CASE REPORT

Nagoya J. Med. Sci. **81**. 171–176, 2019
doi:10.18999/nagjms.81.1.171

Estrogen producing ovarian fibrosarcoma: A case report

Mayo Miura[1], Shiro Suzuki[1], Kiyosumi Shibata[2], Hiroaki Kajiyama[1], and Fumitaka Kikkawa[1]

[1]*Department of Obstetrics and Gynecology, Nagoya University Graduate School of Medicine, Nagoya, Japan*
[2]*Department of Obstetrics and Gynecology, Banbuntane Hotokukai Hospital, Fujita Health University, Nagoya, Japan*

ABSTRACT

Fibrosarcoma is an extremely rare malignant sex-cord stromal tumor. Fibrosarcoma is generally unknown as an estrogen producing tumor. This report presents, for the first time, a case of estrogen producing ovarian fibrosarcoma in an 83-year-old female. We performed total hysterectomy, bilateral salpingo-oophorectomy and omentectomy. Histopathologically, the tumor of the left ovary had high cellularity, cellular atypia and 10–15 mitotic counts per 10 high power fields. The tumor contained small components composed of cells that were similar to Sertoli cells. In an effort to examine which component was producing estrogen, we checked aromatase expression; but both components were positive. We could not explain which component was producing estrogen. Postoperative clinical stage was IA. As she was geriatric patient, we did not recommend adjuvant chemotherapy. There were no signs of recurrence or increase in serum estradiol level at two years after the operation.

Keywords: fibrosarcoma, estrogen producing tumor, sex-cord stromal tumor, aromatase

INTRODUCTION

Sex-cord stromal tumors account for almost 7% of malignant ovarian neoplasms.[1] Furthermore, it has been reported that ovarian fibrosarcomas account for approximately 0.02% of malignant ovarian neoplasms including borderline tumors.[2] Ovarian fibrosarcoma is a considerably rare tumor, thereby its clinical pathology is unknown. Within sex-cord stromal tumors, although granulosa cell tumors, thecoma, and Sertoli Leydig cell tumors are well known as estrogen producing tumors, fibrosarcoma is not. We experienced a case of ovarian fibrosarcoma which was producing estrogen, and we report of this case below.

CASE REPORT

The patient was an 83-year-old parous Japanese female who noticed a palpable lower abdominal mass without pain, gastrointestinal symptoms or vaginal bleeding. Her past medical

Received: May 28, 2018; accepted: August 1, 2018

Corresponding Author: Shiro Suzuki, MD, PhD
Department of Obstetrics and Gynecology, Nagoya University Graduate School of Medicine, 65 Tsuruma-cho, Showa-ku, Nagoya 466-8550, Japan
Tel: +81-52-744-2261, Fax: +81-52-744-2268, E-mail: shiro-s@med.nagoya-u.ac.jp

history included hypertension and spinal canal stenosis. Her family doctor pointed out a large solid mass with transabdominal ultrasound. The size of the tumor was 11 cm × 7.8 cm × 11 cm and motility was well. By magnetic resonance imaging (MRI), there was ovarian tumor exhibiting mild low intensity on T1 and T2 weighted images, and the inside of the tumor had low intensity on the T1 weighted image and high intensity on the T2 weighted image (Fig. 1A, B). An approximately 6 cm intramural myoma and endometrial thickening of the uterine wall were also detected. The endometrial cytological test was negative. Almost the whole tumor was enhanced by contrast-enhanced computed tomography (CT), but the inside part was not enhanced (Fig. 1C). There were no signs of metastasis, lymph node enlargement or ascites. No serum tumor marker was elevated. Pretreatment tumor markers were as follows: CA125 = 16.8 U/ml, CA19–9 = 6.0 IU/ml, CA72–4 = 0.9 IU/ml and CEA = 2.9 ng/ml. However, the sex hormone estradiol (E2) was elevated (60 pg/ml).

