Case report:

Ovarian sclerosing stromal tumour: Report of a new entity with immunohistochemical study.

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Abstract:

Sclerosing stromal tumour (SST) is a rare benign sex cord stromal tumour occurring in women in their second and third decades. Patients usually present with menstrual irregularity and pelvic pain. Microscopically, this tumour is characterized by epithelioid and spindle cells arranged in pseudolobules separated by areas with fibrous deposition of various amount. Presence of 'staghorn like' proliferating vasculature is the hallmark feature of this tumour. The main differential diagnoses are thecoma and fibroma. Immunohistochemistry can be used to differentiate these tumours. This relatively new entity should be kept in mind while reporting ovarian tumour in a young female. We have described SST in an 18 year old female in this case report.

Keywords: Sclerosing stromal tumour; sex cord stromal tumour; vimentin, inhibin;calretinin.

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Introduction:

Sclerosing stromal tumour (SST) is an extremely rare benign ovarian sex cord stromal neoplasm with distinctive clinical and pathological features of unknown aetiology. This entity was first identified in 1973 by Chalvardjian and Scully. It accounts for approximately 8% of all primary ovarian neoplasm generally occurring in young women and girls in the second and third decades of life.[1,2] The tumour is composed of an admixture of epithelioid and spindle cells of ovarian stromal origin.[3] It was included as a subtype of ovarian sex cord stromal tumour in WHO 2003 classification of female genital tumours.[4]

SST is usually but not invariably hormonally inactive. Occasional cases have been reported with estrogenic and androgenic activity. Unusual presentation may occur with virilization and precocious puberty. It may be associated with pregnancy, rarely with Meig's syndrome and endometrial carcinoma. Majority of the patients have the complaints of menstrual irregularities, pelvic pain and ovarian mass effect, but may be asymptomatic.[2-4] The tumour is usually unilateral and well circumscribed. This microscopically heterogeneous tumour has most striking features of distinct cellular and hypocellular areas and peculiar vascular architecture. Cellular areas comprise fibroblast-like and luteinized theca-like cells arranged in pseudolobules. Intervening hypocellular areas consist of oedematous and collagenous stroma.[1,5-6] Tumours are immunohistochemically positive for vimentin, SMA, desmin, CD99, estrogen

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and progesterone receptors, and sex cord markers, such as inhibin and calretinin. Surgery is the main therapeutic modality.[5,6] Exceptionally one patient was reported with low grade malignancy in 1990[4] and another one case with recurrence having features of capsular disruption, necrosis and significant mitotic activity.[3] Here we have described a case of SST in an 18-year-old female.

Case report:

Clinical summary

A regularly menstruating 18 years old unmarried female had history of lower abdominal pain for 1 year duration. She had complaints of menorrhagia since the same duration. On clinical examination, a mass was palpable in the lower abdomen which was gradually increasing in size in the last 6 months before operation. Ultrasonography revealed a large complex mass, mostly cystic measuring about 15.3x10.8 cm arising from right adnexa. Magnetic resonance imaging showed a huge inhomogeneous cystic mass with solid component, regular and smooth in outline, not separately defined from right ovary, measuring about 15x13x12 cm in the pelvis extending up to the central abdomen and compressing the bowel loops. The lesion contained some internal septation and mixed intensity components from the wall, which showed enhancement after contrast. Mild ascites and right sided moderate hydroureteronephrosis were also present. Radiological opinion was in favor of mucinous cystadenocarcinoma. Routine laboratory parameters including tumour markers were within normal limits. Then the patient underwent right sided salpingo-oophorectomy operation and the resected specimen was sent to the Department of Pathology, BSMMU for frozen section which revealed negative for malignancy. Post-operative period was uneventful. The tumour did not recur in a follow up period over the following 1 year.

Macroscopic findings

The specimen consisted of a resected ovarian cyst with attached fallopian tube. The cyst measured about 17x16x10 cm. Outer surface was grey white, smooth and shiny. Clear fluid came out on incision. Cyst cavity was uniloculated. Cut surface of the cyst wall was grey white, edematous, rubbery in consistency containing small cystic spaces with maximum 2.5 cm of thickness.

Microscopic findings

Hematoxylin and Eosin stained sections showed a benign tumour composed of cellular and hypocellular areas arranged in pseudolobules. These pseudolobules contained lutein cells and spindle cells (figure-1A). Occasional signet ring like cells were present (figure-1B). Hypocellular areas showed edematous stroma with foci of myxoid changes. Numerous thin, branching hemangiopericytoma like blood vessels were also present within cellular areas. Mitoses were infrequent (<1/10HPF). Tumour cells were negative for PAS stain (figure-1C).

