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Sclerosing stromal tumor of the ovary: Report of a case and review of the literature

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Sclerosing stromal tumor (SST) is an extremely rare and distinctive sex cord stromal tumor, occurring predominantly in the second and third decades of life. In this article, our aim is to present clinicopathologic features of STT, and to review the recent literature with regard to differentiating STT from other ovarian stromal tumors. We describe STT in a 17-year-old girl who presented with an abdomino-pelvic mass and irregular menses. A review of the literature for this rare entity emphasizes the importance of histological confirmation of its benign nature. So conservative surgery should be performed and correct intraoperative diagnosis is important. We suggest that frozen section analysis is able to rule out cancer.

Key words: Sclerosing stromal tumor, ovary, immunohistochemistry, frozen section.

Introduction

Sclerosing stromal tumor (STT) is an uncommon subtype of ovarian stromal neoplasm of the sex cord-stromal category that has distinctive clinical, pathologic and radiological features, which differentiates it from other stromal tumors. The tumor occurs predominantly in the second and third decades and is histologically characterized by a prominent network of thin-walled vessels, sclerosis, heterogeneity of the cellular area and ill-defined cellular pseudolobules separated by a densely hyalinized or markedly edematous stroma.[1]

Most of the reported cases have been unilateral and all SSTs encountered to date have been benign[1–5] (Table 1). So conservative surgery should be performed and correct intraoperative diagnosis is important. We suggest that frozen section analysis is able to rule out malignancy.

Case

A 17-year-old girl with mild hirsutism was admitted to the Department of Obstetrics&Gynaecology of Pamukkale University, for menstrual irregularity, metrorrhagia and pelvic pain during the last four months. Physical examination revealed a large, palpable abdomino-pelvic mass. All tumor markers were below cut-off levels. Serum hormonal levels were normal. Ascites was not present. Medical history of the patient was unremarkable. On ultrasonographic examination, the mass was proved to be solid and cystic and measured approximately 10 cm.

At laparoscopy a yellow, lobulated and well-circumscribed cystic mass was found attached to the lower pole of the right ovary. The left ovary was normal. The mass was diagnosed as benign by frozen section analysis and then removed by laparoscopic salpingo-oophorectomy. Postoperative recovery was uneventful.

The specimen demonstrated an 11x5x4 cm oval, sharply demarcated mass with a smooth and intact

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Table 1. Clinical features of patients with sclerosing stromal tumor (SST) of the ovary.

Case no./ Author	Age	Symptom	Size (max; cm)	Location	Gross appearance
1 Joja, 2001	24	Irregular menses	11,5	Left	Cystic and solid
2	15	Hypermenorrhea	6,5	Left	Predominantly solid
3	30	Irregular menses	7	Left	Predominantly solid
4	17	Hypermenorrhea	7	Left	Cystic and solid
5 Kawauchi, 1998	21	Abdominal mass	17	Right	Cystic
6	28	Abnormal vaginal bleeding	14	Left	Predominantly solid
7	19	Abnormal vaginal bleeding	11	Right	Cystic and solid
8	28	Abnormal vaginal bleeding	5	Right	Predominantly solid
9	45	Abnormal vaginal bleeding	7	Left	Cystic and solid
10	17	Abdominal discomfort	14	Right	Cystic
11	24	Abnormal vaginal bleeding	11	Left	Cystic and solid
12	22	Abnormal vaginal bleeding	4,5	Left	Cystic and solid
13	14	Abdominal discomfort	15	Left	Multicystic and solid
14	24	Abdominal discomfort	7	Right	Cystic and solid
15	29	Abnormal vaginal bleeding	Unknown	Left	Unknown
16	19	Abnormal vaginal bleeding	Unknown	Left	Unknown
17 Ihara, 1999	20	Abnormal vaginal bleeding	7	Left	Cystic and solid
18 Torricelli, 2002	17	Irregular menses	8,5	Left	Predominantly solid
19 Matsubayashi, 1999	19	Irregular menses	7,5	Left	Predominantly solid
20	49	Irregular menses	5,5	Left	Predominantly solid
21 Yerli, 2003	34	Amenorrhea, hirsutism	12,54	Right	Predominantly solid
22 Lee, 2001	27	Irregular menses	1	Left	Cystic and solid
23	28	Infertility	3,7	Left	Cystic and solid
24	39	Infertility	6,3	Right	Cystic and solid
25	32	Infertility	6	Left	Solid
26	20	Pelvic pain	11	Right	Cystic and solid
27	19	Irregular menses	7,3	Right	Cystic and solid
28	28	Dysmenorrhea	9	Right	Cystic and solid
29 Fefferman, 2003	10	Pelvic pain	13	Left	Cystic and solid
30 Andrade, 2001	18	Pelvic pain, hirsutism	16	Accessory ovary	Cystic and solid

continued on the next page

Table 1. Clinical features of patients with sclerosing stromal tumor (SST) of the ovary. *(cont. from previous page)*

