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A rare case of Sclerosing stromal tumour with ascites and raised CA 125 mimicking primary ovarian malignancy

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Abstract
Sclerosing stromal tumour is a rare benign sex cord stromal tumour of ovary. A 16 year old female presented with menorrhagia & fever. MRI showed large well defined heterogenous mass lesion of size 9x11x12cm in the lower abdomen and pelvic cavity. There was mild ascites and serum CA 125 levels were elevated which mimicked the possibility of primary ovarian malignancy . Staging laparotomy was done. Macroscopic examination showed an encapsulated solid mass. Cut section showed grey white solid mass with glistening areas. Histopathological examination showed a neoplasm composed of alternating cellular and hypocellular areas and thin branching hemangiopericytoma like vessels. Immunohistochemical analysis showed positive results for Vimentin, SMA & calretinin. Inhibin, CK, CD 34 & Bcl2 were negative in tumour cells. A diagnosis of Sclerosing stromal tumours was given. About 8% ovarian tumours are sex cord stromal tumours and of these sclerosing stromal tumour compromises less than 5 %. Around 208 cases of SSTs are described in literature till now.(1)

Case Presentation

A 16 year old female presented with fever for 4 days duration. There was history of menorrhagia. . Per abdomen Examination showed a nontender non mobile solid mass of size 10x10cm. Routine blood investigtaions were within in normal limits . An ovarian mass measuring 10.48x6.98x8.8cm was found out on USG abdomen. CT abdomen and pelvis showed large solid lesion in the pelvis in the midline & mild ascites with possibility of either ovarian lesion or subserosal fibroid. Magnetic Resonance imaging (MRI) pelvis showed large well defined heterogenous mass lesion of size 9x11x12 in the lower abdomen and pelvic cavity. Multiple T 2 hyper intense non enhancing necrotic areas noted within the lesion. Possibility of Left ovarian fibroma more likely than uterine fibroid and minimal fluid noted in pelvic cavity (Figure 1 ; A& B).Chest Xray was normal.

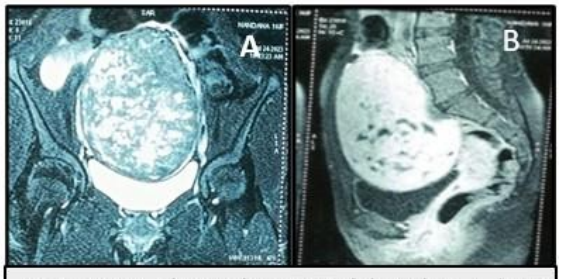

Figure 1: MRI plain and contrast of the Pelvis A large well defined heterogenous T1,T2,T2FS hyper intense mass lesion of size 9x11x12cm in the lower abdomen and pelvic cavity: A :coronal image B: Axial image

Hormonal assays showed elevated levels of CA 125 (1342 IU/ml) .All other assays (Beta hcg (< 1.2) , CEA(1.68ng/ml) , AFP(2.5ng/ml)& LDH (140)) were within in normal limits . Patient undervent staging laprotomy .Intraoperatively , uterus were approximate for size .Right ovary , Right fallopian tube were normal &Left ovary enlarged to size 15x10cm, solid mass with thick capsule .

Gross examination of the specimen received in histopathology showed an encapsulated solid mass measuring 13x10.5x7.5cm with attached stretched out fallopian tube . On cut section , grey white solid growth with glistening areas noted .No normal ovarian tissue identified.(figure 2)

Figure 2 : Encapsulated solid mass ; Cut section grey white and solid with glistening areas.

Microscopic examination showed a neoplasm composed of alternating cellular and hypocellular areas, tumour cells are arranged in nodules separated by edematous and collagenous stroma. Nodules are composed of spindled to epithelioid cells . Spindle cells are having scant cytoplasm, elongated nucleus and bland chromatin. Epithelioid cells are having pale eosinophilic to clear cytoplasm, vesicular nucleus and some showing nucleoli. Numerous thin walled and branching hemangiopericytoma like vessels seen. Hypocellular areas are edematous and collagenous. Mitosis infrequent. No necrosis was seen (Figure 3)

