Mitotically active cellular fibroma of the ovary: a case report and a review of the literature

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Summary

Mitotically active cellular fibroma (MACF) is characterized by increased cellularity, mitotic activity, and less frequently, nuclear atypia, which comprises 10% of ovarian fibromatous tumors. The authors report the case of a 76-year-old woman who presented at the present hospital with a two-month pelvic mass. B ultrasound disclosed a 75 × 52 × 41 mm mass in the right accessories. A hysterectomy and bilateral salpingo-oophorectomy was performed. Histologically, the tumor was composed of a densely cellular proliferation of fibrolastic-like cells with bland nuclear features and arranged in a fascicular pattern. There were more than four mitotic figures per ten high-power fields (HPFs). The histological diagnosis for the mass of the right ovary was MACF. MACF should be distinguished from ovarian fibrosarcoma. MACF is a recent histopathologic entity. Despite the high count of mitotic figures, the clinical course of the tumor is typically uneventful. Long-term clinical follow-up is recommended.

Key words: Ovary; fibroma; Mitotically active cellular fibroma; Outcome.

Introduction

Fibromatous tumors of the ovary are comprised predominantly of fibroma, cellular fibroma, mitotically active cellular fibroma (MACF) and fibrosarcoma [1]. The majority of these neoplasms are benign fibromas and the diagnosis is usually straightforward. The MACF is defined by increased cellularity, mitotic activity, and less frequently nuclear atypia, which should be distinguished from fibrosarcoma as their prognosis and therapy are different [2]. Since the first report described by Irving et al., only three cases have been reported to date [3-5]. Herein, the authors report a patient with a rare ovarian fibrous tumor with a large number of mitotic figures but without severe nuclear atypia.

Case Report

A 76-year-old woman presented with a two-month pelvic mass and requested gynecological consultation. B ultrasound in the locality revealed a 75 × 52 × 41 mm liquid dark area in the right adnexa and the capsule was intact. The patient was then admitted to the present hospital and B ultrasound was repeated. Ultrasound examination showed an irregular low-echo mass measuring 77 × 44 × 62 mm on the right adnexa, which containing fairly abundant, cord-like color blood stream, and irregular echo (Figure 1). The mass had an indistinct capsule. The right adnexa tumor was considered. Serum levels of tumor markers including CA125, CA153, CA199, AFP, CEA, and SCC were within the normal range.

At laparotomy, a 6 × 5 × 5cm solid, grey-white and smooth mass was was detected in the right ovary. The right oviduct, the left ovary and oviduct, and the uterus appeared normal. No ascitic fluid and peritoneal dissemination were observed. Right adnexectomy was performed. Intraoperative frozen section of the right adnexa confirmed an ovarian malignant tumor consistent with Sertoli-Leydig stromal cell tumor. Subsequently, a hysterectomy and bilateral salpingo-oophorectomy were performed.

Macroscopically, the tumor was 9 × 6 × 5 cm and firm, fibrous, well-demarcated. The external surface was smooth. On cut surface, the tumor was grey-white in colour without gross necrosis and hemorrhage. Microscopically, the tumor was comprised predominantly of densely spindle fibroblastic-like cells with focal edematous areas (Figures 2a, 2b). The spindle cells arranged in intersecting fascicles with mild nuclear atypia (Figure 2c). The cells had scant cytoplasm and indistinct borders and nucleoli. Interestingly, the mitotic index varied from five to nine per ten high-power fields (HPF) (Figure 2d). Immunohistochemical analysis showed that tumor cells were positive for vimentin, alpha-inhibin (Figure 3), ER, PR, and focally for CD56 and CD99, while cytokeratin, EMA, CD10, HMB45, S-100, calretinin, CD34, CD117, and Dog-1 were negative. The Ki-67 labeling index reached up to 10%.

