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Rarity does not rule out the diagnosis-huge sex-cord stromal cell tumor of the ovary

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Abstract
Huge borderline ovarian tumors are rare in modern medicine because of the awareness, earlier medical consultation and available ultrasound facility even in rural area. Huge ovarian tumor with rapid growth in reproductive age group will lead the clinician towards a diagnosis of ovarian carcinoma. Ovarian sex cord-stromal tumours are a rare group of tumors and accounts for approximately for 7% of all ovarian tumors. A 44-year-old female presented with abdominal distension and pain. Her examination findings and investigation gave a probable diagnosis of ovarian carcinoma. Staging laparotomy and enucleation of tumor was performed en bloc. Histopathology revealed the tumor as mixed sex cord stromal tumor.

Keywords: Huge borderline, stromal tumor, Histopathology, diagnosis-huge sex-cord, approximately

Introduction
Huge borderline ovarian tumours are rare in modern medicine because of the awareness, earlier medical consultation and available ultrasound facility even in rural area [1]. The commonest diagnosis in a patient with mass abdomen with suspicion of ovarian tumor will be epithelial ovarian tumor unless otherwise proved. Huge ovarian tumor with rapid growth in reproductive age group will lead the clinician towards a diagnosis of ovarian carcinoma. However, sex cord stromal tumors can also be present with mass abdomen of rapid growth. Ovarian sex cord-stromal tumours are a rare group of tumors and accounts for approximately for 7% of all ovarian tumors. These tumours are often found in adolescents and young adults. The constituent cells of these tumors are involved with ovarian steroid hormone production (e.g. androgens, estrogen and corticoids) and therefore can present with hormonal manifestations along with signs and symptoms of a pelvic mass. Here we present a rare case of huge ovarian tumor suspected to be epithelial but later on proved to be a sex cord stromal tumor.

Case Report
A 44-year female, P3L3A3, presented to our out-patient department in July 2019 with complaints of abdominal distension for 1 month which was sudden in onset and rapid in progression. The distension was accompanied with a dull aching, intermittent pain in the abdomen. She gave a history of loss of appetite and loss of weight of 2 kg in the past 1 month. There was no associated urinary or bowel symptoms. She had undergone hysterectomy 6 years ago for Fibroid uterus and Excision biopsy in the right breast for Fibroadenoma 4 years ago. There was no history of any malignancies in the family. Patient had sought medical attention for the same at an outside hospital for which she had undergone ultrasound which showed a large abdomino-pelvic mass probably arising from the ovary, likely adenocarcinoma of ovary. Patient was referred to us for further management.
The patient was moderately built, weighing 61kgs. Physical examination revealed mild pallor, afebrile with a pulse rate of 82bpm and blood pressure of 130/80mmHg and a respiratory rate of 20 breaths/min. Her cardiovascular and respiratory system findings were normal. Her abdomen examination revealed a mass of 32 weeks size gravid uterus with variegated consistency, smooth surface, non-tender, with restricted mobility. Bimanual pelvic examination confirmed the abdomen examination findings.
The ultrasound report showed a large ill-defined heterogenic abdomino-pelvic mass measuring approximately 26 x 18 cms arising from the adnexa extending superiorly, posteriorly and

laterally with both solid and cystic components with septations within and diffusely increased vascularity suggestive of neoplastic etiology arising from the ovary probably Adenocarcinoma of ovary. Magnetic resonance imaging illustrated Large peritoneal complex solid cystic mass lesion measuring 26cms TR x 23 cms CC and 25 cms AP extending from right to left flank proximally extending up to the transverse colon and distally into the pelvis. The lesion shows increased vascularity, causing mass effect and displacement of the omento-mesentery and bowel loops. No abdomino-pelvic adenopathy. Post contrast study revealed moderate enhancement in the solid regions within the tumor with capsular enhancement. The findings may represent large malignant peritoneal malignancy possibility of Carcinoma Ovary. No ascites, macroscopic peritoneal metastasis. No hepatic metastasis. Lower lumbar spondylosis and degenerative disc disease. Her tumor markers Ca-125:11.6U/mL, CEA: 1.27 ng/mL, Ca 19.9: 3.43 U/mL. IOTA ADNEX Model predicted the risk of malignancy in our patient to be 74.3% as shown in figure 1.

