen Fällen bezüglich Krankheitsverlauf und Outcome zu vergleichen.

Introduction

Primary fallopian tube carcinomas are rare, comprising between 0.3 and 1.1% of female genital tract cancers [1]; most are diagnosed at the time of surgery. Sarcomas of the fallopian tube are even more rare. Since the first report on a primary fallopian tube sarcoma by Emil Senger in 1886 [2], only 35 primary uterine tube sarcomas have been documented [3–8]. Including the present case, 19 of the fallopian tube sarcomas fulfilled the histological criteria for leiomyosarcoma [9, 10].

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Unfortunately, progress in establishing valid prognostic factors and developing effective therapeutic regimens has been hampered by the small number of known cases as well as by incomplete reports and follow-up of the published cases. With this report, we intend to contribute a detailed case history including histopathology, and summarize the findings and course of the disease.

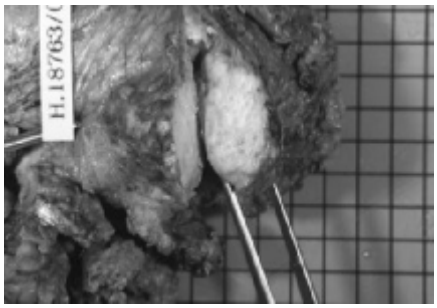

Fig. 1. Cut-in from the surface of the circumscribed tumor.

Case Report

A 59-year-old, single nulli-gravida, with a prior abdominal hysterectomy in 1991 for benign disease, was referred by her local gynecologist because of a newly discovered mass in the right lower quadrant of the abdomen. She had been postmenopausal since 1987, and had repeated abdominal surgery as well as other co-morbidities not related to the abdominal tumor. Previous gynecologic visits on a routine base every 6 months were uneventful. No family history of gynecologic cancer was present.

In the clinic, the patient presented with intermittent constipation for 5 months, a drawing pain in the lower right quadrant of the abdomen for 3 months, a tendency to constipation, but no weight loss nor change in abdominal circumference. Night sweats for approximately 1.5 years were assumed to be due to climacteric symptoms, and hormonal replacement therapy (HRT) was given. Vaginal examination revealed an unsuspicious inner vaginal stump, and towards the right side a plum size mobile mass with and another and larger right lower abdominal mass which was pressure-sensitive and painful. These findings were confirmed by vaginal ultrasound and computed tomography (CT) of the pelvis, which did not show any abnormal lymph nodes or ascites. Doppler showed no signs of pathologic tumor vascularization. The preoperative laboratory studies were normal, as were the serum levels of carcinoembryonic antigen (CEA) and CA 125. Exploratory laparotomy revealed a $6 \times 4 \times 3$ cm solid necrotic mass in the right fallopian tube. The tumor looked like an encapsulated tubo-ovarian abscess. Both ovaries and the left tube were unremarkable, as was the remainder of the abdominal exploration. A total bilateral adnectomy and adhesiolysis were performed. Intraoperative frozen section of the specimen showed tissue necrosis and post inflammatory alterations, not clearly excluding malignant disease but with signs pointing towards a sarcoma. The final histology report confirmed an invasive-destructive leiomyosarcoma of the right tubal wall, pT2b, low differentiation (G3), with tumor infiltration at the vaginal stump as a sign of peritoneal tumor expansion. The right ovary as well as the left tube and ovary showed no signs of malignancy.

Initially, a completion operation with deperitonealization of the small pelvis and hemicolpectomy was considered, but during the postoperative staging a CT of the thorax, abdomen, and small pelvis demonstrated 2 lesions in different lobes of the liver of 1.2 and 1.5 cm diameter, respectively, highly suspicious for liver metastasis. Because an operation with R0 resection was no longer possible, the extensive procedure was cancelled. Postoperatively the patient recovered normally with postoperative absence of disease-related symptoms and relative well-being. As no hard response data for the therapy of leiomyosarcomas of the fallopian tube are available, the option were either 'watchful waiting' with interval staging or experimental chemotherapy. Due to the patient's professional background – she had worked for 30 years in our hospital as an occupational therapist, also leading a self-help group about coping with death for patients and family members – she was familiar and realistic in dealing with cancer at advanced stages. After comprehensive education about her disease and the prospects of further oncologic therapy, she declined additional treatments, citing her past medical experience and the limited options that were available to her.

