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Case Report

A rare case of primary ovarian leiomyosarcoma

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Summary

Primary ovarian leiomyosarcoma (LMS) is very rare, with only 72 cases reported. Its behavior is aggressive, and there is no standard therapy. A 62-year-old woman with a giant pelvic tumor underwent CT and MRI. An irregular, 30-cm, solid tumor that was suspected to be malignant was seen. On laparotomy, the tumor was derived from her right ovary and adhered widely to the retroperitoneum. On pathological examination, it was an ovarian leiomyosarcoma. Adjuvant chemotherapy (docetaxel and gemcitabine) was given. Three months after surgery, CT showed multiple liver metastases. Pazopanib, ifosfamide, doxorubicin, and eribulin were given with no effect, and the woman died 18 months after the primary operation. With the administration of pazopanib, proteinuria of 2.3 g/dl occurred, which made continuous administration impossible. Since ovarian LMS may not respond to chemotherapy for other soft tissue sarcomas, study of more ovarian LMS cases is needed.

Key words: Primary ovarian leiomyosarcoma (LMS); Laparotomy; Adjuvant chemotherapy; Soft tissue sarcomas.

Introduction

Primary ovarian mesenchymal tumors are very rare and aggressive neoplasms that account for fewer than 3% of ovarian malignancies [1]. Primary ovarian leiomyosarcoma (LMS) is derived from smooth muscle or vessels of the ovary [2], and fewer than 100 cases have been reported [3]. Standard therapy has not yet been established. Although some reports showed that debulking surgery seems to prolong overall survival [4, 5], the efficacy of chemotherapy seems to be very limited.

The case of a postmenopausal woman diagnosed with an ovarian LMS, in whom all anticancer drugs that can be administered for soft tissue sarcoma were inefficacious, is presented.

Case Report

A 62-year-old woman visited the present hospital with a three-month history of abdominal distension. Her past history and family history were unremarkable, except for her hypertension. Transabdominal ultrasonography showed an irregular, giant, and solid mass in her abdominal cavity. On pelvic examination, movability of the tumor was poor. The endocervical smear showed no intraepithelial lesions of malignancy, and the endometrial smear showed no atypical cells derived from endometrial glands.

In order to further characterize the mass, blood tests including tumor marker assays, MRI, and CT were performed. Serum concentrations of LDH (442 IU/l) and CRP (13.08 mg/dl) were elevated. All tumor marker (CA125, CEA, and CA19-9) levels were normal. MRI showed an irregular intensity mass that was suspected to be malignant (Figure 1A). On enhanced CT, although no metastasis was seen, the right ureter was deviated because of the pressure caused by this huge mass (Figure 1B).

