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A case report of primary ovarian fibrosarcoma

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ABSTRACT

Background: Ovarian fibrosarcoma is a rare malignant tumor that should be distinguished from benign fibrous ovarian tumors and other malignancies, as it has a predilection for early and aggressive metastasis.

Case: A 52-year-old woman presented with a large adnexal mass comprised of atypical spindle cells with increased mitotic activity, high Ki-67 index, and positive vimentin staining, consistent with primary ovarian fibrosarcoma. The patient required multiple laparotomies for large volumes of recurrent, rapidly growing disease. She died 15 months after initial surgery.

Conclusion: Ovarian fibrosarcoma is an important diagnostic consideration when evaluating adnexal masses. Further study is required to clarify the impact of potential prognostic factors and establish optimal management and treatment.

Keywords: Ovarian fibrosarcoma, ovarian tumor, pelvic pain

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Introduction

Ovarian fibrosarcoma is a very rare type of malignant ovarian tumor, documented mostly in case reports. Disease prognosis and 'best practice' in terms of diagnosis and treatment are yet to be established[1, 2]. Prognosis is generally very poor, with early metastasis and survival usually less than 2 years[1]; however, there are rare case reports documenting long-term survival beyond 5 years[10, 11]. Here we present a case of primary ovarian fibrosarcoma with aggressive behavior and review the current literature.

Case

A 52-year-old parous woman presented with a history of pelvic/lower back pain and pressure, increasing over several months. Abdomino-pelvic examination was remarkable for a mass in the posterior cul-de-sac. Imaging studies, including pelvic ultrasound and MRI, demonstrated an 11 x 15 cm right adnexal mass with a hypervascular appearance and areas of necrosis. The differential diagnosis included degenerating leioyoma and benign ovarian tumor. A CA125 level at that time was 62 U/mL.

Three months later she presented to emergency with acute abdominal pain. CT scan reported a 16 x 18 cm complex ovarian mass (Figure 1). A total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed on an urgent basis because of significant symptoms. The large right ovarian mass was resected, with intra-operative spill occurring as a result of significant adhesions.

On gross examination the mass was 24 x 23 x 10 cm with a disrupted capsule and surface adhesions. The cut surface appeared variegated and was soft with extensive areas of hemorrhage and necrosis. Histology showed sheets of highly cellular, atypical spindle cells displaying a herringbone pattern. Numerous mitotic figures (>20 mitoses per 10 high power fields) were identified. There were extensive areas of necrosis. Immunoperoxidase stains were performed to rule out leimyosarcoma, carcinosarcoma, sex-cord stromal tumor, and rhabdomyosarcoma. Neoplastic cells were diffusely and strongly positive for vimentin. All other immunohistochemical markers were negative, and the tumor was diagnosed as fibrosarcoma.

The patient was referred to gynecologic oncology. She did not pursue further treatment, given the absence of any definitive survival advantage with adjuvant chemotherapy or radiotherapy.

Follow up PET and CT scans three months later revealed a 2.5 x 3.7 cm hypermetabolic mass in the left upper quadrant (Figure 2). No other distant metastases were noted. A laparotomy was performed approximately 5 months from her initial surgery. An 11 x 5.5 x 6.8 cm friable, soft omental mass was resected (Figure 3). There were significant adhesions to the bowel mesentery but no other visible disease was noted in the abdomen and pelvis. Histomorphology and immunoprofile of this lesion were similar to the initial ovarian mass (Figure 4) and a high Ki-67 index of 60-70% was noted (Figure 5), in keeping with recurrent fibrosarcoma. The patient recovered well after surgery and chose not to receive chemotherapy, in the absence of clear prognostic benefit.

Outcome and follow up

PET and CT scans performed 2 months after the second surgery showed diffuse metastatic disease, including hypermetabolic bilateral pelvic lymph nodes (0.9 x 0.7 cm) and hypermetabolic mass lesions in the right pelvis (2.7 x 1.4 cm) and left upper quadrant of the abdomen (5.3 x 1.3 cm). The case was discussed by a multidisciplinary tumor board, and the option of combination chemotherapy was once again offered. The patient opted instead for alternative therapy in another

country (high-dose Vitamin C, glutathione, and Vitamin B17 injections along with stem cell transfusion). She received four weeks of treatment, beginning approximately 5 months after her second surgery.