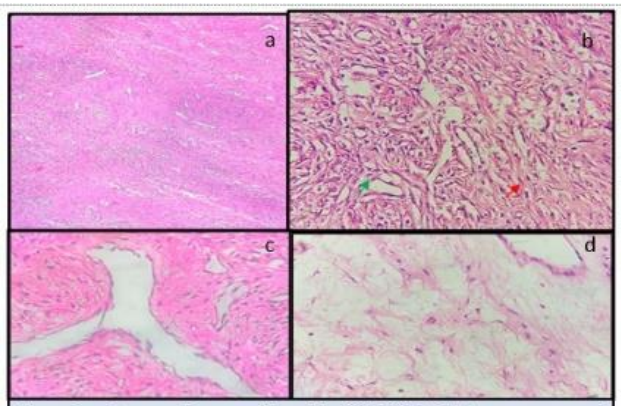

Figure 3 : a:Tumour cells arranged in nodules (H&E, 4X) b:Cellular areas composed of 2 population of tumor cells ; spindle cells with scant cytoplasm and bland chromatin (red arrow) & epithelioid cells having moderate amount of eosinophilic to clear cytoplasm and vesicular nucleus (green arrow) (H & E, 40X) c : branching hemangiopericytoma like vessels (H & E 40X) d : hypocellular areas showing of edematous collagenous areas (H &E, 40X)

Immunohistochemical analysis was done which showed positive results for vimentin and SMA and partial positivity for Calretinin . Inhibin and CK, CD 34 & Bcl2 were negative(Figure :4).

Final diagnosis was given as sclerosing stromal tumour of left ovary measuring 13x10.5x7.5cm. On follow up She was asymptomatic and her cycles were regular after the surgery .

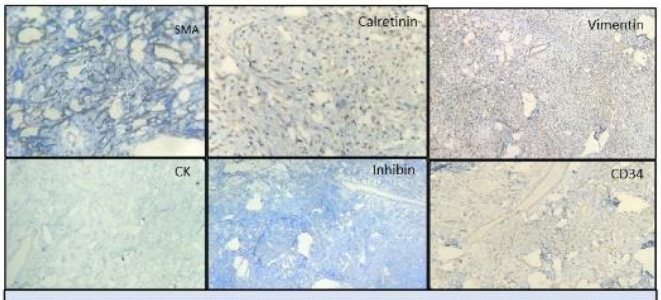

Figure 4 : IHC RESULTS :Tumour cells were positive for Vimentin , SMA & Calretinin . CK , Inhibin & CD 34 were negative in tumour cells .

Discussion

Sclerosing stromal tumour of ovary represents an extremely rare subtype of sex cord stromal tumour in young female, typically seen during second and third decades. Benign sexcord stromal tumours such as fibroma and thecoma are uncommonly encountered in this age. Presenting complaints includes abnormal uterine bleeding or symptoms related to ovarian mass. Hormonal symptoms are uncommon, but few cases were reported with virilization and precoucious puberty. Majority of these tumours are unilateral. Rarely Meigs syndrome is associated with this tumours.

Meigs Syndrome is a triad of pleural effusion, ascites and ovarian tumour which is usually benign such as fibroma or fibroma like tumours (Thecoma and granulosa cell tumour) . Pseudo-Meigs syndrome is ascites , pleural effusion associated with other benign cysts of the ovary (such as struma ovarii, mucinous cystadenoma and teratomas), leiomyoma of the uterus, and secondary metastatic tumours [(2)]. Our case is ovarian tumour with mild ascites and no pleural effusion. But there was also elevated levels of serum 125. So this is a rare presentation of Sclerosing stromal tumour of ovary with elevated serum CA 125 . Probable mechanisms for the ascites in these tumours are production of ascitic fluid by the tumor; lymphatic obstruction; hormonal stimulation; release of inflammatory mediators and tumor torsion. Pleural effusion is said to be caused by the migration of fluid and protein , perhaps by lymphatic channels across the diaphragm. In the present case, pleural effusion was not present, which was possibly due to the minimal amount of ascitic fluid [(3)]

CA125 antigen is a tumor marker normally produced in tissues such as epithelium of the fallopian tubes, endometrium, endocervix, ovaries, and mesothelial cells of the pleura, peritoneum & pericardium .It is elevated in some physiologic conditions such as menstruation or pregnancy and in some benign conditions such as endometriosis, peritonitis, cirrhosis with ascites, PID, uterine leiomyoma, pericarditis & pleuritis . This tumor marker levels (normal up to 35 IU/mL) increase in malignant ovarian tumors [(4)]

The precise mechanism of serum CA 125 level elevation is not clearly understood till now. Some tumors express CA 125, which is absorbed into the circulation resulting in elevated serum levels. An inflammation of the peritoneum or pleura have been associated with elevated serum CA 125 levels, possibly through the stimulation of mesothelial cells to produce CA 125. Elevated intrabdominal pressure caused by tumor growth can also result in mesothelial expression of CA 125 [(6)]

The most common clinical features include menstrual irregularities, pelvic pain, and nonspecific symptoms related to an ovarian mass. Masculinization or anovulation may be present in some patients, as they are sometimes associated with estrogen and androgen secretion.