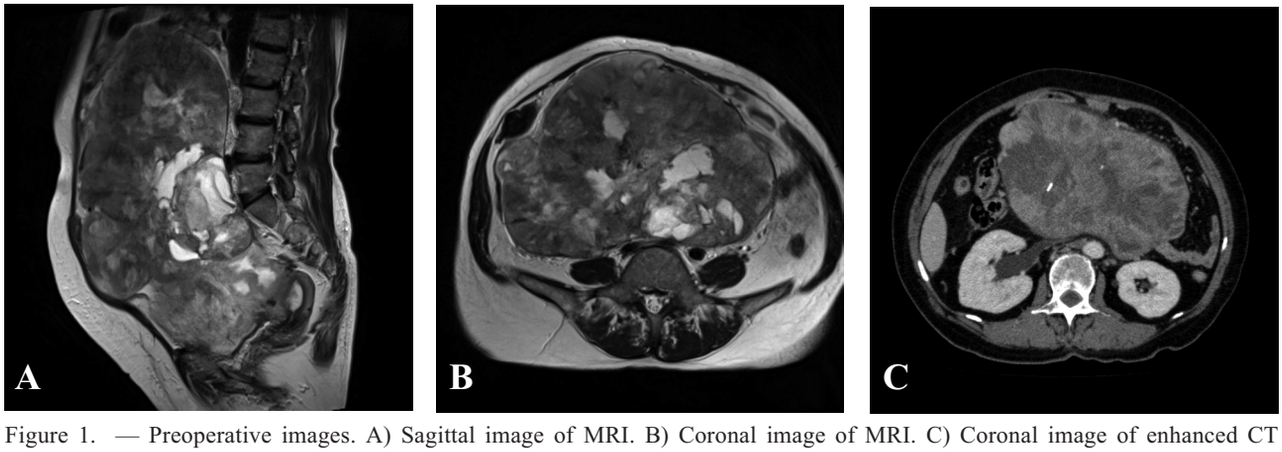

Figure 1. — Preoperative images. A) Sagittal image of MRI. B) Coronal image of MRI. C) Coronal image of enhanced CT MRI shows an irregular, solid mass, highly suspicious of malignancy. Since CT shows hydronephrosis of the right ureter, adhesion of tumor to the retroperitoneum is suspected.

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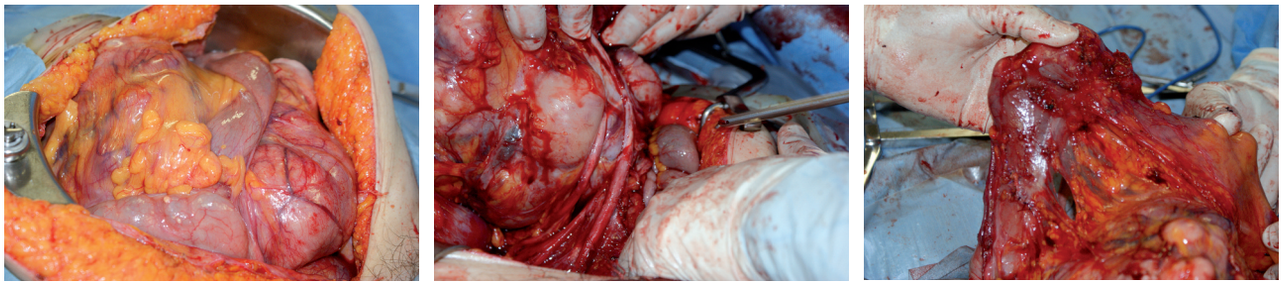

Figure 2. — Findings at operation. A giant tumor adheres widely to small bowel and the cecum. The ureter is deviated and adheres to the back of the tumor.

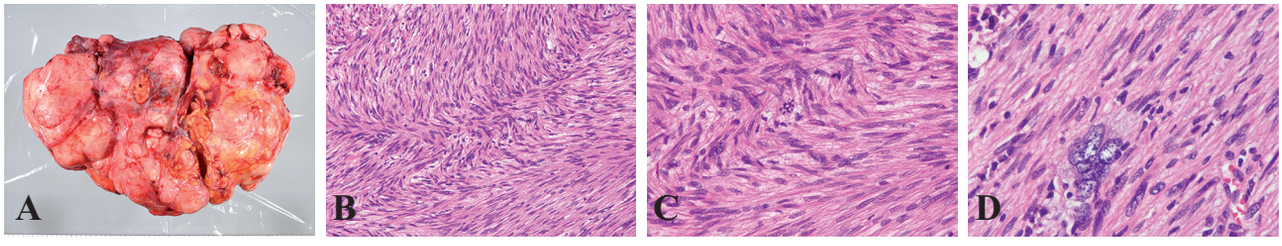

Figure 3. — Pathological findings A:) Macroscopic findings of the tumor. B), C), D): Microscopic findings. Hematoxylin-Eosin staining; magnification ×100 (C), magnification ×400 (C, D).