Six weeks following completion of this therapy she presented with acute abdominal pain. A CT scan of her abdomen and pelvis revealed that the recurrent pelvic and abdominal disease had grown significantly, from 2.7 and 5.3 to 15 and 17 cm in size respectively, with areas of necrosis and extensive hemorrhage (Figure 6 A, B, C).

The patient decided to pursue a second course of alternative therapy abroad. Unfortunately she required an urgent laparotomy a few days into treatment, including an emergency bowel resection, colostomy, and partial removal of abdominal mass. She was flown home to Canada several days post-operatively, where she recovered from surgery. She was ultimately discharged home upon her request, with palliative care support in place. She succumbed to disease soon thereafter, approximately 15 months following her initial surgery for resection of the mass.

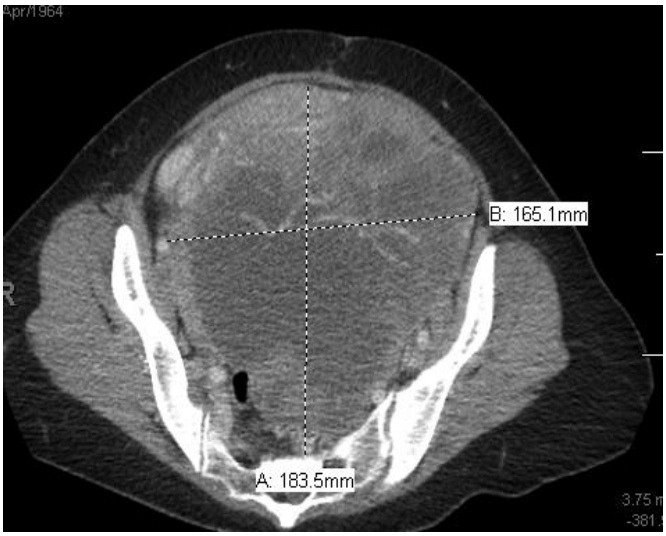


Figure 1. Complex ovarian mass.

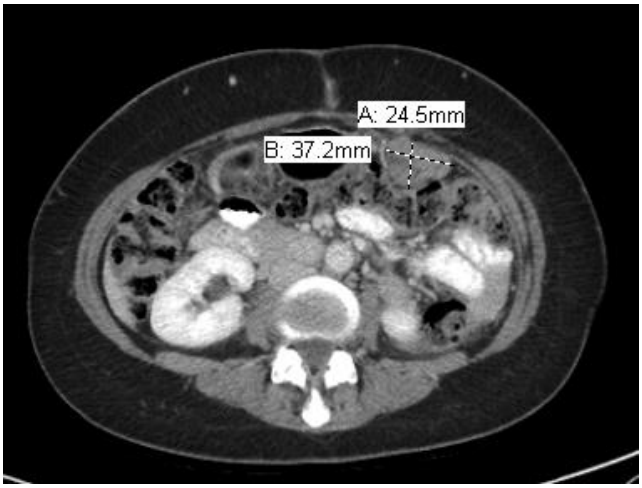


Figure 2. Left upper quadrant mass, suspicious for recurrent disease.

