# Ovarian fibrothecoma with massive edema

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**Abstract : We report a rare case of ovarian fibrothecoma with massive edema. The patient was a 59-year-old woman with a left ovarian mass measuring 11x10x7 cm. Magnetic resonance images revealed a solid mass showing unhomogeneous content with predominantly high signal intensity on T2-weighted image. Microscopically, the ovarian mass was composed of a cellular area and an edematous hypocellular area. The latter accounted for more than 75% of the tumor. In the cellular area, spindle-shaped or plump tumor cells were randomly distributed or arranged in a fascicular fashion. These cells contained abundant intracytoplasmic lipid. There was dense collagenous connective tissue in the stroma of the cellular areas. In contrast, in the edematous areas spindle or stellate cells were scattered. Alcian blue stain revealed only a small amount of stromal mucin even in the edematous areas. The microscopic findings were consistent with that of fibrothecoma with massive edema. The present case must be differentiated from massive edema of the ovary and sclerosing stromal tumor of the ovary. Immunohistochemistry was not helpful in distinguishing them. The age of the patient and careful histologic observation are important. J. Med. Invest. 47 : 148-151, 2000**

***Key words*** **:** *thecoma, fibroma, myxoma, stromal cell, edema*

## INTRODUCTION

Both thecoma and fibroma of the ovary are included in stromal tumors of the ovary. Thecoma is histologically composed of lipid-containing cells that resemble theca interna cells. Fibroma is composed entirely or almost entirely of spindle, oval, or round cells forming variable amounts of collagen. The differentiation between thecomas and fibromas is occasionally imprecise because of the histological and immunohistochemical overlap between them. Therefore, the term" fibrothecoma "has been frequently used (1). Ovarian tumors of the thecoma-fibroma group have been reported to show myxoid change or degeneration (2,3). Recently, we encountered a case of fibrothecoma with massive edematous change, which was difficult to distinguish from massive edema of the ovary, ovarian myxoma, and sclerosing stromal tumor. Although varying degrees of intercellular edema may be observed in fibrothecoma (1), the edema in the present case was excessive. We herein report this rare case and discuss the differential diagnosis.

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## CASE REPORT

The patient was a 59-year-old Japanese woman with a complaint of abdominal discomfort without pain. She reached menopause at 45 years of age. Magnetic resonance images (MRI) revealed a grip-sized, well-demarcated, solid mass in the front of the uterus. Unlike typical fibroma and fibrothecoma (4), the mass showed unhomogeneous content with predominantly high signal intensity on T2-weighted MRI, indicating an abundant fluid component (Figure 1). Laboratory examination of the serum related with hormonal activity was not performed, because she clinically showed no abnormal hormonal state. Under

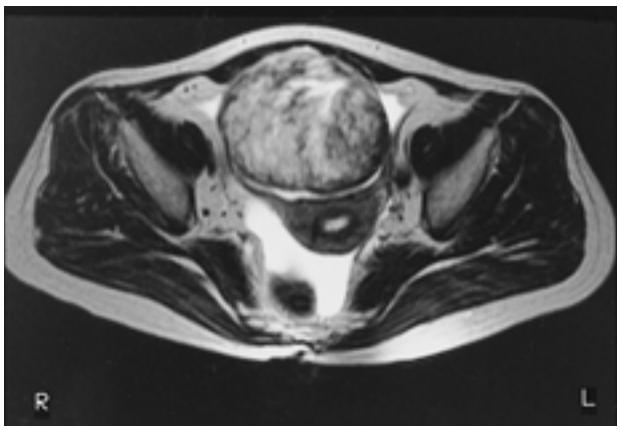


Fig. 1. Magnetic resonance images show an unhomogeneous mass with predominantly high signal intensity on T2-weighted image.

the diagnosis of ovarian tumor, hysterectomy and bilateral oophorectomy were performed. The operation revealed a left ovarian mass without adhesion to the surrounding tissues and clear yellowish ascites measuring 200 ml.