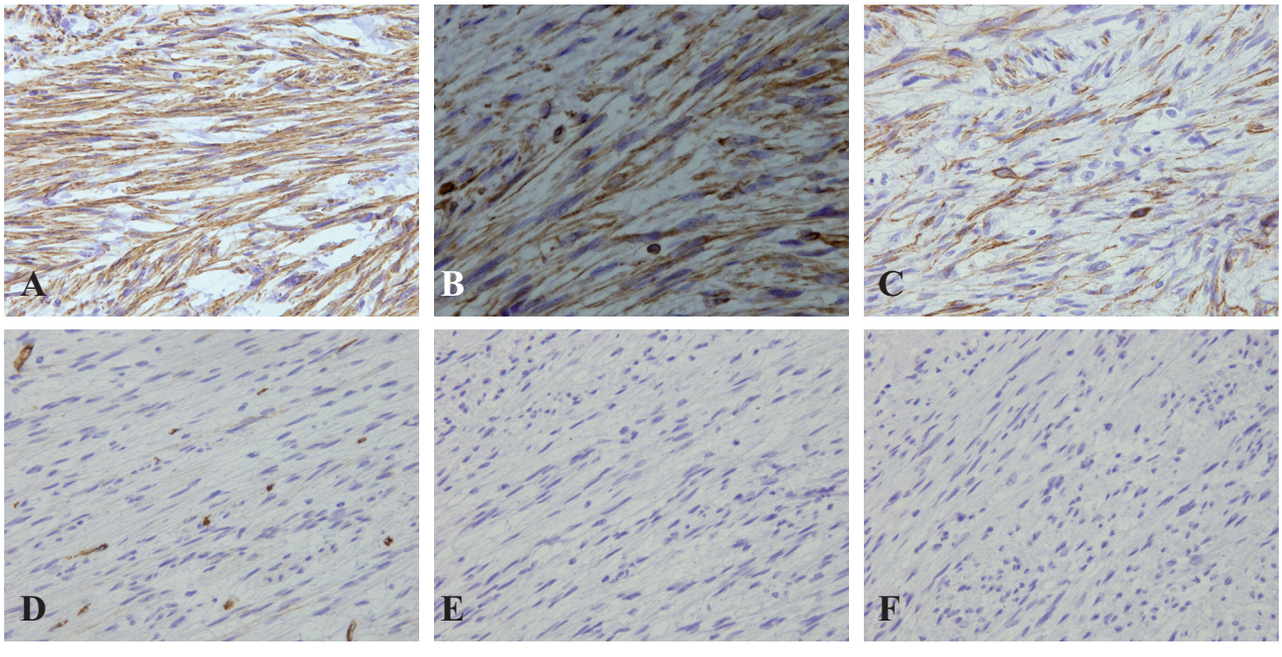

Figure 4. — Immunohistochemistry. Smooth muscle actin (A), vimentin (B), and desmin (C) are positive. CD34 (D), C-kit (E), and S-100 (F) are negative.

After the work-up, a laparotomy was performed. The adult head-sized tumor was derived from the right ovary. The surface of the tumor was white and relatively smooth. The uterus and left ovary were normal in size, and their movability was good. The huge right ovarian tumor adhered widely to retroperitoneum and ileum, and it pressed the right ureter, as seen on the preoperative images (Figure 1C). Thus, the right ureter was separated from the retroperitoneum, and adhesiolysis of the ileum was performed before tumorectomy. Finally, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. Since the ileum became ischemic after adhesiolysis, a functional end-to-end anastomosis that connected the ileum to the ascending colon was performed to prevent bowel perforation (Figure 2).

