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CASE REPORT

Ovarian fibrosarcoma : A Case Report

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Abstract

This case report aims to report and discuss cases of ovarian fibrosarcoma. Ovarian fibrosarcoma is a rare case that generally occurs in women who have menopause. In the case of ovarian fibrosarcoma, the patient was 43 years old, had two children, and had no complaints during menstruation. The patient has lost weight in the last six months. The patient has performed debulking surgery optimally. On the PA results, it looks macroscopic, a piece of brownish-white tissue, densely rubbery, with a size of 15x12x5 cm, a solid white part is visible, and there is a yellowish-white part and anger, there is a 0.5-1.5 cm cavity filled with a yellowish liquid. On microscopic examination of the tumor, the tissue section appears to consist of a diffuse proliferation of tumor cells with hypercellular and hypocellular areas. Based on the results of macroscopic and microscopic examination of the tumor tissue, a skewed sarcoma is established in fibrosarcoma. The patient underwent chemotherapy after tumor surgery. Although there is no clear consensus on the administration of fibrosarcoma chemotherapy, several published case reports have demonstrated a lower probability of recurrence and a better prognosis in patients undergoing chemotherapy.

***Keywords:** Ovarian fibrosarcoma; Tumor; Chemotherapy*

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PRELIMINARY

Globally, epithelial ovarian cancer still represents the majority of disease (approximately 80%–90%), compared to germ cell tumors and stromal tumors of the genital cord, which are relatively rare. Sex cord-stromal tumors (SCSs) make up nearly 7% of malignant ovarian neoplasms. Ovarian fibrosarcoma accounts for approximately 0.02% of malignant ovarian neoplasms, including borderline tumors.[1] Reported cases of ovarian fibrosarcoma are minimal, and clear diagnostic criteria have not been established.[2] Fewer than 100 cases have been reported to date. [3] Due to the limited number of cases of fibrosarcoma, clear criteria for differentiating them have not been established.[2]

Fibrosarcoma malignant potential is usually based on the cell growth pattern, nuclear atypia, and mitotic rate per 10 hpfs.[2] Although the malignant potential of ovarian fibromas is determined by the number of mitoses, the presence of cellular atypia, and the growth pattern, the clinical and histological distinction between cellular fibroma and fibrosarcoma may be imprecise due to the rarity of cases. [4] The most appropriate treatment has not been determined, and the median survival is less than two years due to early hematogenous metastases and local recurrence. [4]

Ovarian fibrosarcoma is a sporadic tumor, yet to exist without generally agreed treatment guidelines. We present a 43-year-old nulliparous woman with ovarian fibrosarcoma. Optimal debulking surgery is performed, and the tumor specimen is examined. The patient underwent chemotherapy after tumor surgery. Although there is no clear consensus on the chemotherapy of fibrosarcoma, several published case reports have demonstrated a lower probability of recurrence and a better prognosis in patients undergoing chemotherapy.

Primary spindle cell sarcoma is one of the least reported tumors. Based on the Surveillance Database Epidemiology End Results (SEER), only 3299 cases of primary spindle cell sarcoma were identified from 1973–2017, and most of these cases originated in the respiratory system.[5] Ovarian sarcoma is very rare, accounting for less than 3% of ovarian neoplasms. [6] Less than 100 cases of primary ovarian sarcoma have been reported. [7] Patients with ovarian fibrosarcoma usually have poor survival due to distant metastases via the bloodstream and tumor recurrence. [8] Therefore, this disorder is under-studied. We present a case of primary ovarian fibrosarcoma at a relatively young age (regular menstrual cycles) or premenopausal.

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RESULTS

This case of ovarian fibrosarcoma was found in a 43-year-old woman who was a patient sent from the oncology polyclinic at Dr. M. Djamil Padang with a diagnosis of pro-chemotherapy ovarian fibrosarcoma I. The patient complained of decreased appetite, weakness, and weight loss in the last six months. The patient has been married for about 15 years and has two children. The patient had no history of heart, lung, liver, or kidney disease, diabetes mellitus, hypertension, or history of allergies. There is no family history of hereditary, infectious, or psychiatric illnesses. Menstrual history, menarche at 12 years old, regular cycles, 5-7 days duration, and no complaints of pain.