With the working diagnosis of ovarian tumor, probably borderline, the patient was taken up for staging laparotomy. Intraoperative findings were: a huge ovarian tumor of size 28 x 20cm, loculated, with solid areas and bosselated surface. The lower extent of the tumor could not be delineated with suspicion of dense adhesion of the bladder. Posterior wall of the bladder was forming the cyst wall, causing inadvertent bladder injury during dissection, which was recognized and repaired. Left ureter was traced densely adherent to the posterior wall of cyst, and separated from the cyst. Bowel adhesions were present which was released. Omental adhesions were present on anterior wall of the cyst for which adhesiolysis was done. Peritoneal wash was given. Omental biopsy taken. The entire tumor was removed en bloc. Other ovary could not be visualized, probably buried in the retroperitoneum.

Her post-operative period was uneventful without any urinary complaints and complete suture removal was done on post-operative day 8. Histopathological examination revealed mixed sex cord stromal cell tumor of the ovary with mixed theca cells. Immuno Histo Chemistry was negative for inhibin, least chance for granulosa cell component in the tumor. Hence the final diagnosis of the patient is the coma-fibroma and the patient is on regular follow up.

Discussion

Sex cord ovarian tumors account for 7% of all ovarian tumors [2]. As per the WHO guidelines, they have been divided into pure stromal tumors, pure sex cord tumors, and mixed sex cord stromal tumors [3]. They are a heterogenous group of tumors formed by diverse group of cells arising from the primitive sex cord and stromal cells. Theca cells, fibroblasts, and Leydig cells are the stromal cells and Granulosa cells and Sertoli cells belong to the primitive sex cords.

Granulosa cell tumors is the commonest sex cord tumors and accounts for 70% of sex cord tumors [4]. Sex cord stromal cell tumors are usually hormonally active tumors as they develop from the connective tissue of the ovaries and testes. The tumors from the granulosa cells and theca cells are usually hyper estrogenic, and from Sertoli cells and Leydig cells are hyper androgenic [5]. Our patient gave a past history of fibroid uterus and fibroadenoma breast which could have given us a suspicion of sex cord stromal tumor. These tumors unlike the more common epithelial ovarian tumors are found to be associated with various syndromes such as Peutz-Jegher syndrome, Gorlin syndrome, Meigs syndrome and even Cushing's syndrome [6-8].

The tumor most commonly present in the 4th and 5th decades, as in our case. In a study by Haroon *et al* on clinico-pathological spectrum of ovarian sex cord-stromal tumors in a developing country, the mean age of the patients was 44.3 +/-16.8 years.[2] The most common clinical presentation reported in many studies is abdominal lump with pain (54-61%) and abdominal distension (55%) [2, 9] The size usually reported in literature is >10cm, but it can vary from small to large mass as presented in our case as a huge tumor [9, 10]. GCT presents at an early stage in 81% of cases (Stage I: 71%) [10]. Our patient presented in stage I with a tumor of size >25cms.

GCTs grossly appear unilateral, solid or partially cystic, the cut surface maybe grey white or yellow, with necrosis and hemorrhage often present. Histologically, they are divided into adult and juvenile subtypes. In the adult subtype granulosa cells appear round, pale, scanty cytoplasm and with coffee bean grooved nuclei. Call Exner bodies is the pathognomonic histopathological finding in which, the cells arrange themselves in clusters or rosettes around a central cavity filled with eosinophilic fluid. The juvenile subtype is characterized by a follicular or diffuse growth pattern, with extensive luteinization and presence of lipid in the granulosa and/or theca cell elements.