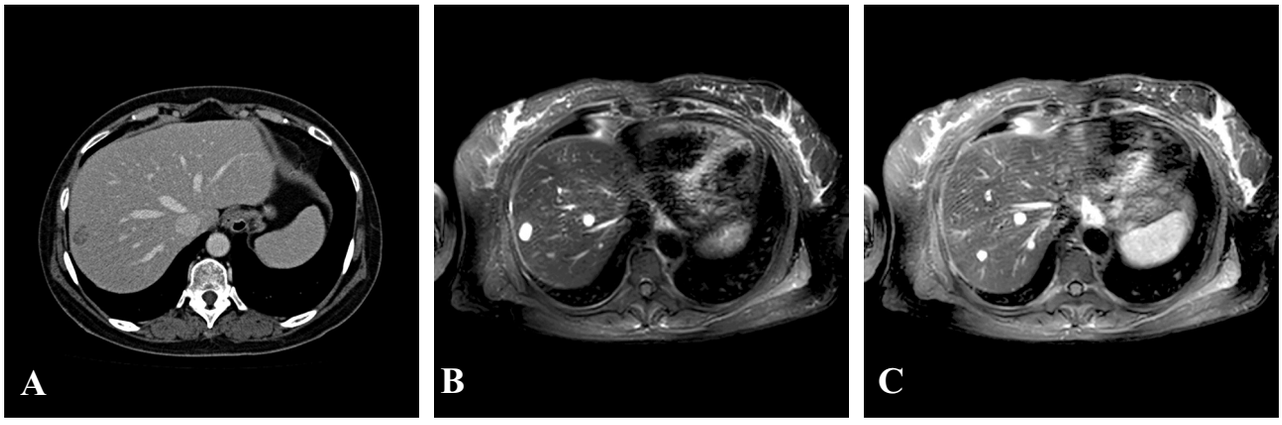

Figure 5. — CT (a) and MRI (b, c) findings when DG chemotherapy was finished. Multiple liver metastases are seen.

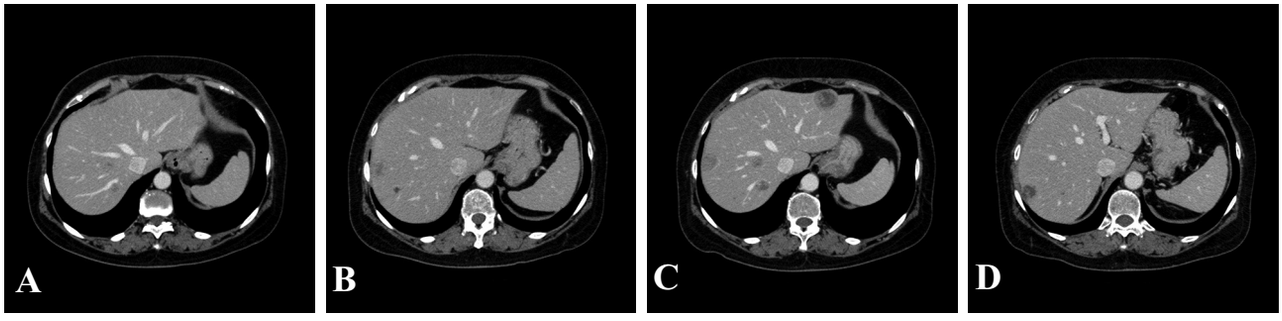

Figure 6. — CT findings of liver metastases. A, B) The period after. pazopanib was administered. C, D) The period after IAP chemotherapy was completed. Multiple liver metastases have grown.

The tumor weighed 4.5 kg, and it was 30 cm in size. The cut surface of the tumor was fibrous and solid. The necrotic component was unclear. Microscopic examination of the tumor showed atypical cells derived from smooth muscle cells (Figure 3). There were giant cells with 8 mitoses/HPF and spindle cells. On immunohistochemical examination of the tumor, the tumor cells showed strong expressions of smooth-muscle actin, vimentin, and desmin (Figure 4), while they were negative for CD34, C-kit, and S-100.

The tumor was diagnosed as a LMS. Microscopic examination of the uterus and left ovary showed no abnormalities. Although FIGO2008 staging was Stage 1A, the adhesion of this tumor to peritoneum was considered a risk factor for recurrence. Thus, combination chemotherapy of docetaxel and gemcitabine was performed; 80 mg/m^2 of docetaxel was administered on Day 1, and 1 g/m^2 of gemcitabine was given on Days 1 and 8. Both anticancer drugs were administered by drip infusion, and the interval of one cycle was 21 days.