30 Andrade, 2001	18	Pelvic pain, hirsutism	16	Accessory ovary	Cystic and solid
31 Mikami, 2003	36	Abdominal mass	5	Right	Cystic and solid
32	32	Infertility	7	Right	Cystic and solid
33 Cashell, 1991	27	Hirsutism (Pregnancy)	3	Left	Solid
34 Tiltman, 1985	21	Abdominal pain	14	Right	Cystic
35	32	Pelvic pain (Pregnancy)	4	Right	Solid
36	18	Adnexal mass (Pregnancy)	20	Right	Cystic
37 Valente, 1985	17	Pelvic pain	12	Left	Cystic and solid
38 Lam, 1988	15	Adnexal mass	13	Right	Cystic and solid
39 Ismail, 1990	29	Infertility	R: 14, L:10,5	Bilateral	Solid
40 Marelli, 1998	30	Pain, tenderness	5	Right	Solid
41	18	Irregular menses	8	Right	Solid
42	15	Irregular menses	6	Right	Solid
43	14	Polymenorrhea	10	Right	Cystic and solid
44	19	Pain, metrorrhagia	6	Left	Solid
45	21	No symptoms	10	Right	Solid
46	23	No symptoms	5	Right	Solid
47	26	No symptoms	15	Right	Cystic and solid
48 Kim, 2003	16	Irregular menses	6	Left	Solid
49	26	Abnormal vaginal bleeding	6	Left	Solid
50	39	Irregular menses, pain	5,5	Left	Solid

outer surface. The cut surface revealed solid, cystic and edematous areas. No haemorrhage or necrosis was observed.

The specimen was fixed in 10% neutral formalin. The paraffin-embedded tissue sections were stained with haematoxylin and eosin, Periodic Acid Schiff and mucicarmine. Immunohistochemical analysis for inhibin, vimentin, smooth muscle actin, desmin, cytokeratin, estrogen and progesterone was performed by using avidine-biotin peroxidase complex method. The tumor was composed of ill-defined cellular pseudolobules separated by a densely hyalinized or markedly edematous stroma (Fig. 1). The lobules were composed of two-cell population: rounded polyhedral cells with eosinophilic or vacuolated cytoplasm and spindle shaped fibroblasts (Fig. 2). Mitotic figures were absent. Cellular areas revealed a rich thin-walled vascular network (Fig. 3). Periodic Acid-Schiff and mucicarmine stains were negative. Immunohistochemical analysis demonstrated positivity for inhibin (Fig. 4), vimentin and smooth muscle actin and negativity for cytokeratin, estrogen and progesterone. At the periphery of the mass, residual ovarian tissue with primordial follicles and follicle cysts was apparent. The diagnosis of sclerosing stromal tumor of the ovary was made.

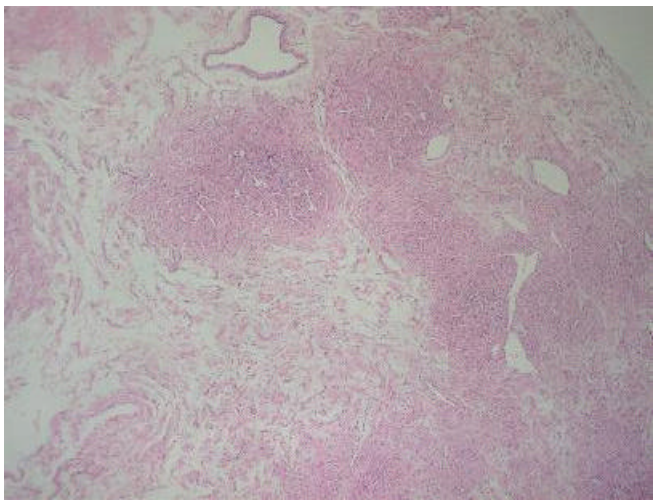

Figure 1. Cellular pseudolobules separated by a densely hyalinized or markedly edematous stroma with prominent vasculature (H&E, x40).