## PATHOLOGIC FINDINGS

Grossly, the resected left ovary weighed 590 g, and contained a solid mass measuring 11x10x7 cm. The mass occupied most of the left ovary and compressed normal ovarian tissue to the periphery (Figure 2). The border between the mass and the normal ovary was clear, but it was not encapsulated. The cut surface of the mass was whitish-gray in color, and showed a fascicular pattern. There was no evidence of myxoid appearance, hemorrhage, or necrosis. The right ovary was of normalsize, and no myxoedematous change was seen. The uterus and bilateral fallopian tubes were grossly unremarkable.

The resected ovaries, fallopian tubes and uterus were fixed in buffered 10% formalin, embedded in paraffin and cut at 4 μm thickness. Microscopically, the left ovarian mass was composed of a cellular area (Figure 3) and an edematous hypocellular area (Figure 4). The latter accounted for more than 75% of the tumor. In the cellular area, spindle-shaped or plump tumor cells were ramdomly distributed or arranged in a fascicular fashion. These cells contained abundant intracytoplasmic lipid, demonstrated by oil red-O stain. Reticulin fibers were rich in this area, and partially showed a box-in-appearance pattern. There was dense collagenous connective tissue in the stroma of the cellular areas. In contrast, in the edematous area spindle or stellate cells without atypia were scattered. Alcian blue stain revealed a small amount of stromal mucin in both areas. Mitotic figures were not observed. Capillaries showing a hemangiopericytomatous pattern were not observed.

An immunohistochemical study was performed on formalin-fixed, paraffin-embedded sections using the labeled streptavidin biotin (LSAB) method. The

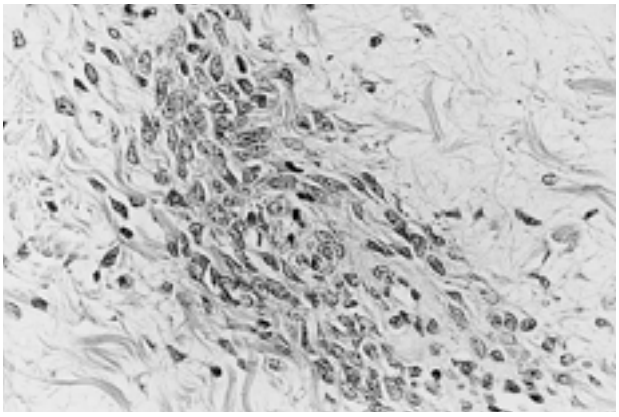

Fig.3. Cellular area shows proliferation of spindle-shaped or plump tumor cells. (HE, ×100)

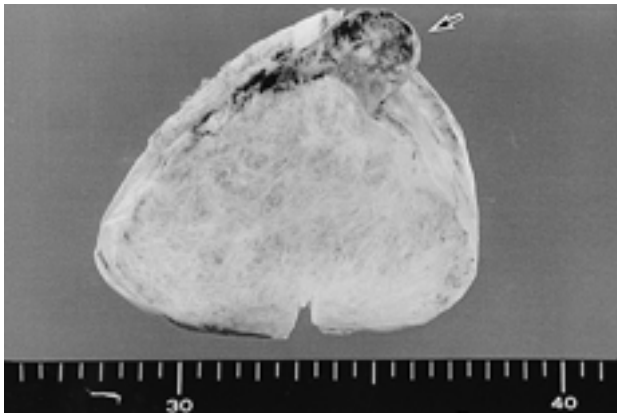


Fig. 2. The mass is clearly demarcated from normal ovary (arrow) and has pushed it to the periphery.

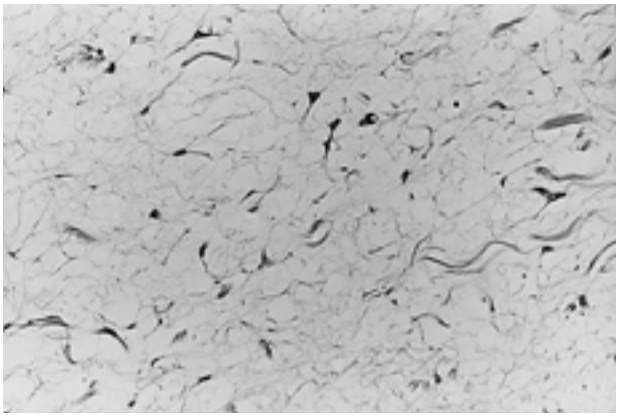

Fig.4. In the edematous area, spindle or stellate cells are scattered. (HE, ×100)

antibodies used in the study are listed in Table 1. Vimentin was positive for more than half of the tumor cells in the cellular area. Alpha-smooth muscle actin (α-SMA) showed positivity in 10% to 20% of the tumor cells in the cellular area, especially in centrally located tumor cells. Progesterone receptor was positive for the nuclei of the tumor cells. Estrogen receptor, desmin and cytokeratin AE1/AE3 were negative. The labeling index of MIB-1 was approximately 0.7%.