Based on the physical examination results, the blood pressure was relatively high. Namely, 165/102 mmHg and other vital signs were within normal limits. On physical inspection of the abdomen, there was no swelling in the stomach, tenderness, or loss of pain; on percussion tympanic examination and auscultation, normal positive bowel sounds were made. Analysis of the genitals was carried out, a calm V/U was found, and no vaginal bleeding was found. Based on the results of the laboratory conducted on October 10, 2022, there was an increase in platelet levels to 417000 mm3, and the consequences of an examination of Hb, Leukosit, hematocrit, SGOT, SGPT, Ur, and Cr levels were within normal limits, can be seen in table 1. The chest photo obtained results show no abnormalities.

Table 1. Labor Examination Results

Examination	Normal Value	Results
Hb	12 – 16	12,9 gr/dL
Leukosit	5000 - 10.000	8,680 mm3
Trombosit	150.000 - 400.000	417000 mm3
Hematokrit	37 – 43	41%
SGOT	<32	17
SGPT	<31	21
Ur	1-50	28
Cr	0.6-1.2	11.5

The patient had an optimal debulking operation on September 14, 2022. Next, two tissue bags and one site fluid tube were examined, which were carried out at the Anatomical Pathology Section of RSUP Dr. M. Djamil Padang. On the results of PA on September 16,

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2022, the first bag looks macroscopic, a piece of brownish white tissue, densely rubbery, with a size of 15x12x5 cm, a solid white part is visible, and there is a yellowish white part and anger, there is a 0.5-1.5 cm cavity filled with a yellowish liquid, shown in figure 1. Macroscopic appearance of 2 pieces of omentum tissue, in the form of sheets of brownish yellow, dense rubber with a size of 11x8x2 cm, no KGB found, shown in figure 2.

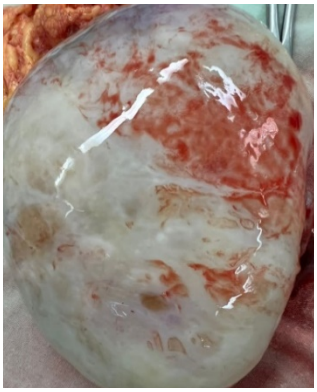

Fig 1 Ovarian fibrosarcoma macroscopic appearance

A piece of brownish-white ovarian tissue measuring 15x12x5 cm

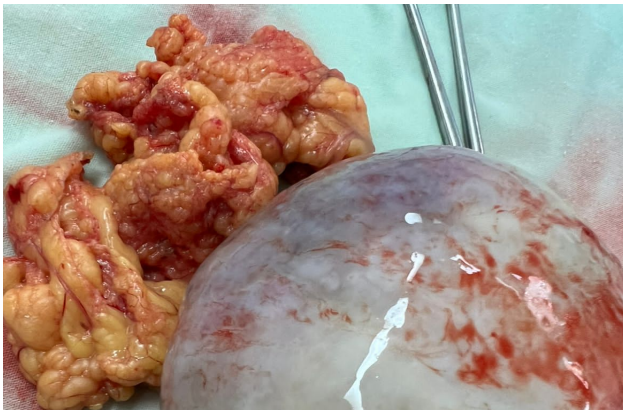

Fig 2 Omentum Tissue Microscopic Image

It looks brownish, has a yellow sheet, and is a thick solid with a size of 11x8x2 cm.

On microscopic examination of the tumor, it appears that pieces of tissue consist of a proliferation of tumor cells that are spread diffusely with hypercellular and hypocellular areas, shown in Figure 3. Based on the macroscopic and microscopic examination of tumor tissue, a skewed sarcoma is established in fibrosarcoma. On microscopic examination of omental tissue, the tissue appears to consist of stroma, fatty tissue, with connective tissue septa, which are partially fibrotic with fibroblast cells that experience dysplasia so that a diagnosis of mild-moderate dysplasia of omental fibroblast cells was established.On microscopic examination of ascitic fluid, the distribution and grouping of cells with round, pleomorphic, and vesicular nuclei, there are apparent nuclei, shown in Figure 4. You can also see the distribution and group of lymphocyte cells. Based on the results of the microscopic examination, the diagnosis of metastases of a tumor in the ascitic fluid was established.

On November 11, 2022, he came to do chemotherapy I. The patient came and said he had no complaints at this time. On the physical examination results, vital signs, abdomen, and genitalia were within normal limits. On November 12, 2022, a follow-up was carried out with the results of a physical examination; vital signs, abdomen, and genitalia were within normal limits. Followed by general condition monitoring and post-chemotherapy treatment, and the

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patient is planned to go home. This case report has received informed consent from the patient for publication.