After three months, during which the patient traveled extensively, she returned for restaging. Ultrasound of the liver confirmed progress of metastasis (now $2.1 \times 2.2 \times 2.8$ cm). Additionally, the CT scan showed a suspicious lymph node in the right axilla, 2 small suspicious lesions in the lung, a pathologic lumbar fracture at L1, multiple mesenteric nodes up to 6.0×2.5 cm in diameter, and local progress at the vaginal stump (now 6.0×3.5 cm). The bone metastasis and pathologic spine fracture were treated with the bisphosphonate pamidronate disodium 90 mg (q28). Local radiation of the lower thorax and upper lumbar spine with up to 30 Gy was initiated. One month later, after further progression of the disease with multiple liver metastases as well as intestinal infiltration and a suspicious metastatic lesion in the left adrenal gland, the patient consented to receive a chemotherapy with gemcitabine 900 mg/m^2 (d1+8) and docetaxel 100 mg/m^2 (d8), both q21, according to the results of a phase II trial [11]. After only 2 cycles without obvious response, the patient developed a recto-vaginal fistula which was closed at laparotomy. Because of peritoneal metastasis and involvement of the small and large bowel, the operation had to be expanded and a recto-sigmoid resection with deep anastomosis, a descendo-rectostomy, and an ileocecal resection with end-to-end anastomosis were performed. Recovery was uneventful until at the 9th day when the patient developed an anastomosis insufficiency at the site of the ileotransversostomy, which then was re-operated on with uneventful recovery. Due to massive progressive disease, decrease in her general condition and lack of additional therapeutic options, the patient was discharged to a hospice after pain therapy adjustment and died 4 weeks later, 8 months and 4 days after her initial diagnosis.

Histopathology

Macroscopic Histology

Macroscopically (fig. 1), the tumor measured $6 \times 4 \times 3$ cm and showed a mostly white to gray partially necrotic and hemorrhagic surface with an implied trabecular pattern.

Microscopic Findings

Formalin-fixed and paraffin-embedded tissue blocks of the tumor and surrounding tissues were cut into 4 µm-thick sections and stained with hematoxylin and eosin. The slides were stained for vimentin, desmin, smooth muscle actin, estrogen- and progesterone-receptor, S-100, and CD34. The proliferation rate was assessed by staining for the Ki67 antigen (MIB1, Dako, Hamburg, Germany). Immunohistochemistry was performed on an automated immunostainer (Ventana Medical systems, Tucson, AZ, USA). Histologically, the tumor was composed of fascicles of spindle cells with abundant cytoplasm. The nuclei were fusiform to round, and showed a hyperchromatic chromatin with partially multiple nuclei. Nuclear pleomorphism was prominent, and frequent mitotic figures were observed (20 mitotic figures / 10 high power fields) (fig. 2). Additionally, confluent areas of necrosis were prominent (fig. 2). In peripheral areas of the tumor, smooth muscle bundles of the muscular wall of the tube were visible (fig. 3). The tumor cells were immunohistochemically positive for vimentin (fig. 4), and showed a faint staining for smooth muscle actin (fig. 5), desmin, as well as S-100 protein and MIB1 (fig. 6). The proliferation rate was 80%.

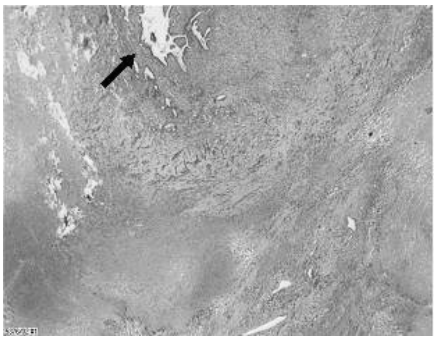

Fig. 2. Part of the fallopian tube (arrow) with extensive necrosis.

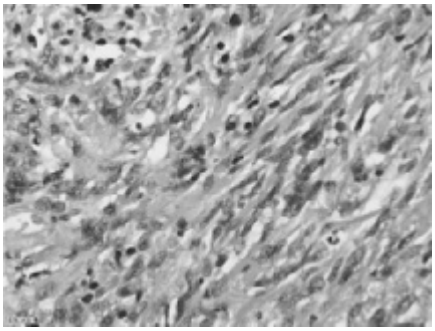

Fig. 3. Tumor cells are composed of fascicles of spindle cells (enlargement of fig. 2).