## DISCUSSION

Microscopic examination of the thecoma revealed oval or rounded tumor cells with abundant pale or vacuolated cytoplasm. They usually contain moderate to large amounts of lipid demonstrated by an oil red-O stain. The nuclei vary from round to spindle shaped and exhibit little or no atypia. Reticulin stain highlights an investment of individual cells by reticulin fibers, namely a box-in-appearance. Fibroma is composed of spindle, oval or round cells with variable amounts of collagen. The tumor cells may contain small quantities of lipid, similar to that of thecoma. Since the differentiation between thecomas and fibromas is occasionally imprecise due to the histological overlap between them, some have used the designation" fibrothecoma "for tumors in the intermediate zone between thecoma and fibroma (1). The ovarian mass in the present case demonstrated both spindle cells associated with collagen bundles and lipid containing cells with a box-in-appearance which indicate fibroma and thecoma, respectively. Therefore, the histologic findings inthe present case were consistent with fibrothecoma, with the exception of the massive edema.

Edema may be observed in fibrothecoma (1, 2), but fibrothecoma showing massive edema as in the present case is unusual. The massive edema if fibrothecoma may be induced by a stasis of lymphatic drainage, such as massive edema of the ovary (2, 5). A partial intermittent torsion has been thought as a cause. Samanth et al. reported that ovarian tumors larger than 10 cm in diameter tended to be associated with myxoid change, and insisted that a discrepancy between arterial supply and venous and lymphatic drainage could lead to stromal edema.

Fibrothecoma with massive edema must be differentiated from massive edema of the ovary, ovarian myxoma and sclerosing stromal tumor. Massive edema of the ovary is characterized by a proliferation of ovarian stromal cells with marked intercellular edema preserving the overall structure of both the ovarian cortex and medulla, probably secondary to intermittent torsion (5). Massive edema of the ovary almost always contains follicles, corpora lutea and corpora albicantia. The present case displaced such structures. The patient 's age is also important to differentiate between the lesions. Massive edema affects young women with an average age of 22 years (5), whereas 84% of the patients with thecoma are postmenopausal (1). Fibromas occur at all ages, but are most frequent during middle age (1). The age of our patient was not suggestive of massive edema of the ovary.

Ovarian myxoma has recently been reported as a new distinct pathological entity that shows a myxoid, moderate cellular proliferation of spindle and stellate cells interspersed with areas of fibrosis, hemorrhage and delicate vascular spaces (3). Myxoid change has also been reported in fibrothecoma in up to 40% of cases (2). Costa *et al*. insisted that ovarian myxoma may be at one end of the spectrum of differentiation in the thecoma-fibroma group of tumors, because the myxoid change in fibrothecoma was indistinguishable histologically and immunohistochemically

Table 1. Antibody Used for Immunohistochemical Staining

| Antibody | Clone | Dilution | Source |
|---|---|---|---|
| AE1/AE3 | AE1 and AE3 | 1:50 | Dako, Capinteria, USA |
| Desmin | D33 | 1:50 | Dako, Glostrup, Denmark |
| αSmooth Muscle Actin | 1A4 | 1:400 | SIGMA, Saint Louis, USA |
| CD34 | Q-BEND-10 | 1:50 | Novocastia Lab Ltd, Newcastle, UK |
| Factor VIII | F8/86 | 1:50 | Dako, Glostrup, Denmark |
| Estrogen Receptor | ED1D5 | 1:50 | Dako, Marseille, France |
| Progesteron Receptor | PR10A9 | 1:50 | Dako, Marseille, France |
| Vimentin | V9 | 1:20 | Dako, Glostrup, Denmark |
| MIB-1 | MIB-1 | 1:100 | Immunotech, Marseille, France |

from ovarian myxoma (2). The stromal change seen in the present case was mainly edematous. Myxoid change was not prominent, because there was little alcian blue-positive stromal material.