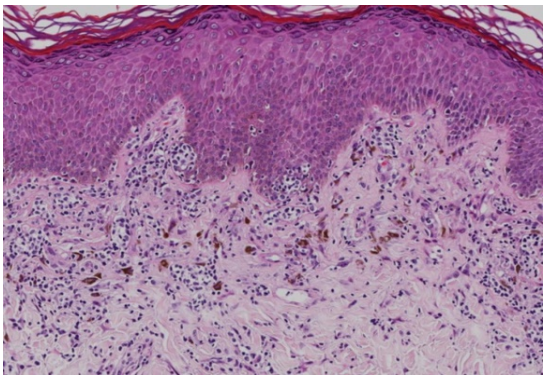

Fig 4 Microscopy of the Ovary

These cells with spindle to pleomorphic nuclei, partly hyperchromatic, partly vesicular, coarse chromatin, distinct nuclei, and apical mitoses found in hypermetric capillaries are also seen.

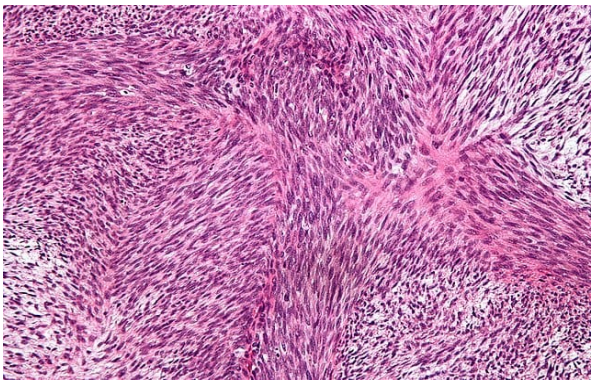

Fig 4 Metastases in Omentum Microscopically

The distribution and grouping of cells with round, pleomorphic, vesicular, and duck nuclei are evident. Also visible distribution and grouping of lymphocyte cells

DISCUSSION

Primary spindle cell sarcoma is one of the least reported tumors. Based on the Surveillance, Epidemiology, and End Results (SEER) database, only 3299 primary spindle cell sarcoma cases were identified between 1973 and 2017, and most of these cases originated in the respiratory system. [1] Ovarian sarcoma is very rare, accounting for less than 3% of ovarian neoplasms.[2] To the best of our knowledge, less than 100 cases of primary ovarian sarcoma have been reported to date.[3] Patients with ovarian fibrosarcoma usually have poor survival due to distant metastases via the bloodstream and tumor recurrence.[4] Therefore, this disorder is still under-studied.

Presented is a case of primary ovarian fibrosarcoma at a relatively young age. Spindle cell sarcoma comprises a group of malignant soft tissue tumors with potentially deleterious growth, local recurrence, and a significant risk of distant metastases. Spindle cell neoplasms characterize it. Spindle cell sarcoma is classified into different subtypes based on their morphology, immunophenotype, genetics, and differentiation. [9] Based on differentiation, spindle cell sarcomas consist of two subgroups: well-differentiated and undifferentiated. Leiomyosarcoma, fibrosarcoma and myofibroblastic sarcoma are examples of well-differentiated spindle cell sarcoma, whereas synovial sarcoma is the most common poorly differentiated spindle cell sarcoma.[9]

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Ovarian fibrosarcoma is very rare. Its origin is believed to be the stromal cells around the sex cord of the ovary. Malignant transformation of fibromas is another possible origin of ovarian fibrosarcoma. Patients with fibrosarcoma are usually menopausal and postmenopausal women who complain of pelvic pain, abdominal enlargement, or a rapidly growing abdominal mass, but can also present with abdominal pain, vaginal bleeding, or pelvic swelling, but in the cases reported, the patient is not yet menopausal. This case occurs at a relatively young age. [9] Summary of reported cases of ovarian fibrosarcoma can be seen in Table 2.

Based on a study of 31 cases of ovarian fibrosarcoma, the median age of patients diagnosed with ovarian fibrosarcoma was 49 years.[10] In later cases, ovarian fibrosarcoma may also appear in children. The youngest patient reported was nine years old and associated with the DICER1 syndrome.