Thecomas are clinically similar to granulosa cells and produce estrogen. They are unliteral and found in postmenopausal women. They vary in size from small to large (5-10cm diameter), rubbery, yellow to orange depending on the lipid content. Histologically, sheets of round to oval cells with pale cytoplasm containing lipid are frequently seen with hyaline bands interspersing cells. Treatment is surgical excision as they are virtually never malignant and hence have excellent prognosis with a 5-year survival rate of 100%.

Fibromas may appear as pure forms which are non-functioning or else may contain theca cells and therefore secrete estrogen. They are usually seen in middle aged and perimenopausal women. Grossly, they are unilateral, fibrous solid growths, with hard grey to white whorled cut surface. They are mostly extensively calcified making it difficult to cut. Histologically, they are seen as well differentiated fibroblasts in collagenous stroma.

Sex cord stromal tumors have a spectrum of imaging manifestations due to the various histologic appearances and arrangements of tumor cells. Imaging reports in these tumors vary from solid masses, tumor with hemorrhagic or fibrotic changes, multilocular cystic lesions or even complete cystic lesions [11]. MRI finding in our patient illustrated a solid tumor with cystic areas. Hence imaging modality may not accurately diagnose a case as sex cord stromal tumor.

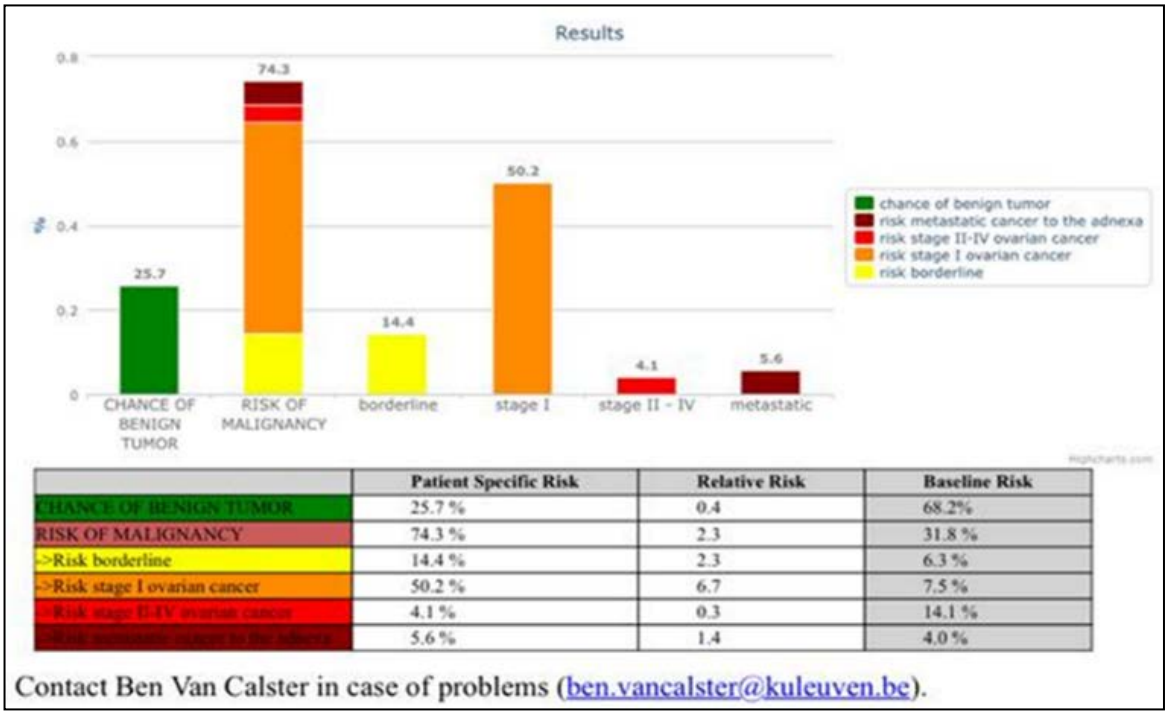
Of all the tumor markers reported to have stained granulosa cell tumors, inhibin has been proven to be the most useful [12]. Inhibin is a hormonal polypeptide, containing α and β subunits. It is present in ovarian granulosa and lutein cells and its function is to suppress the pituitary gonadotropins [13]. In an immunohistochemistry study by Deaver *et al* in 53 subjects with sex cord stromal tumors 45 tumors (85%) were positive for inhibin and staining in 53% were 3+ to 4+. Of the cases negative for inhibin, all but one was fibromas or fibro the comas. This report gives us a picture in our case as immunohistochemistry for inhibin was negative, the tumor preponderance is towards fibromas or fibrothecomas. However, in their study one case of metastatic adult granulosa cell tumor had inhibin negative.[14]