We performed laparotomy and the intraoperative rapid diagnosis was fibrosarcoma of the left ovary. Considering she was elderly, we performed total hysterectomy, bilateral salpingo-oophorectomy and omentectomy. There was no peritoneal metastasis. Her serum E2 level had decreased to <10 pg/ml a week after operation.

Grossly, the cut surface of the tumor was softly yellowish and homogenous, and the central

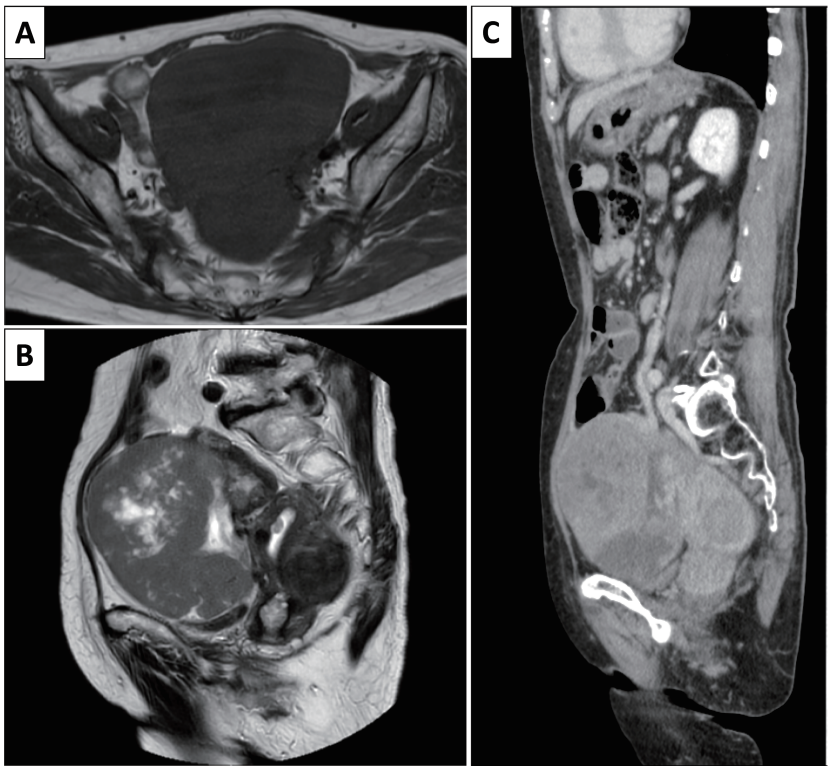

Fig. 1 Imaging findings

T1 weighted (A), and T2 weighted (B) MRI. The tumor was solid and measured 11 cm in diameter. An approximately 6 cm intramural myoma and endometrial thickening of the cervix and corpus uterine were also detected. (C) By contrast CT, the whole tumor was enhanced but the inner part was not enhanced. The left ovarian artery continued to the tumor.