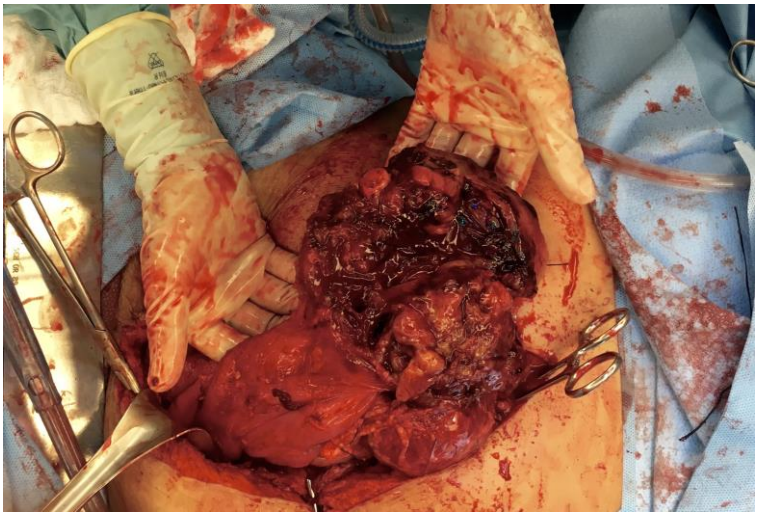
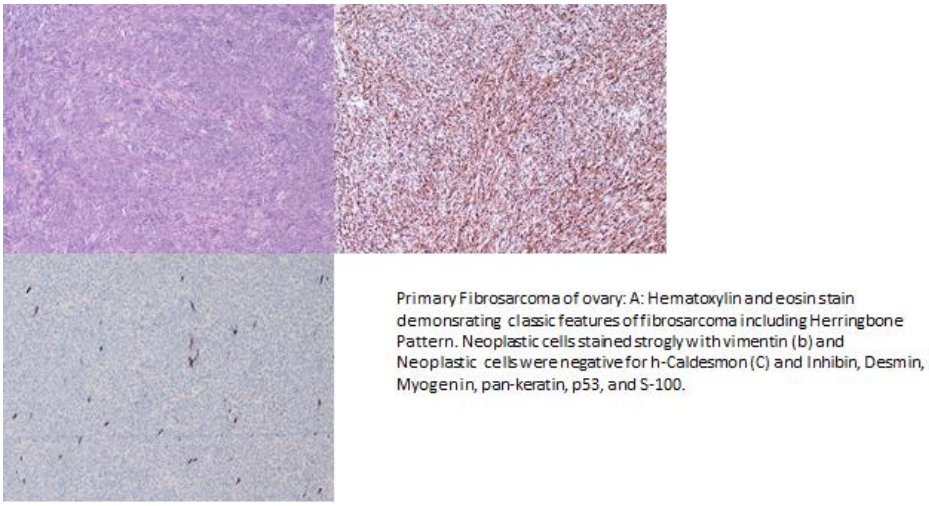


Figure 3. Recurrent tumor.



Primary Fibrosarcoma of ovary: A: Hematoxylin and eosin stain demonsrating classic features of fibrosarcoma including Herringbone Pattern. Neoplastic cells stained strogly with vimentin (b) and Neoplastic cells were negative for h-Caldesmon (C) and Inhibin, Desmin, Myogenin, pan-keratin, p53, and S-100.

Figure 4. Immunostaining of recurrent resected tumor.

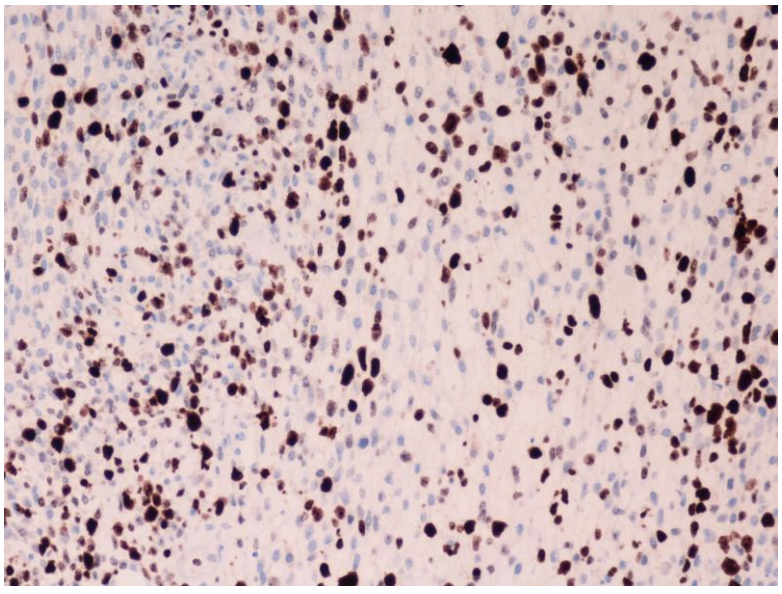


Figure 5. Stained cells exhibiting high Ki-67 index.