Immunohistochemistry was done. SMA and desmin were positive focally in blood vessels and fibroblast like spindle cells (figure-2A and 2B). Cytoplasm of the tumour cells was diffusely positive for vimentin (figure-2C). Inhibin was positive focally with weak intensity in around 5-10% of tumour cells' cytoplasm, especially in the plump vacuolated cells (figure-2D). Calretinin was negative in tumour cells (figure-2E). CD34 was found positive in blood vessels delineating peculiar ectatic and proliferating vascular pattern but negative in tumour cells (figure-2F).

Discussion:

Sclerosing stromal tumour is a relatively rare subtype of ovarian sex cord stromal tumour proposed to be originated from the perifollicular myoid stromal cells residing normally in the theca externa and ovarian cortical stroma.[4,7] Previous immunohistochemical studies supported the smooth muscle differentiation of the specialized gonadal stromal tissue.[2] This benign ovarian tumour predominantly involves the young age group ranging from about 14 to 51 years.[5,8] Grossly, the tumour may transform the involved ovary into a solid, or predominantly solid mass with cystic degeneration, or a unilocular cyst containing clear fluid. SST may contain polygonal lutein cells with eosinophilic cytoplasm showing clinical evidence of steroid hormonal activity. Despite of presence of such type of cells, the tumour is considered hormonally inactive in nature as these active appearing cells do not always secret clinically significant amounts of steroid hormones.[9] Features of masculinization or anovulation may be present in those cases occasionally associated with oestrogen and androgen secretion.[8] CT and MRI are the imaging modalities of choice for better visualization of ovarian tumours, that are larger than 5-10 mm in size.[10] Our presenting case was clinically and radiologically suspected as a malignant one due to having an enlarging mass attained at a huge size within short period and a heterogenous hypointense and hyperintense pelvic lesion containing internal

septations on MRI impression.

SST has characteristic histologic features to separate the entity from other types of sex cord stromal tumour. It does not require any immunohistochemical or ancillary tests for diagnosis except those cases with overlapping microscopic features.[5] The benign neoplasm is marked by presence of cellular and paucicellular areas with pseudolobular appearance of the former one. Cellular areas are composed of an admixture of fibroblast like spindle cells with elongated vesicular nuclei, and round to oval cells or epithelioid cells. The later neoplastic cells, often plump to polygonal in appearance, having eosinophilic, sometimes vacuolated cytoplasm due to presence of lipid and round nuclei, are termed to as 'luteinized theca like' cells. Occasional foci of signet ring like cells may be revealed which may show prominent luteinization, especially during pregnancy.[3] Thin walled ectatic branching 'hemangiopericytoma like' vascular channels are seen scattered throughout both the cellular areas as well as the intervening fibrotic stroma.[2,5]

SST and thecoma are supposed to be of closely related entity on the basis of antigenic determinant and morphology. IHC has little role in differentiating these two entities.[6,7] SST may be considered as a neoplasm in transition arising from typical or luteinized thecoma which may be evolved into ovarian myxoma or end stage SST.[9] SST with prominent signet ring like cells can mimic signet ring stromal tumour. However, these signet ring cells show negative reaction for lipid, whereas signet ring like cells in SST are lipid rich.[11] SST may also develop from pre-existing fibroma.[6] Thus, differentiation of SST from other stromal tumours may impose a diagnostic challenge.

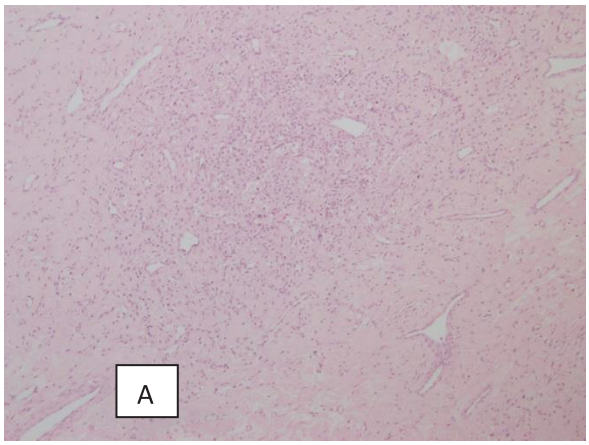
Inhibin, calretinin and α glutathione S transferases (GST) are the biomarkers used for diagnosis of sex cord stromal tumours related to steroidogenesity of cells. Highly vascular sclerosing stromal tumour may mimic a vascular tumour, such as hemangiopericytoma, which is excluded by presence of inhibin and calretinin positivity. Inhibin is more specific (97%), whereas calretinin is more sensitive (97%) marker for sex cord stromal tumours. Stronger expression for inhibin and calretinin goes in favor of thecoma over fibroma. Vacuolated cells and scattered single cells of SST show marked intracytoplasmic positivity for GST. On other hand, thecoma show diffuse staining and fibroma show no staining for GST. Intensity of expression for GST is a reflection of inhibin as well as calretinin positivity, which correlates with degree of luteinization.[1-2,5-6,12] Massive ovarian edema is another differential diagnosis of SST. The possibility can be excluded by presence of preserved ovarian tissue within edematous areas and absence of cellular heterogeneity.[1] In present case, no preserved ovarian tissue was seen.