Ovarian fibrosarcoma usually occurs unilaterally and is generally larger and predominately dense, with extensive hemorrhage and necrosis, capsular damage, and infiltrative margins with adhesions to other pelvic organs. Microscopically, ovarian fibrosarcomas have the general characteristics of fibrosarcomas in other organs.[10]. Fibrosarcoma is often associated with trisomy 12 or 18. Ovarian fibrosarcoma usually has a poor prognosis because of early distant metastases and resistance to some adjuvant chemotherapy.[4, 5, 10]

Table 2 Ovarian Fibrosarcoma Case Summary

Author	Age	Immunohistochemistry	Operation	Other therapy	Recurrent	Survive
Huang*dkk*2	46	Spindle cell morphology is arranged in a storiform configuration. There was no marked cellular atypia, hemorrhage, or necrosis. Ki67 no data and mitotic rate >5 per 10 HPF.	TAH, BSO and LND	Kemoterapi (epirubisin/ifosfamid/ dacarbazine)	None	72 bulan (hidup)
Ozdemir*dkk*3	50	Positive and negative vimentin for SMA and desmin. Ki67 30%–40% and mitotic rate 5–6 per 10 HPF.	TAH and BSO	None	None	6 bulan (hidup)
Garcia Jiménez*dkk*5	55	Positive for vimentin and negative for CD117 and SMA. Ki67 60% and mitotic rate <1–2 per 10 HPF.	TAH, BSO and omentektomi	Kemoterapi (ifosfamid/adriamisin)	Yes (14 month, hearth)	14 bulan (hidup)
Gultekin*dkk*6	52	Positive for inhibin, calretinin and SMA, and negative for EMA, CK, desmin and CD10. Ki67 9% and mitotic rate 4 per 10 HPF.	TAH and BSO	None	None	12 bulan (hidup)
lebih hijau*dkk*9	52	Positive for vimentin and negative for h-Caldesmon, inhibin, desmin, myogenin, pan-keratin, p52, and S100. Ki67 60%–70% and mitotic rate >20 per 10 HPF.	TAH and BSO	None (alternative medicine: high doses of vitamin C, glutathione, vitamin B17 and stem cell transfusion)	Yes (3 months, omental and 7 months, flank and abdomen)	15 months (died)

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Prat dan Scully10	61	No data. Ki67 no data and mitotic rate 4 per 10 HPF.	TAH, BSO andomentektomi	Radiasi	Yes (18 months, heart)	18 months (deceased)
	59	No data. Ki67 no data and mitotic rate 8 per 10 HPF.	TAH, BSO andomentektomi	None	Yes (1 month, sigmoid colon)	4 months (died)
	42	No data. Ki67 no data and mitotic rate 25 per 10 HPF.	TAH, BSO and omentektomi	None	Yes (1 month, ureter)	13 months (live)
	65	No data. Ki67 no data and mitotic rate 10 per 10 HPF.	Ooforektomi	None	Yes (6 months, hip)	13 months (died)
	73	No data. Ki67 no data and mitotic rate 7 per 10 HPF.	No	Chemo (unspecified)	Yes (2 months, pelvis and peritoneum)	2 months (died)
	49	No data. Ki67 no data and mitotic rate 5 per 10 HPF.	TAH, BSO and omentektomi	None	Yes (44 months, pelvis and peritoneum)	48 months (died)
Choi*dkk*14	44	Positive for vimentin and negative for SMA and S100. Ki61 <1% and mitotic rate 17 per 10 HPF.	TAH, BSO and omentektomi	kemoterapi (Adriamisin / cisplatin)	No	120 months (life)
	34	Positive for vimentin and negative for SMA and S100. Ki67 20% and mitotic rate 8 per 10 HPF.	TAH, BSO and omentektomi	kemoterapi (Etoposide/ifosfamid/ cisplatin)	No	60months (life)
sinar*dkk*18	23	Positive for vimentin and CD34. Ki67 no data and mitotic rate 10–12 per 10 HPF.	Ooforektomi right	None	No reported	No reported
Celýk*dkk*19	49	Positive for vimentin and S100 and negative for desmin. Ki67 is not reported and the mitotic rate is 4 per 10 HPF.	TAH, BSO and omentektomi	kemoterapi (paclitaxel/cisplatin)	Yes (36 months, hip and heart)	42 months (died)
Testa*dkk*20	44	Positive for vimentin and inhibin. Ki67 no data and mitotic rate 7 per 10 HPF.	TAH, BSO and omentektomi	kemoterapi (ifosfamid/adriamycin)	No	50months (life)
	50	Positive for vimentin and inhibin. Ki67 12% and mitotic rate 5-7 per 10 HPF.	TAH, BSO and omentektomi	None	No	5months (life)
Fukuda*dkk*21	54	Positive for vimentin and weakly positive for -inhibin. Ki67 5.4%–8.2% and mitotic rate 3–6 per 10 HPF.	Ooforektomi right	None	Yes (14 months, hip)	22 months (life)
Grauso*dkk*22	58	Positive for vimentin, SMA and calretinin and negative for CD34, CD3, TAH, BSO and CK and EMA. Ki67 20% and mitotic rate 7-8 per 10 HPF	omentektomi	None	No	24 months (life)
Melendez-Zajgla*dkk*11	9	Positive for vimentin and negative for inhibin. Ki67 no data and mitotic rate 4 per 10 HPF.	Eksisi tumor (no reported)	No reported	No reported	No reported