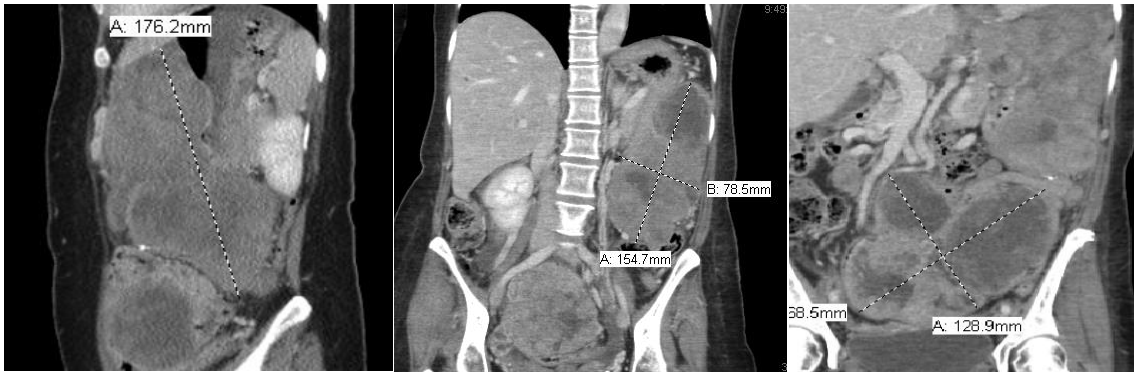


Figure 6 A, B, C. Extensive recurrent metastatic tumor in the abdomen and pelvis, with areas of necrosis and hemorrhage.

Discussion

Fibrous ovarian tumors can be classified as fibromas, mitotically active cellular fibromas (MACF), or fibrosarcomas[7]. Fibrosarcomas arise either *de novo* from the ovarian sex cord stroma, or rarely as a malignant transformation of a benign ovarian fibroma. Benign fibromas are by far the commonest type of spindle cell ovarian neoplasm, and are characterized by mild nuclear atypia and 3 or fewer mitotic figures per 10 high power fields (HPFs)[3]. MACF has been more recently identified as a distinct entity[5] that resembles fibrosarcoma in its high degree of mitotic activity; however, MACFs lack significant cytological atypia[16]. MACF is considered benign and has a favorable prognosis. Malignant fibrosarcomas, on the other hand, exhibit marked nuclear atypia with 4 or more mitotic figures per 10 HPFs[3]. In our case, the high degree of nuclear atypia, increased mitotic activity (>20 per HPF), high Ki-67 index, herringbone pattern, and extensive areas of necrosis on histology and negative immunohistochemical profile for other spindle cell lesions were all consistent with a diagnosis of fibrosarcoma.

Our patient presented with a symptomatic, unilateral pelvic mass rapidly increasing in size, suggestive of a malignant process[1-3]. Based on several case reports, it appears that patients with ovarian fibrosarcoma are often postmenopausal (average age 49 years) and typically present with pain or increasing abdominal girth[1-3,15].

There are no diagnostic immunohistochemical markers for fibrosarcoma[17,18]; rather, as in our case, this diagnosis should be considered after excluding other malignant tumors. The tumor in this case was negative for H_caldesmon and epithelial markers, effectively ruling out leiomyosarcoma and sarcomatoid carcinoma. It was positive for vimentin, with a high Ki-67 proliferation index of 60-70% and negative staining for ER/PR, smooth muscle actin, cytokeratins, inhibin, p53, or other unique or specific stains. It is important to distinguish fibrosarcoma from leiomyosarcoma, as both of these are malignant spindle cell lesions. Unlike in the instance of fibrosarcoma, specific treatment (chemotherapy or radiation therapy) can be recommended for selected cases of advanced or recurrent leimyosarcoma, with a goal of local control and extended disease free interval.

Due to the rarity of fibrosarcomas, there is a paucity of information regarding prognostic markers. Similar to other malignant spindle cell lesions, prognosis may be impacted by tumor size and degree of mitotic activity[3]; degree of proliferative activity based on Ki-67 index[1, 4]; ruptured tumor capsule; stage of disease at presentation; or optimal debulking at time of surgery[15]. Unfortunately, the limited data available shows great variability in these factors

Table 1. Clinical features and prognosis of ovarian fibrosarcoma cases in the literature