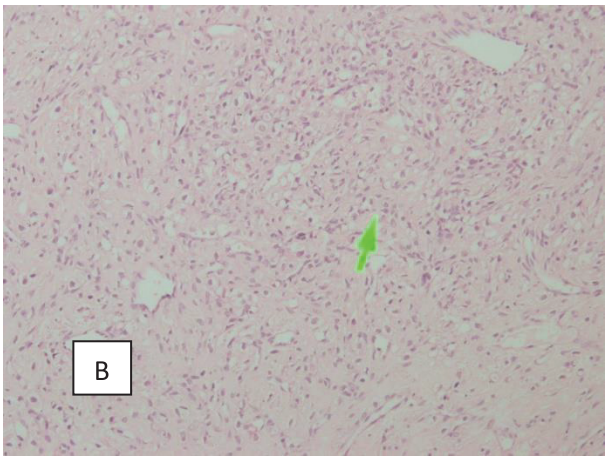
In ovarian stromal tumour, vimentin, smooth muscle actin (SMA) and desmin may show cytoplasmic positivity. SMA and desmin often show positive staining in blood vessels wall as well as focal perivascular and stromal fibroblast like cells in SST with marked intensity. SMA and desmin is weakly and focally positive in thecoma. In fibroma, SMA staining is delicate wispy in nature with moderate intensity and desmin reactivity is negative. Staining of CD34 highlights complex branching vascular architecture in SST along with ovarian non neoplastic stromal cells. In fibroma and thecoma, tumour stromal cells may be positive for CD34. Sometimes presence of signet ring like cells create confusion for Krukenberg tumour. These malignant signet ring cells are positive for EMA, pancytokeratin, PAS, negative for inhibin and show atypical mitosis and nuclear features.[2,5,7,12] Other less reliable marker used for SST are CD99, CD56, WT1, S100, estrogen and progesterone receptors. FOXL2 and TFE3 reactivity has recently been reported in a subset of tumours.[3,9,11] Reticulin stain outlines tumour cell nests and aggregates in granulosa cell tumour along with reticulin fibres deposition. In thecoma and fibroma, it reveals pericellular reticulin staining pattern. Collagen fibres are found abundantly deposited in fibroma as highlighted by Masson's trichrome stain.[5] In our case, reticulin stain was positive around blood vessels and scattered around individual cells in perivascular areas. The present case also showed positivity for Masson's trichrome stain in collagenized areas. This special stain revealed deposition of fine collagen fibres in cellular areas which became thick collagen bundles at the periphery of the cellular areas. After consideration of clinical features, histomorphology, IHC findings and special staining patterns, the case was decided to be diagnosed for sclerosing stromal tumour.

Ancillary investigation is not practically applied for the diagnosis of SST. A small subset of tumours has revealed presence of trisomy 12, FHL2-GLI2 fusion genes in tumour cells on FISH studies.[3]

Conclusion:

Preoperative assumption of sclerosing stromal tumour is difficult because of the rarity of the tumour. The tumour can simulate malignancy clinically and radiologically. Frozen section can play an important role for exclusion of malignancy and avoid further unnecessary surgical intervention. In cases of ovarian tumours in young female, SST should be borne in mind. It can be diagnosed mainly on the basis of peculiar heterogeneous cellular, vascular and sclerotic pattern. We can differentiate SST from fibroma, thecoma and granulosa cell tumour with special stains and immunohistochemistry in case of diagnostic dilemma.





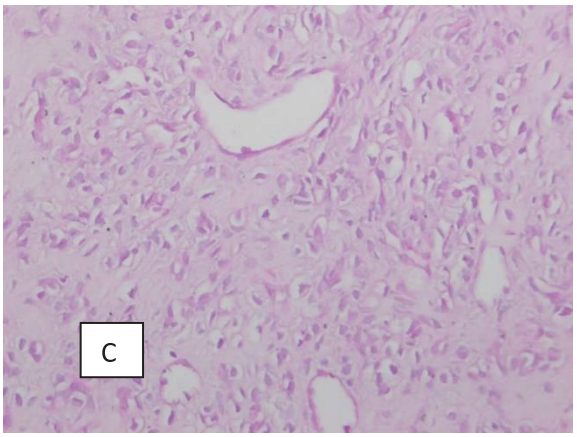


Figure 1(A): H&E x100, stain of SST shows a cellular pseudolobular area composed of an admixture of spindle shaped and polygonal lutein cells; Figure 1(B): H&E x200, stain of the tumour shows an arrow head demonstrating occasional scattered signet ring like cells; Figure 1(C): Plump to polygonal cells with vacuolated cytoplasm are negative in PAS stain (x400).