Discussion

Ovarian stromal tumors are comprised of a pure proliferation of fibroblastic cells usually consisting of fibromas, cellular fibromas (CFs), and hardly ever of fibrosarcomas [1]. The majority of these neoplasms are benign fibromas and rarely pose any diagnostic difficulty and are readily considered benign in most cases. However, about 10% of fibromatous tumours exhibit increased cellularity, mitotic activity, and less frequently, nuclear atypia [4]. The presence of one or a combination of these features may result in difficulty to classify a case within the group of fibromatous tumors. In 1981, Prat and Scully studied 17 cellular fibrothecomatous lesions of the ovary and identified the mitotic count as the most important feature for distinguishing between benign and malignant lesions [6]. They

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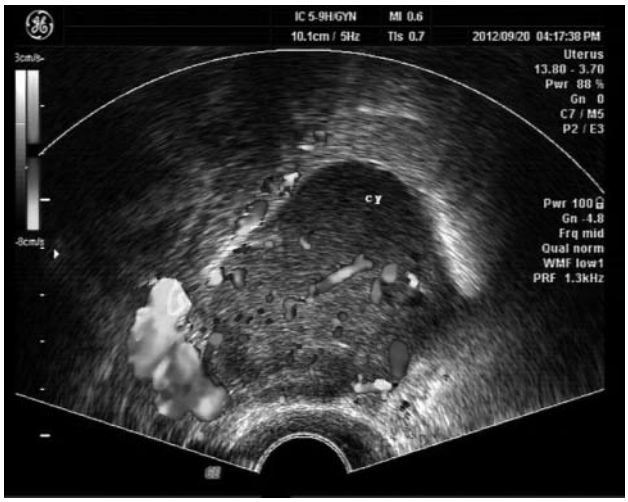

Figure 1. — B ultrasound showing an irregular low-echo mass measuring 77 × 44 × 62 mm on the right adnexa, which containing fairly abundant, cord-like color blood stream and irregular echo.

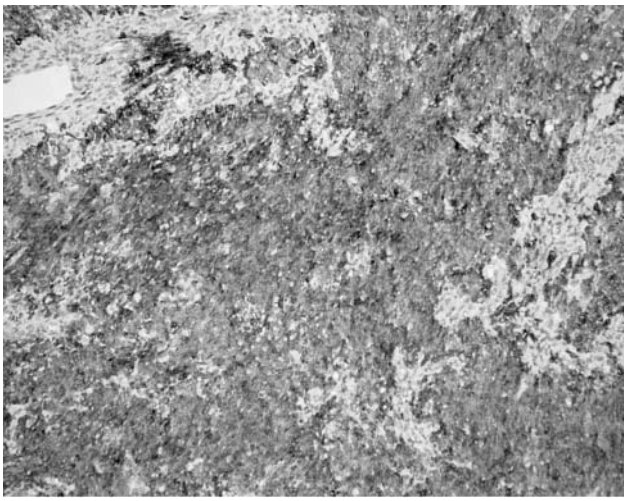

Figure 3. — Tumor cells immunoreactive with alpha-inhibin.