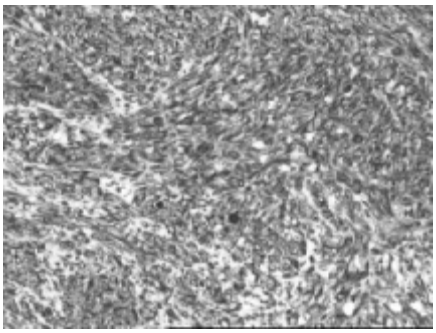

Fig. 4. Immunohistochemistry: antibody reaction against vimentin.

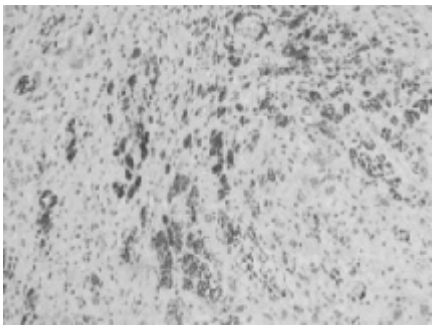

Fig. 5. Immunohistochemistry: antibody reaction against smooth muscle actin.

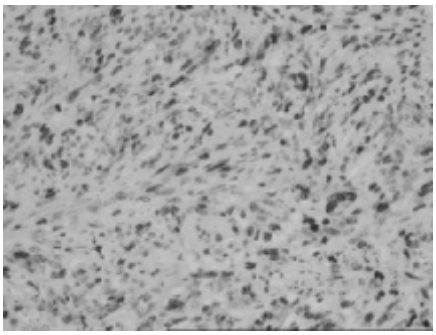

Fig. 6. Immunohistochemistry: antibody reaction against MiB1.

Discussion

Leiomyosarcoma of the fallopian tube is a very rare disease. Only about 19 case reports have been published worldwide since its initial description more than 120 years ago. The most recent publication was in 2005 [12]. Our case is the first case report with primarily diagnosed metastasis. Since the quality of all case reports is varying, e.g. with pathologic findings first discovered post mortem and limited or incomplete data regarding therapy and outcome, no conclusions based on these publications can be drawn at the present time. In any case, it appears that leiomyosarcomas of the fallopian tube seem to have a rapid and progressive course of disease with limited therapy options.

For non-metastasized leiomyosarcomas of the tube, initial surgical intervention with the target of complete resection (R0) is standard. Similar to therapy offered to uterine sarcomas, abdominal hysterectomy, bilateral salpingo-oophorectomy, and pelvic and peri-aortic selective lymphadenectomy are performed. Cytologic washings can also be obtained from the pelvis and abdomen for staging of disease. Intraoperatively, a thorough examination of the diaphragm, omentum, and upper abdomen should be performed. As metastatic leiomyosarcomas can only be treated within a palliative concept, an operation might be considered for tumor debulking.

No structured data of any therapy including chemotherapy or outcome for leiomyosarcomas of the fallopian tube are available at present. Therefore, rare diseases like this would benefit from a centralized case registry with course of disease, treatment, and outcome. Results from case series or evidence-based trials are not available. Experience with specific therapies is limited and has to be individually adjusted to every case. Therapeutic options can be ascertained from the web site of the National Cancer Institute [13]. Options might also be found for similar entities like uterine sarcoma [14]. Chemotherapy regimens such as gemcitabine/docetaxel [11] or the GOG-150 phase II trial with cisplatin/ifosfamide/mesna (CIM) [15] can be considered, although CIM showed no statistical significance regarding recurrence rate or survival vs. whole abdominal irradiation therapy [16]. Therapy in our case was adjusted to the individual course of disease: bisphosphonates ± radiation for bone metastasis, conservative treatment of liver metastasis, palliative surgical approach to symptomatic bowel and other intra-abdominal symptoms, and adequate pain therapy including an interdisciplinary approach. Repeated presentations to an interdisciplinary tumor board should be standard to help assure quality of care at a maximum level of competence. For rare entities such as leiomyosarcomas of the fallopian tube, more comprehensive case reports are necessary with sufficient documentation. This can support the accumulation of data regarding therapy and outcome over time for an improved treatment of this disease in the future.

Supplemental Material

Color representations of all figures can be found at *www.karger.com/DOI=264625.*

Conflict of Interest

All authors had no conflict of interest in writing this paper.

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