Conclusion

Sclerosing stromal tumor is a rare, benign subtype of ovarian stromal tumors that differs from the others both clinically and pathologically. As a distinct entity,

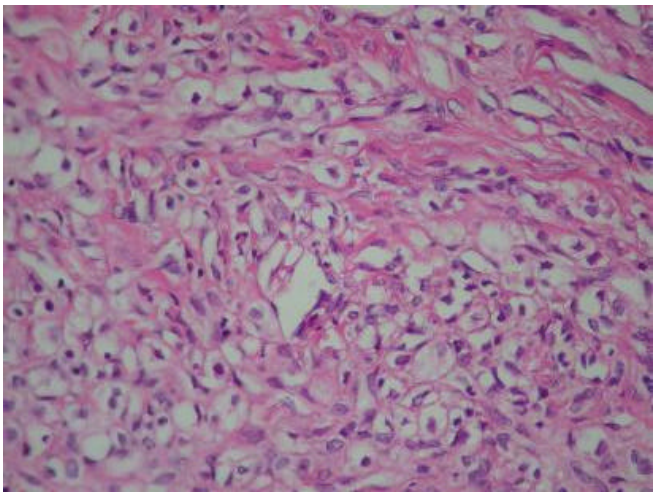

Figure 2. Spindle cells mixed with large rounded vacuolated cells (H&E, x400)

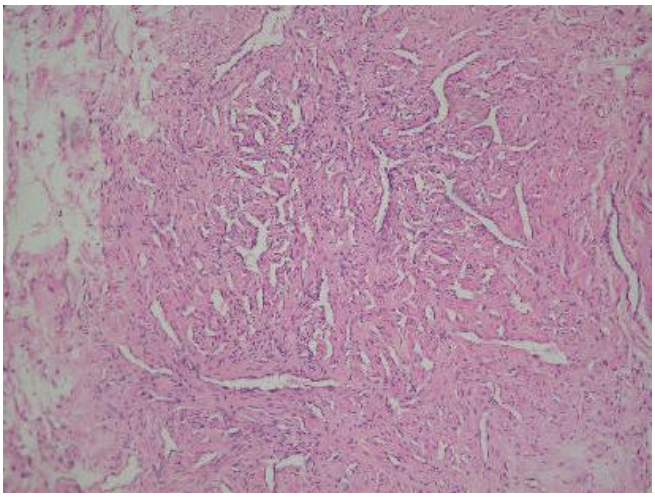

Figure 3. Richly vascularized pseudolobule (H&E, x100).

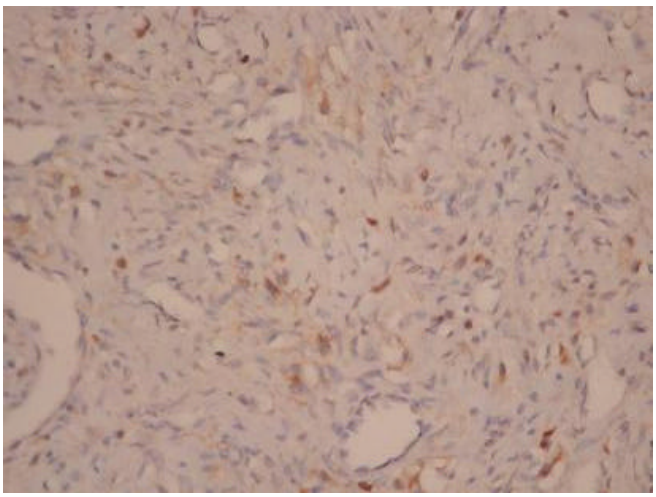

Figure 4. Tumor cells demonstrating positivity for inhibin (x200).

it was first described in 1973 by Chaldvardjian and Scully.[1]

The tumor is characterized by cellular pseudolobules, prominent interlobular fibrosis, frequently marked vascularity and a dual cell population: Collagen-producing spindle cells and lipid-containing round or ovoid cells. The heterogeneity due to the variation in cellular size and shape are helpful features in the differential diagnosis of STT, and contrasts with the relative homogeneity of thecoma and fibromas.[1,6–8] Also SSTs do not have hyalinized plaques, as do fibromas and thecomas. The finding of a thick rim of compressed residual ovarian tissue at the periphery of the mass suggests a slow growing benign tumor. On the other hand, thecomas and fibromas generally occur in the fifth or sixth decades of life when the ovaries are atrophic, so it is hard to identify residual ovarian tissue at the periphery of the tumor.[8, 9]

In the literature, reports of ovarian SSTs are rare. Of these, bilateralism is fewer. Our tumor developed in the right ovary as in most reported cases in the literature. The most common presenting clinical symptoms include menstrual irregularity, pelvic pain and non-specific symptoms related to the ovarian mass and our patient is complained of these symptoms.[6,10] Some patients have presented with anovulation or masculinization, which resolved spontaneously once the tumor was removed.[11] To our knowledge, all SSTs reported to date have been benign and hormonal activity may be present, but recurrence has not been described.[1,2,6,12,13]