Authors	*Age*	*Symptoms*	*FIGO stage*	*Tumor size (cm)*	*Ki-67 index*	*Mitotic figures per 10 HPF*	*Surgery or other initial therapy*	*Other therapy*	*Prognosis*
Prat *et al*[3]	61	NR	Ia	10	NR	4	TAH BSO Oment.	Radiation	Rec. in liver at 18 months; died at 18 months without further therapy
	59	NR	IIb	NR	NR	8	TAH BSO Oment.	None	Rec. in sigmoid colon at 1 month; treated with 2° surgery and radiation; died at 4 months
	42	NR	IIb	NR	NR	25	TAH BSO Oment.	None	Rec. on ureter at 1 month; treated with radiation; still alive at 13 month follow up
	65	NR	Ia	NR	NR	10	Ooph.	None	Rec. in pelvis at 6 months; no further therapy; died at 13 months
	73	NR	III	6	NR	7	Chemo (not specified)	None	Rec. in pelvis and peritoneum at 2 months; 2° chemotherapy; died at 2 months
	49	NR	Ia	NR	NR	5	TAH BSO Oment.	None	Rec. in pelvis and peritoneum at 44 months; 2° chemotherapy; died at 48 months
Huang *et al*[10]	46	Vaginal bleeding	Ia	8	NR	>5 (>25 in some areas)	TAH RSO	LSO LND Epirubicin/ ifosfamide/ dacarbazine	TF at 72 months
Choi *et al*[11]	44	Abdominal pain	Ia	18	<1%	17	TAH BSO Oment.	Adriamycin/cisplatin	TF at 120 months
	34	Abdominal pain	Ib	13	20%	8	TAH BSO Oment.	Etoposide/ Ifosfamide/ cispatin	TF at 60 months
Ray *et al*[12]	23	Abdominal pain	Ia	25	NR	10-12	Right Ooph.	None	NR
Gultekin *et al*[15]	52	Abdominal pain	Ia	10	9%	3-6	TAH BSO	Patient declined	TF at 12 months
Celyk *et al*[19]	49	Abdominal pain	IIIc	12	NR	>3	TAH BSO Oment.	Paclitaxel/ cisplatin	Rec. in pelvis and liver at 36 months; no further therapy; died at 42 months
Testa *et al*[20]	44	Unknown	IIIb	NR	NR	7	TAH BSO Oment.	Ifosfamide/ adriamycin	TF at 50 months
	50	Unknown	Ia	NR	12%	5-7	TAH BSO Oment.	None	TF at 5 months
Jimenez *et al*[21]	55	Vaginal bleeding	Ic	23	60%	<1-2	TAH BSO Oment.	Ifosfamide/ adriamycin	Rec. in liver at 14 months; secondary surgery; alive with tumor at 14 months
Ozdemir *et al*[22]	50	Abdominal pain	Ia	4	30-40%	5-6	TAH BSO	None	TF at 6 months

NR, not reported; TAH, total abdominal hysterectomy; BSO, bilateral salpingooophorectomy; Oment., omentectomy; Rec., recurrence; Ooph., oophorectomy; RSO, right salpingooophorectomy; LSO, left salpingooophorectomy; LND, lymph node dissection; TF, tumor free.

among documented cases, making it difficult to correlate them to disease progression and survival[1, 10, 11, 18]. Regardless of the lack of independent prognostic factors, overall prognosis for ovarian fibrosarcoma is poor[1, 2, 3]. Early hematologic metastasis is common, and in most cases, there is local recurrence within 2 years of the first diagnosis[1]. Some investigators have seen longer tumor free intervals in patients who had complete resection of a Stage I ovarian fibrosarcoma[10, 11, 18]; however, other authors report recurrence as early as 1 month from initial surgery [3]. Those tumors that behave more aggressively seem to be larger, with higher FIGO stage at initial diagnosis, greater degree of mitotic activity, and higher Ki-67 index. Table 1 details the clinical features and corresponding prognosis of published cases of fibrosarcoma.

Based on the available literature, the widely accepted initial treatment for ovarian fibrosarcoma is primary surgery. The aim of surgery should be optimal tumor debulking, with complete resection of the tumor as a goal. Treatments in case reports have included surgery (ranging from adnexectomy to radical debulking) and, in some cases, adjuvant chemotherapy (with either cisplatin-based combination therapy or a combination of mesna, doxorubicin, ifosfamide, and DTIC)[10, 11, 15, 18, 19]. Investigators in some cases believe that adjuvant chemotherapy may improve long-term survival[1, 10, 11, 19].

Conclusion

Primary ovarian fibrosarcomas are very rare tumors and have a generally poor prognosis. The scarcity of documented cases creates difficulty in establishing prognostic factors. Established management, treatment options or guidelines do not yet exist for this disease. Until larger studies can be performed on a greater number of cases, management of ovarian fibrosarcoma will continue to be individualized.

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