After three cycles of chemotherapy, CT showed multiple liver metastases (Figure 5). Pazopanib was selected as second-line chemotherapy, and 600 mg of pazopanib was given orally daily. On Day 15, the platelet count decreased to 30×10^3/μl. The chemotherapy was stopped for two weeks and then restarted. However, recurrent Grade 3 thrombocytopenia and proteinuria (2.3 g/dl) occurred. In addition to these adverse events, the multiple liver metastases grew, and it was decided to change the regimen. Since the third-line chemotherapy that combined ifosfamide (D1-5, 1 g/m^2), adriamycin (D1, 20 mg/m^2), and cisplatin (20 mg/m^2) showed no effect (Figure 6), eribulin was administered as fourth-line chemotherapy. After three cycles of eribulin (21-day cycle, D1, 1.2 mg/m^2), PET-CT imaging was performed and showed a 7-cm recurrent tumor appeared at her mesentery. The patient developed ileus, and it was decided that chemotherapy could not be continued. Although she had been asymptomatic until she was diagnosed with ileus, the disease then progressed aggressively. Opioids and octreotide were administered as symptomatic treatment. The patient died 18 months after the initial diagnosis.

Discussion

Ovarian LMS is a very rare mesenchymal neoplasm that accounts for less than 1% of ovarian sarcomas [6]. Some reports showed that ovarian LMS is derived from smooth muscle cells of vessels in the ovary [2, 7]. Only 72 cases of ovarian LMS have been reported so far [3]. They are generally considered to be high-risk cancers for which there are no management recommendations [3, 7]. Although the histopathological findings of ovarian LMS include coagulative necrosis, cellular atypia, and mitotic index greater than 10 [7], some reports showed that the presence of mitotic index greater than 5 with significant atypia leads to the diagnosis of ovarian LMS [8, 9]. In addition to these findings, positive

staining for desmin, smooth-muscle actin, and vimentin supports the diagnosis of ovarian LMS [1, 7]. Thus, the authors were able to diagnose the current neoplasm as ovarian LMS.

Because of the limited data, it is reasonable to manage ovarian LMS in a manner similar to uterine LMS [10]. Based on some reports, surgery is the preferred first-choice treatment [3, 4, 9]. Resection of recurrent tumor has tended to be selected as a treatment option for relapse. On the other hand, there is no recommended standard chemotherapy. Since the NCCN guideline for uterine sarcoma recommends chemotherapy that combines docetaxel and gemcitabine [11], a combination of docetaxel and gemcitabine was selected as first-line chemotherapy in the present case. Despite debulking surgery and chemotherapy, the patient developed liver recurrence only three months after surgery.

For more than 30 years, doxorubicin and ifosfamide have been used to treat soft-tissue sarcoma [12, 13]. In 2014, the European Organisation for the Research and Treatment of Cancer (EORTC) 62012 study showed that the combination of doxorubicin and ifosfamide for advanced or metastatic soft-tissue sarcoma did not prolong overall survival compared with single-agent doxorubicin [12]. Thus, single-agent doxorubicin tends to be considered first-line chemotherapy for soft-tissue sarcoma.

In the present case, the combination of doxorubicin, ifosfamide, and cisplatin (IAP therapy) was given as third-line chemotherapy, referring to some previous reports [14, 15]. Although the agents may have been given late, the IAP therapy was ineffective. Some reports recently showed that some new agents, for example, pazopanib [16], trabectedin [17], and eribulin [18] prolonged progression-free survival of recurrent soft-tissue sarcoma cases that were resistant to anthracycline. Although these anticancer drugs have been used as an option for salvage chemotherapy, there is no evidence that these agents prolong overall survival in LMS. In the current case, although pazopanib was used as second-line chemotherapy and eribulin was used as fourth-line chemotherapy, these drugs showed no effect. In addition to their lack of effect, thrombocytopenia and proteinuria of 2.3 g/dl occurred with pazopanib. These adverse events made the continuous administration of pazopanib impossible. Proteinuria and elevated serum creatinine levels with pazopanib in the therapy of soft tissue sarcoma were reported by the EORTC study [19]. Thus, although the patient survived 18 months in the present case, multiple anticancer drugs showed no effect.

In conclusion, although this was only one case, the chemotherapy that are performed for other soft tissue sarcomas may not be useful in the treatment of ovarian LMS. In order to establish the standard therapeutic regimen for ovarian LMS, more ovarian LMS cases need to be studied.

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