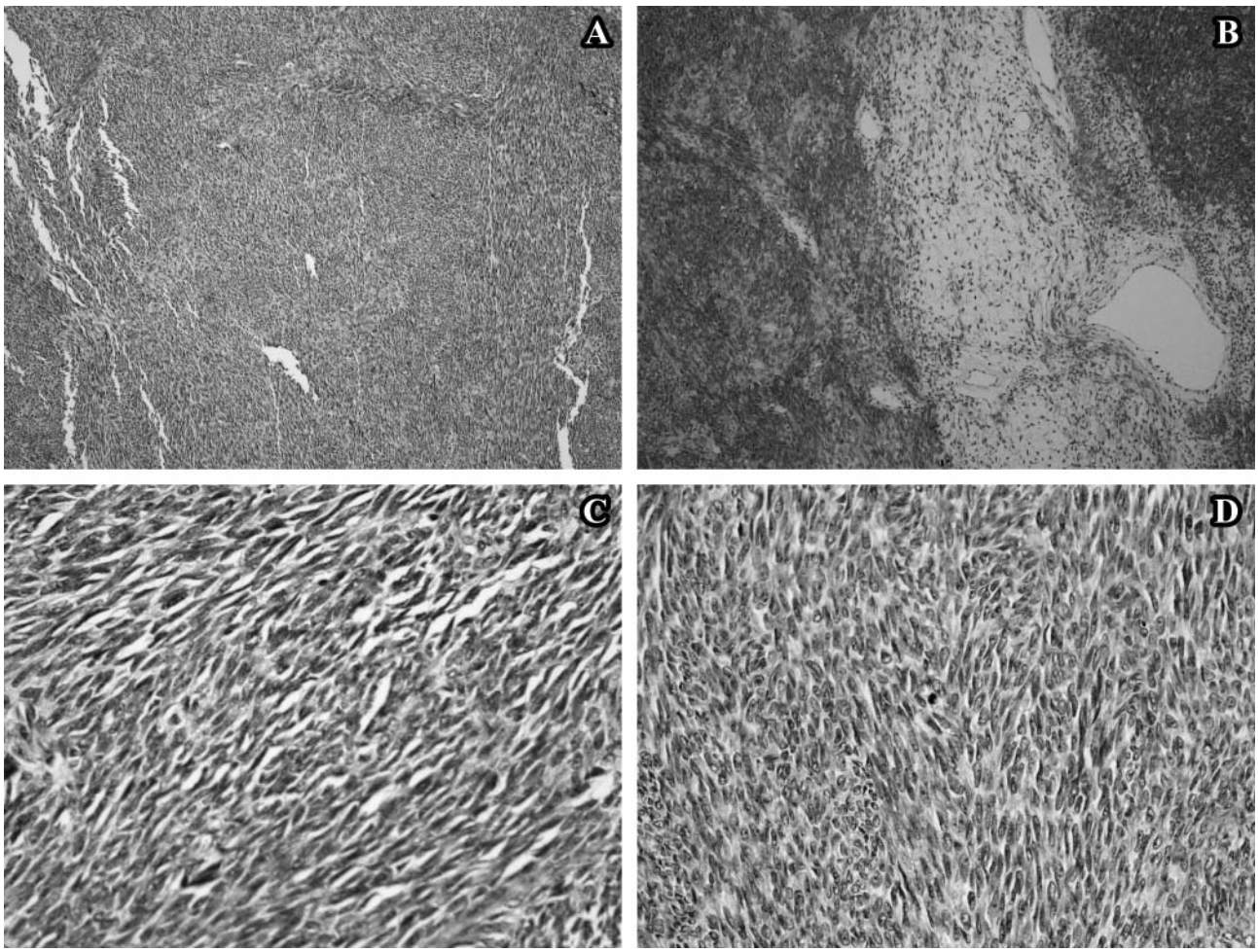

Figure 2. — Histopathologic features of MACF. a) tumor is composed predominantly of densely spindle fibroblastic-like cells which is arranged in intersecting fascicles. b) Focal edematous and sparse cell areas are seen within the tumor. c) On high-power field, the tumor cells are spindle with oval or spindle nuclear and scant cytoplasm, but no moderate and severe atypia. d) Mitotic figure can been readily seen within the tumor.

suggested that a tumor containing fewer than three mitotic figures per ten HPFs should be diagnosed as a cellular fibroma whereas a tumor containing more than 4 mitotic figures per 10 HPFs should be diagnosed as a fibrosarcoma. Tsuji *et al*. [7] suggested that the proliferative activity labeled by MIB-1 in tumor cells was an additional useful parameter for distinguishing between fibromas and fibrosarcomas of the ovary.

Since the Prat and Scully study, subsequent ovarian fibrosarcoma with a benign clinical course have been reported in the literature. In 2001, Huang et al [8] reported a case of primary ovarian fibrosarcoma that was free from disease for six years. In the following year, Cinel *et al.* [9] reported a 45-year-old postmenopausal woman with ovarian fibrosarcoma which showed densely cellular and average six mitotic figures per ten HPFs. The patient had shown no evidence of recurrent disease for five years. Choi *et al*. [10] in 2006 reported two cases of primary ovarian fibrosarcoma. After surgery, both patients received several courses of combination chemotherapy. Neither patient demonstrated any evidence of disease recurrence during follow-up for ten years and five years, respectively. These collecting cases showed the diagnosis was based primarily on a mitotic count of four or more mitotic figures per 10 HPFs, not more than nuclear atypia showing mild to moderate atypia in these reported cases.

In a 2006 study, Irving *et al*. [2] reviewed 75 cases of cellular fibroma of the ovary and they found 40 cases of celluler fibroma characterized by four or more than mitoses per ten HPFs but with no or mild atypia and were classified as MACF. The entity had an uneventful clinical outcome except for local recurrence in three cases which they presented with ovarian surface adhesions or extraovarian involvement.