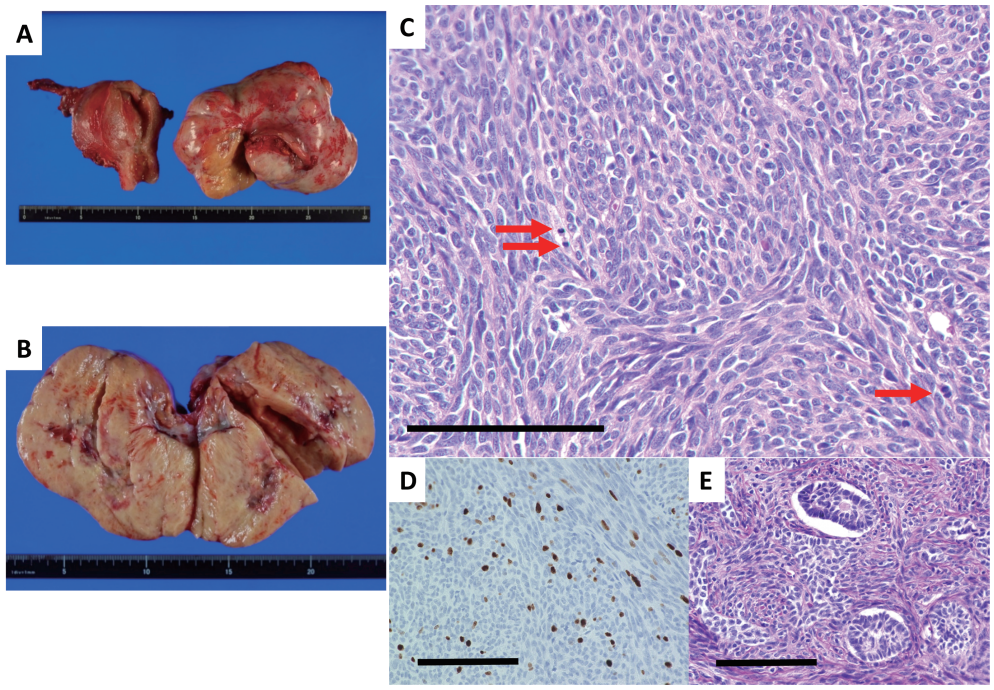

Fig. 2 Macroscopic and histological findings
Macroscopic appearance (A) and the cut surface view (B) of the tumor. It was yellowish, and the inside was suspected liquefactive degeneration. (C) Histological features. A proliferation of spindle cells containing atypical swelled nuclei and high cellularity was observed. The mitotic count was 10–15 per 10 HPFs (arrows: mitosis). (D) The Ki67 proliferation index was 7–8% positive. (E) Another small component composed of cells resembling Sertoli cells. Original magnification, ×400 (scale bars: 200 μm).

part was necrotic (Fig. 2B). Microscopically, a proliferation of spindle cells containing atypical swelled nuclei and high cellularity was observed. The mitotic count was 10–15 per 10 high power fields (HPFs) (Fig. 2C). The Ki67 proliferation index was 7–8% positive (Fig. 2D). The tumor was diagnosed as ovarian fibrosarcoma. Another small component of the tumor contained cells that were similar to Sertoli cells (Fig. 2E). However, the component was too small to diagnose as a Sertoli-Leydig cell tumor. There was no pathological finding that suggested thecoma or granulosa cell tumor. The cytology examination of the peritoneal fluid showed no sign of malignant cells.

For immunohistochemical examination, tissue sections were stained with CD56, inhibin-α, WT-1, calretinin, vimentin, progesterone receptor, estrogen receptor and aromatase. The fibrosarcoma component was positive for CD56, inhibin-α, WT-1, calretinin, vimentin and aromatase, negative for estrogen receptor. The expression of progesterone receptor in the fibrosarcoma component was variable. It was negative to diffuse positive, but strong positive in particular around the cells similar to Sertoli cells. On the other hand, the small component containing cells similar to Sertoli cells was positive for inhibin-α, WT-1, calretinin, vimentin and aromatase, and negative for CD56, progesterone receptor and estrogen receptor (Fig. 3). The contralateral ovary was negative for aromatase.

This case was diagnosed as fibrosarcoma of the left ovary. The clinical FIGO (International Federation of Gynecology and Obstetrics) stage was IA. As the patient was elderly, she did not