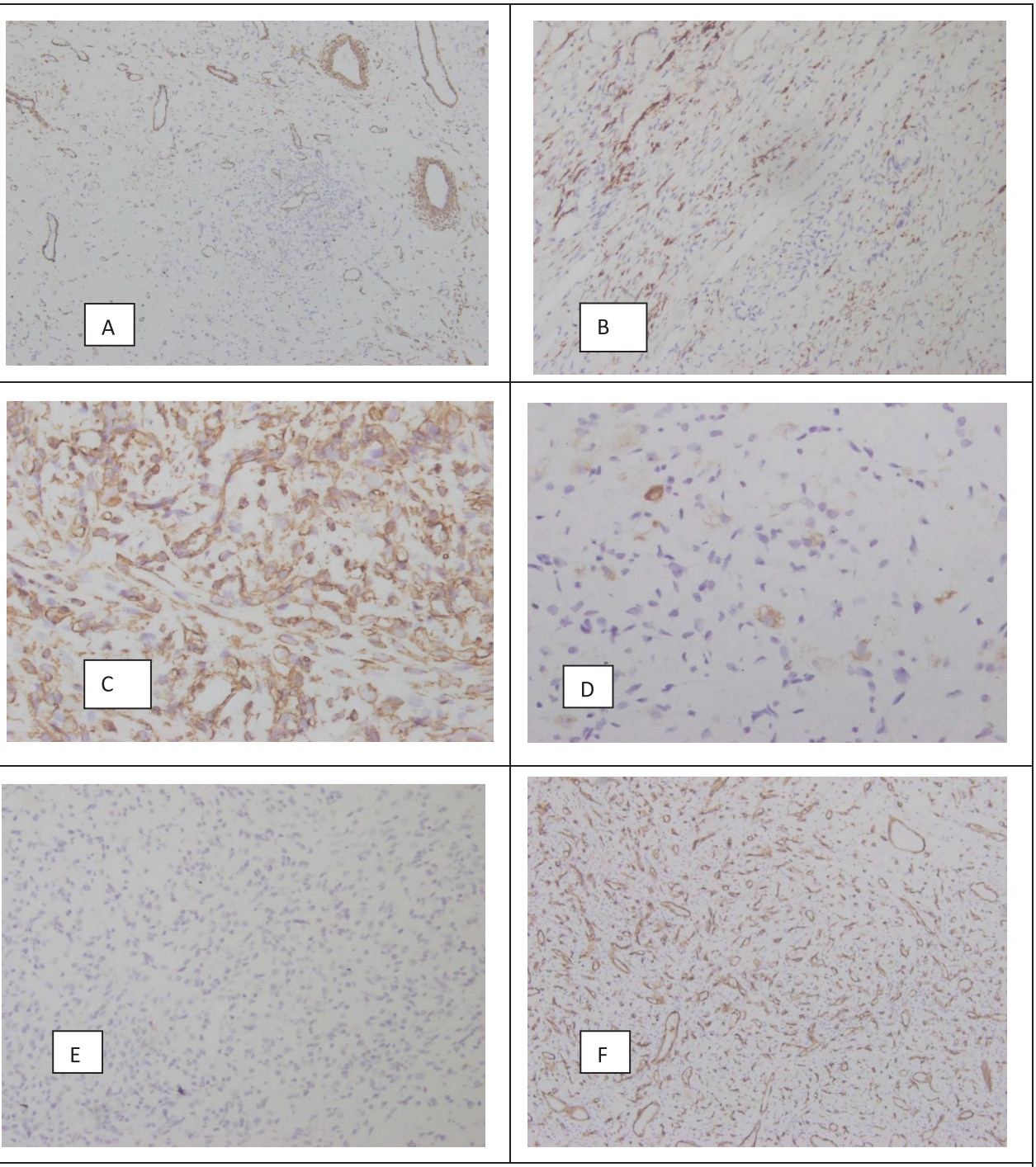


Figure 2(A): Blood vessels and spindly cells are marked by immunostain SMA (x100), perivascular plump tumour cells are SMA negative; Figure 2(B): Spindly tumour cells and blood vessels are positive for desmin (x200); Figure 2(C): Tumour cell are diffusely positive for vimentin (x400); Figure 2(D): Scattered epithelioid lutein cells with vacuolated cytoplasm are weak to moderately positive for inhibin (x400); Figure 2(E): Tumour cells are negative for calretinin (x200); Figure 2(F): CD34 is negative in tumour cells but positive in blood vessels wall highlighting the rich vascularity (x100).

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