The etiology of SSTs is not well understood. Ismail et al., proposed a probable hypothesis that it might be developed from pre-existing ovarian fibromas. Another hypothesis was proposed by Damajanov et al., on the basis of ultrastructural features, postulated that SSTs are derived from the pluripotent immature stromal cells of the ovarian cortex.[(5)] There is another concept that SSTs are derived from a population of muscle specific actin positive elements from the theca externa, namely, the perifollicular myoid stromal cells.[(6)] Tiltman and Haffeyee proposed that SSTs and thecoma are probably closely related entities as they share similar morphological features and immunohistochemistry such as smooth muscle actin and vimentin[(6)] .Fish studies on SST have revealed subset of tumour cells with trisomy 12 .Recently recurrent FHL2-GLI2 fusion gene have been demonstarted 17 of the 26 SST and other GLI2 rearrangement in additional 15 % of the cases [(7)]

Tumour size varies from 1.5 to 19 cm.Grossly tumour is well circumscribed and usually show solid to white cut surface .Central edema and cyst formation may be seen in some cases .

It is difficult to distinguish SST consisting of solid and cystic areas from ovarian malignancy by radiological and macroscopic examination. USG and CT finding of SST show an increased peripheral vascular structures mimicking malignant tumour . So the distinct histomorphological appearance and IHC are important in the diagnosis of SST.

Microscopic picture of SST is heterogenous in contsrast to other stromal tumors like thecoma and fibroma which are homogenous. Histologically it is characterized by c psuedolobular architecture, alternating hypocellular and hyper cellular areas, prominent vascularity (hemangiopericytoma like), collagenous to myxoid stroma & dual population of lipid containing round or ovoid cells and spindle cells .[(8)]

The important differential diagnoses include other sex cord-stromal tumors including fibroma, thecoma,

lipid cell tumor, vascular tumors , solitary fibrous tumour, subserosal leiomyoma, malignant tumors such as Krukenberg's tumor, and non-neoplastic conditions such as massive odema of ovary.

Sex cord-stromal tumors such as fibroma, thecoma and granulosa cell tumour can be differentiated from SSTs, based on different histopathological findings. Massive ovarian edema might be confused with SSTs. However, this confusion can be resolved by finding the entrapped ovarian tissue within the edematous stroma in massive ovarian edema.

Sometimes the edematous stroma of these tumors contains cells resembling signet ring cells which can be mistaken for Krukenberg tumour of ovary. But they can be differentiated as the latter are mostly bilateral, occur usually in the 6th and 7th decades and does not have pseudo-lobular pattern of sclerosing stromal tumour. Furthermore, signet ring cells of Krukenberg tumour contain mucin rather than lipid and the cells may exhibit nuclear atypia and mitotic activity.[1] Typical parauterine leiomyomas show spindle cells arranged in interlacing fascicles and bundles with individual cells are having cigar shaped nuclei .No branching vessels are seen in leiomyoma .Solitary fibrous tumor ia a benign spindle cell neoplasm. It is a microscopically characterised by haphazardouly arranged spindle cells in a collagenous matrix admixed with branching staghorn shaped vessels . They have characteristic NAB2-STAT6 gene rearrangement .It is positive for CD34 , nuclear STAT 6 &Bcl2 .In our case , there was staghorn vessels spindle cells arranged in collagenous matrix, but immunohistochemical analysis showed negative results for CD 34 and Bcl2 .So we eliminated the possibility of solitary fibrous tumour of ovary .

Epithelial ovarian cancers are mostly seen in the postmenopausal period. They are distinguished from benign ovarian tumours by their invasive nature of growth and metastatic potential .[9]

The prominent vascularity, sclerotic and edematous stromal changes are constant features of these tumours . So Vascular tumours are also included in the differential diagnosis . But inhibin positivity suggests the diagnosis of Sex cord stromal tumour .[10]

On IHC, SSTs show positivity for vimentin, smooth muscle actin, inhibin, calretinin, estrogen receptor (ER) ER, progesterone receptor (PR) PR, and vascular endothelial growth factor (VEGF). They are negative for S100 and epithelial markers.

Immunohistochemistry of desmin and smooth muscle actin is useful in distinguishing sclerosing stromal tumors from thecomas and fibromas. It is being postulated that SST is derived from a population of muscle-specific actin-positive elements from the theca externa, namely the perifollicular myoid stromal cell.

Inhibin, Calretinin, CD34, and α-glutathione S-transferase (αGST) positivity help us to differentiate sclerosing stromal tumors from thecomas, fibromas and other sex cord stromal tumors. Inhibin is positive in ovarian sex cord stromal tumors. CD34 stains the endothelium of often dilated and branching vascular architecture and it helps in differentiating SST from thecoma and fibroma. αGST is diffusely positive in thecomas and it is negative in fibromas [1].Treatment of SST includes enucleation or unilateral salpingo-oophorectomy. Recurrence of these neoplasm is extremely rare. [11]

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