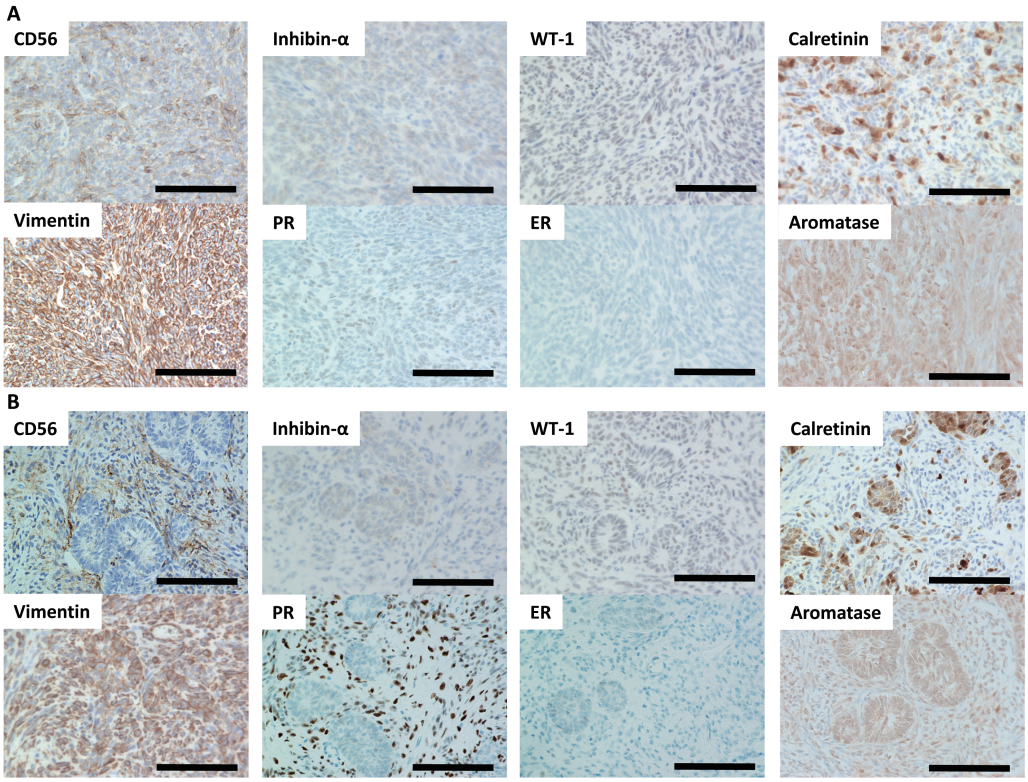

Fig. 3 Immunohistochemical findings
Immunohistochemical examination of the major component that was diagnosed as ovarian fibrosarcoma (A) and minor component that was similar to Sertoli cells (B). Original magnification, ×400 (scale bars: 200 μm).

receive adjuvant chemotherapy. There were no signs of recurrence or increase of serum E2 level at two years after the operation.

DISCUSSION

Ovarian fibrosarcoma is a rare tumor and natural estrogen production by fibrosarcomas is also a rare phenomenon. According to a report by Prat J et al, there was no evidence of estrogen overproduction in any of the 16 ovarian fibrosarcoma cases. The patients with ovarian fibrosarcoma ranged in age from teenagers to over 80 years old.[3] Our patient was an elderly female. Although she did not complain of vaginal bleeding, we observed a myoma and endometrial thickening on transvaginal ultrasonography. Therefore, we checked the cytological examinations of the uterine cervix and corpus; both results were negative. These observations were derived from estrogen overproduction. Fibroma are thought to be deficient in secreting estrogen; however, Foth D et al reported a case in which a bilateral ovarian fibroma and endometrial adenocarcinoma of the uterine corpus were secreting E2.[4] Moreover, two case reports were published in which ovarian epithelial carcinoma produced estrogen.[5,6] Therefore, it does not seem so peculiar that ovarian fibroids produce E2. E2 is generally secreted by thecoma cells,[1] but there were no pathological findings suggesting thecoma or granulosa cell tumor in this case. In an effort to examine which

component was producing E2, we checked aromatase expression; however, both components were positive. We could not determine which component was producing E2. Intratumoral production of aromatase does not necessarily mean ectopic estrogen production. The estrogenic effect by the tumor could be explained by hidden Leydig-cell tumor. To our knowledge, this report presents, for the first time, a patient with an estrogen producing ovarian fibrosarcoma.