Whereas fibroma and thecoma are rarely encountered in the first three decades of life, most of the SSTs occur during second and third decades. Thecoma is typically an estrogenic tumor with peak incidence in the sixth decade and lutein cells are distinct. Fibroma is a non-functioning tumor, which may have diffuse edema. In contrast to thecomas, STTs have been only occasionally associated with estrogen and rarely androgen secretion. Clinical manifestations like infertility and irregular menses suggested the presence of hormone production and several reports described the presence of steroid function in this type of ovarian tumor.[10] Our patient had menstrual irregularity and pelvic pain pre-operatively. Although menstrual irregularity is not an

enough evidence for hormone production itself; our patient was asymptomatic and there were no signs of recurrence and menstrual irregularity five years after the surgery, indicating some endocrine involvement. SSTs may have a potential for hormone production which is not always manifest or may be of a subclinical nature.[14]

Vascular tumors are included in differential diagnosis due to prominent vascularity, but inhibin positivity suggests the diagnosis of SST. On the other hand ''massive ovarian edema'' may be confused with SST. But preserved ovarian tissue within the edematous stroma and absence of heterogeneity favors the diagnosis of massive ovarian edema.[8] In addition to differential diagnosis, the edema of STT is zonal in contrast to that seen in massive ovarian edema or an edematous fibroma.

Infrequently the vacuolated cells and the presence of 'signet-ring' cells in association with edematous stroma may be mistaken for signet-ring cells of Krukenberg tumor of the ovary. But, these malignant tumors occur typically in women in the sixth and seventh decades, are mostly bilateral, and lack the pseudolobulated pattern of sclerosing stromal tumor on cut surfaces. Furthermore, signet-ring cells of Krukenberg tumors contain mucin rather than lipid and they may exhibit mitotic activity and nuclear atypia.[1]

The etiology of SSTs is unknown. Based on the ultrastructural features, SSTs were thought to arise from pluripotent immature stromal cells of the ovarian cortex.[15] However SSTs are proposed to be derived from a population of muscle-specific actin-positive elements from the theca externa, namely the perifollicular myoid stromal cells. The vascular, sclerotic and edematous stromal changes are constant features of these tumors and relate to the local elaboration of some vascular permeability and growth factors like VPV and VEGF.[12] On the other hand Ismail et al suggested that endocrine milieu might be responsible for the morphology of SST and they may be developed from pre-existing ovarian fibromas.[10]

Recently, Tiltman suggested that STTs and thecomas share some morphologic features and many antigenic determinants like smooth muscle actin, vimentin, and thus are probably closely related entities.[14] Although overlap exists between these stromal tumors on the basis of immunohistochemistry and some morphologic features, distinctive clinical and pathological features of the STT almost always allows a specific differential diagnosis.

In the literature calretinin, inhibin, CD34 and alpha glutathione S-transferase positivity (a-GST) was reported to be useful to differentiate STT from thecoma, fibroma and other sex cord stromal tumors.[14,15] Inhibin has been shown to be a useful marker for ovarian sex cord stromal tumors. CD 34 stains the endothelium of often dilated and branching vascular architecture, and clearly distinguishes SSTs from thecoma and fibromas. a-GST positivity within scattered cells appears to be useful in the distinction of SST from diffuse staining thecomas and no staining fibromas.[14] Immunohistochemical analysis for inhibin, actin, vimentin, estrogen and progesterone receptors using formalin-fixed and paraffin-embedded materials showed predominant positivity for a-smooth muscle actin and consistent positivity for inhibin and vimentin, suggesting a stromal origin of the SST. Estrogen and progesterone receptors were not expressed in our case, although menstrual irregularity was disappeared soon after the removal of the tumor.

It is difficult to distinguish SSTs consisting of solid and cystic areas from ovarian malignancies on the basis of radiological and macroscopic examination, as these tumors additionally appear very vascular giving the impression of malignant tumors. Radiologically, especially on sonograms the appearance of SSTs may be suspected to be malignant ovarian tumors because they show a mixed pattern, with cystic and solid components.[7,16] Some recent reports suggested that MRI findings might be more specific in distinguishing this benign neoplasm from malignant ovarian tumors and other sex-cord stromal tumors and useful for the preoperative diagnosis of SST to avoid excessive surgical intervention.[6–9,17,18] Malignant ovarian tumors usually occur in older women and often show high values of serum tumor markers. On the other hand, MRI findings may not be useful in the assessment of pelvic masses during pregnancy.

In conclusion, especially MRI findings of unilateral ovarian mass in a young patient with menstrual irregularity, which reveals a solid/cystic

mass and a high degree of peripheral vascularization may be helpful to allow the preoperative diagnosis. The definite diagnosis of SST is made only by pathologic evaluation but at least a diagnosis of benign ovarian tumor is possible intraoperatively via frozen section analysis by examining the background of pseudolobular pattern, heterogeneity of the cellular areas and densely hyalinized or markedly edematous stroma.

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