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In contrast to the case of epithelial ovarian cancer, there is no universally accepted screening procedure for gynecological sarcoma. Prat and Scully[11] concluded that the mitotic index is the most crucial factor for diagnosing fibrosarcoma because the assessment of nuclear and cellular pleomorphism is unreliable. They stated that a benign cellular fibroma has a mitotic index of 1–3/10 HPF, whereas a mitotic index of 4/10 HPF should be defined as a malignant fibrosarcoma. [12] The finding in our patient, defined as malignant based on microscopic findings, was a diffusely distributed proliferation of tumor cells with areas of hypercellular and hypocellular after optimal debulking surgery. However, a study by Huang et al [6] demonstrated that the mitotic index is not the only prognostic predictor of ovarian fibrosarcoma. Studies show that in patients with a low mitotic index (<4), distant metastases may also occur in a short time and, therefore, suggest that there are other factors for patient survival.[6]

Guidelines for the treatment of ovarian fibrosarcoma have not been developed. As Miles, et, al also said, fibrosarcoma is treated with optimal surgery because it is not sensitive to chemotherapy and radiation.[13,14] However, some literature shows that chemotherapy or radiation can prolong patient survival. Most extended patient survival was reported by Choi et al[15] which included two cases of primary ovarian fibrosarcoma with prolonged survival after treatment with chemotherapy after surgery. One point was free of disease, without evidence of recurrence, ten years after diagnosis, and the other remained disease free five years later. The chemotherapy regimens used were adriamycin/cisplatin and etoposide/ifosfamide/cisplatin.[15]

The Gynecologic Cancer Inter Group consensus for ovarian sex cord-stromal tumors states that postoperative chemotherapy is recommended for advanced or metastatic cancer and relapses, with a regimen of bleomycin, etoposide, and cisplatin for three to six cycles or carboplatin/paclitaxel.[16,17] However, this recommendation was made by studying granuloma cell tumors as the most common sex cord-stromal tumors. It is unclear whether these recommendations apply to ovarian fibrosarcoma because it belongs to a different subclassification.

The prognosis for ovarian fibrosarcoma is generally poor, and patients with this fibrosarcoma usually do not survive long after surgery. A study by Huang et al., which included 31 ovarian fibrosarcoma patients, showed the median overall patient survival was 42 months, and the median disease-free survival was 18 months. Huang et al. and Choi et al. reported several cases of ovarian fibrosarcoma with long-term survival.

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However, no prognostic factors for ovarian fibrosarcoma have been established due to the rarity of the disease. According to the most extensive study of ovarian fibrosarcoma conducted by Huang et al., the FIGO stage and treatment are independent prognostic factors for survival. Previously International Federation of Gynecology and Obstetrics (FIGO) Staging at diagnosis (FIGO stage IA-IC) was associated with better survival compared to more advanced stages (HR 0.231; 95% CI 0072 to 0743). Total hysterectomy with bilateral adnexectomy and omentectomy with chemotherapy after surgery is preferred over other treatment combinations because they are associated with better survival.

Our patient was diagnosed with fibrosarcoma histopathologically. These factors may contribute to the poor prognosis of our patients. Our patient underwent chemotherapy of six planned cycles. Although there is no substantial evidence to support the use of adjuvant chemotherapy or radiation therapy, the previously mentioned studies support adjuvant chemotherapy for better survival. Therefore, we recommend personalized adjuvant chemotherapy in cases of ovarian fibrosarcoma due to insufficient evidence supporting a particular regimen.

CONCLUSION

1. Ovarian fibrosarcoma is a rare entity. Although the diagnostic criteria were established in 1981, less than 100 cases have been reported.
2. The diagnosis of ovarian fibrosarcoma is made by exclusion. The clinician must exclude other tumors with spindle cell appearance by immunohistochemical staining.
3. There is no clear evidence to support the use of adjuvant chemotherapy or radiation to treat ovarian fibrosarcoma. However, the available studies suggest that adjuvant chemotherapy can prolong patient life.

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