Ovarian stromal tumors tend to express CD56, inhibin-α, WT-1, calretinin and vimentin. Both components in this case exhibited features of sex cord stromal tumors. Grauso F et al reported the immunophenotype of ovarian fibrosarcomas; 47% were inhibin-α positive, 17% were progesterone receptor positive and 17% were estrogen receptor positive.[7] The immunophenotype of this case corresponded with ovarian stromal tumors. As Sertoli-stromal cell tumors have hollow tubules, it is not rare to be misdiagnosed as endometrioid adenocarcinoma. Ohishi Y et al reported that sertoli-stromal cell tumors were CD56 positive, but no immunoreactive cells were observed in endometrioid adenocarcinoma.[8] The small component in this case was thought to be different from endometrioid adenocarcinoma.

The diagnostic criteria of fibrosarcoma are generally that the mitotic counts are 4 or more per 10 HPFs,[3] and tumors containing 1–3 mitotic figures per 10 HPFs are suggested to be fibroma. In our patient's case, the tumor contained 10–15 per 10 HPFs. The MIB-1 index of this case was 7–8%. In a previous report, the MIB-1 labelling index for cellular fibromas ranged from 0.5 to 4.0 with a median of 2.3, while that for fibrosarcoma ranged from 3.0 to 10.8 with a median of 6.6.[7] The Ki-67 index was considered to improve the accuracy of the diagnosis, but was not found to be a prognostic factor for survival. Huang L et al reported that FIGO stage and treatment modality, particularly total hysterectomy, bilateral adnexectomy and an omentectomy followed by adjuvant chemotherapy, may be prognostic factors for patients with ovarian fibrosarcoma.[9] There have been limited reports demonstrating survival benefits of adjuvant chemotherapy in patients with ovarian fibrosarcoma. Moreover, there is no evidence for adjuvant chemotherapy regimens or the optimal number of cycles. We did not recommend adjuvant chemotherapy due to stage IA and her age. Accumulation of more ovarian fibrosarcoma cases is needed.

DISCLOSURE

The authors declare no conflicts of interest associated with this manuscript.

REFERENCES

1 Colombo N, Parma G, Zanagnolo V. Management of ovarian stromal cell tumors. *J Clin Oncol*. 2007;25:2944–2951.
2 Aoki D. Annual report of gynecologic oncology committee, Japan society of obstetrics and gynecology, 2013. *J Obstet Gynaecol Res*. 2014;40:338–348.
3 Prat J, Scully RE. Cellular fibromas and fibrosarcomas of the ovary: a comparative clinicopathologic analysis of seventeen cases. *Cancer*. 1981;47:2663–2670.
4 Foth D, Nawroth F, Schmidt T, et al. Bilateral ovarian fibromas and endometrial adenocarcinoma in a postmenopausal patient with growing were uterine myomas. *Maturitas*. 2001;39:259–264.
5 Tokunaga H, Akahira J, Suzuki T, et al. Ovarian epithelial carcinoma with estrogen-producing stroma. *Pathol Int*. 2007;57:285–290.
6 Katoh T, Yasuda M, Hasegawa K, et al. Estrogen-producing endometrioid adenocarcinoma resembling sex cord-stromal tumor of the ovary: a review of four postmenopausal cases. *Diagn Pathol*. 2012;7:164.
7 Grauso F, Messalli EM. Ovarian fibrosarcoma: case report and latest trends in diagnostic and therapeutic management. *Eur J Gynaecol Oncol*. 2015;36:742–745.
8 Ohishi Y, Kaku T, Oya M, et al. CD56 expression in ovarian granulosa cell tumors, and its diagnostic

utility and pitfalls. *Gynecol Oncol*. 2007;107:30–38.

9 Huang L, Liao LM. Clinicopathologic characteristics and prognostic factors of ovarian fibrosarcoma: the results of a multi-center retrospective study. *BMC Cancer*. 2010;10:585.