Since the first study published by Irving *et al*. in 2006, only three cases of MACF have been reported to the best of the authors' knowledge. Kaku *et al*. [3] in 2007 reported a unique fibrous tumor of the ovary which showed two-circumscribed component. Of the component, there were 17 mitotic figures per 10 fields HPFs but no obvious atypia which consistented with MACF. The patient had shown no evidence of the disease for one year after surgery. In 2009, Bucella *et al*. reported a case of MACF with recurrence accurring six years after primary surgery [4]. Monterio *et al*. [5] in 2012 reported a 13-year-old girl with significant ascites who was not given any additional treatment and was remained well with no signs of recurrence after 3 years of follow-up. These results further suggested that MACF was associated with a favorable outcome.

Considering the benign nature of MACFs, a more aggressive treatment was not recommended. However, in the study by Irving *et al*. [2], local recurrence was observed in a small proportion of cases with ovarian surface adhesions/rupture or extraovarian involvement. In addition, long-term local recurrence can also be seen in the MACF case reported by Bucella *et al*. [4], which showed no tumoral rupture or surgical difficulty. Thus, the long-term clinical follow-up is recommended.

Since current experience with primary ovarian MACF is so highly limited, treatment modalities are still not well established. Regular follow-ups with transabdominal pelvic ultrasound every six to 12 months seems reasonable. Besides, prognostic factors for MACF have also not yet been characterized, thereafter, further studies with a large number of cases are required for the identification of prognostic factors for ovarian MACF.

References

[1] Irving J.A., McCluggage W.G.: "Ovarian spindle cell lesions: a review with emphasis on recent developments and differential diagnosis". *Adv. Anat. Pathol.*, 2007, *14*, 305.

[2] Irving J. A., Alkushi A., Young R. H., Clement P. B.: "Cellular fibroma of the ovary. A study of 75 cases including 40 mitotically active tumors emphasizing their distinction from fibrosarcoma". *Am. J. Surg. Pathol.*, 2006, *30*, 929.

[3] Kaku S., Takeshima N., Akiyama F., Furuta R., Hirai Y., Takizawa K.: "A unique fibrous tumor of the ovary. Fibrosarcoma or mitotically active cellular fibroma?". *Anticancer. Res.*, 2007, *27*, 4365.

[4] Bucella D., Limbosch J., Buxant F., Simon P., Fayt I., Anaf V., No l JC.: "Recurrence of mitotically active cellular fibroma of the ovary". *Obstet. Gynecol. Int.*, 2009, *2009*, 803062. doi: 10.1155/2009/803062. Epub 2009 Jan 12.

[5] Monterio S.B., Costa A., Paiva V.: " Mitotically active cellular ovarian fibroma with Meigs syndrome and elevated CA-125. Towards fertility preservation". *Pediatr. Adolesc. Gynecol*., 2012, *25*, e107.

[6] Prat J., Scully R. E.: "Cellular fibromas and fibrosarcomas of the ovary: a comparative clinicopathologic analysis of seventeen cases". *Cancer*, 1981, 47, 2663.

[7] Tsuji T., Kawauchi S., Utsunomiya T., Nagata Y., Tsuneyoshi M.: " Fibrosarcoma versus cellular fibroma of the ovary: a comparative study of their proliferative activity and chromosome aberrations using MIB-1 immunostaining, DNA flow cytometry, and fluorescence in situ hybridization". *Am. J. Surg. Pathol.*, 1997, *21*, 52.

[8] Huang Y. C., Hsu K. F., Chou C. Y., Dai Y. C., Tzeng C. C.: "Ovarian fibrosarcoma with long-term survival: a case report". *Int. J. Gynecol. Cancer.*, 2001, *11*, 331.

[9] Cinel L., Taner D., Nabaei S. B., Oquz S., Gökmen O.: "Ovarian fibrosarcoma with five-year survival: a case report". *Eur. J. Gynaecol. Oncol*., 2002, *23*, 345.

[10] Choi W. J., Ha M. T., Shin J. K., Lee J. H.: "Primary ovarian fibrosarcoma with long-term survival: a report of two cases". *J. Obstet. Gynaecol. Res.*, 2006, *32*, 524.

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