Sclerosing stromal tumors are rare ovarian neoplasms occurring predominantly in young women, and their hypocellular and edematous area may be confused with edematous area of fibrothecoma (8). The histologic features of sclerosing stromal tumor are a pseudolobular pattern of cellular areas and hypocellular areas, prominent vasculature with a hemangiopericytomatous pattern and cellular heterogeneity of vacuolated luteinized theca-like cells and spindle-shaped fibroblast-like cells in the cellular area (8-11). In the present case these findings were not observed.

Immunohistochemistry of fibrothecoma has been described by some studies (3, 8, 10). The tumor cells are strongly positive for vimentin, occasionally and focally positive for $\alpha$-SMA and desmin (3, 8, 10). The nuclei of thecoma cells are also positive for estrogen and progesterone receptors (8). Fibrothecoma is negative for cytokeratin, CEA, EMA, Factor VIII-related antigen, and S-100 protein (8, 10). Immunohistochemical findings in the present case were identical with those previously described with the exception of the negative reactivity for estrogen receptor. However, massive edema and sclerosing stromal tumor also reveal similar reactivity (5, 8, 10). Therefore, an immunohistochemical study is not helpful for distinguishing fibrothecoma from massive edema or sclerosing stromal tumor.

We reported a rare case of ovarian fibrothecoma with massive edema, which must be differentiated from massive edema of the ovary and sclerosing stromal tumor of the ovary. Immunohistochemistry was not helpful in distinguishing between them, however, it was possible histologically to distinguish under careful observation. The age of the patient was also important.

## REFERENCES

1. Scully RE, Youg RH, Clement PB : Tumors of the ovary, maldeveloped gonads, fallopian tube and broad ligament. Washington DC, AFIP, 1996, pp. 189-201
2. Samanth KK, Black WC : Benign ovarian stromal tumors associated with free peritoneal fluid. Am J Obstet Gynecol 107 : 538-45, 1970
3. Costa MJ, Morris R, DeRose PB, Cohen C : Histologic and immunohistochemical evidence for considering ovarian myxoma as a variant of the thecoma-fibroma group of ovarian stromal tumors. Arch Pathol Lab Med 117 : 802-8, 1993
4. Troiano RN, Lazzarini KM, Scoutt LM, Lange RC, Flynn SD, McCarthy S : Fibroma and fibrothecoma of the ovary : MR imaging findings. Radiology 204 : 795-8, 1997
5. Nogales FF, Martin-Sances L, Mendoza-Garcia E, Salamanca A, Gonzalez-Nunez MA, Pardo Mindan FJ : Massive ovarian oedema. Histopathology 28 : 229-234, 1996
6. Turcinov D, Damjanov I : Massive edema of the ovary. Pathol Res Pract 182 : 124-9, 1987
7. Roth LM, Deaton RL, Sternberg WH : Massive ovarian edema. A clinicopathologic study of five casesincluding ultrastructural observations and review of theliterature. Am J Surg Pathol 3: 11-21, 1979
8. Kawauchi S, Tsuji T, Kaku T, Kamura T, Nakano H, Tsuneyoshi M : Sclerosing stromal tumor of the ovary : a clinicopathologic, immunohistochemical, ultrastructural, and cytogenetic analysis withspecial reference to its vasculature. Am J Surg Pathol 22 : 83-92, 1998
9. Shaw JA, Dabbs DJ, Geisinger KR : Sclerosing stromal tumor of the ovary : an ultrastructural and immunohistochemical analysis with histogenetic considerations. Ultrastruct Pathol 16 : 363-77, 1992
10. Saitoh A, Tsutsumi Y, Osamura RY, Watanabe K : Sclerosing stromal tumor of the ovary. Immunohistochemical and electron-microscopic demonstration of smooth-muscle differentiation. Arch Pathol Lab Med 113 : 372-6, 1989
11. Chalvardjian A, Scully RE : Sclerosing stromal tumors of the ovary. Cancer 31 : 664-70, 1973