According to recent reports, calretinin which is widely used in mesothelioma panels, may also be useful in diagnosis of ovarian sex cord stromal tumors [15]. Calretinin is a 29KDa calcium binding protein that was discovered originally in neuronal tissue

and later found in mesothelial cells and in ovaries. Granulosa cell tumors have a potential for clinically malignant behavior. The mainstay of treatment however is complete surgery i.e. hysterectomy with bilateral salpingo-oophorectomy with staging for early stage and debulking surgery for advanced stage or recurrent disease [16]. Majority of the patients have excellent prognosis with >100% having a 10year survival rate. However, they do have a tendency of late recurrence, even 10-20 years after diagnosis [11].

Conclusion

This case report shows that huge ovarian tumors in post hysterectomy patients in perimenopausal age groups, rarely can be non- epithelial (as in our case). Timely surgical intervention can give best prognosis in these cases.



	Patient Specific Risk	Relative Risk	Baseline Risk
CHANCE OF BENIGN TUMOR	25.7 %	0.4	68.2%
RISK OF MALIGNANCY	74.3 %	2.3	31.8 %
->Risk borderline	14.4 %	2.3	6.3 %
->Risk stage I ovarian cancer	50.2 %	6.7	7.5 %
->Risk stage II-IV ovarian cancer	4.1 %	0.3	14.1 %
->Risk metastatic cancer to the adnexa	5.6 %	1.4	4.0 %

Fig 1: IOTA- ADNEX report of the patient

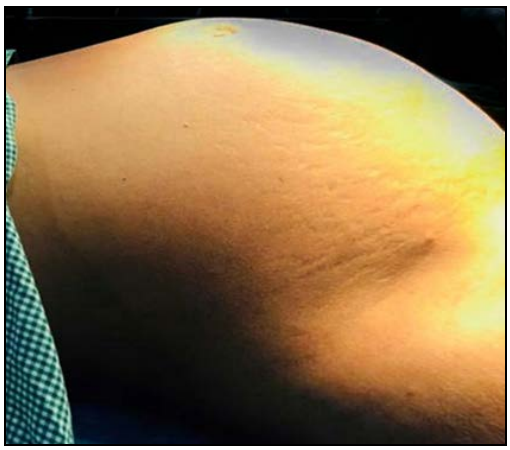


Fig 2: Abdomen examination showing the ovarian mass

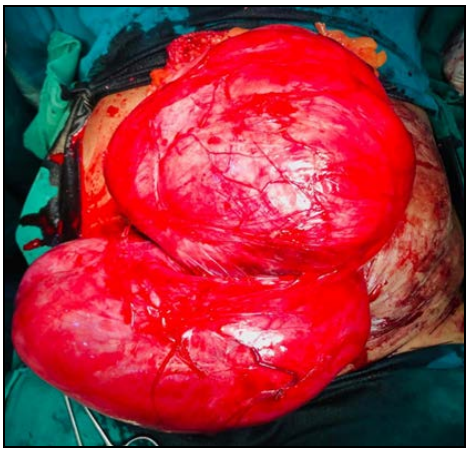


Fig 3: Intra operative finding of ovarian tumor

Fig 4: Cut section of ovarian tumor showing the solid areas

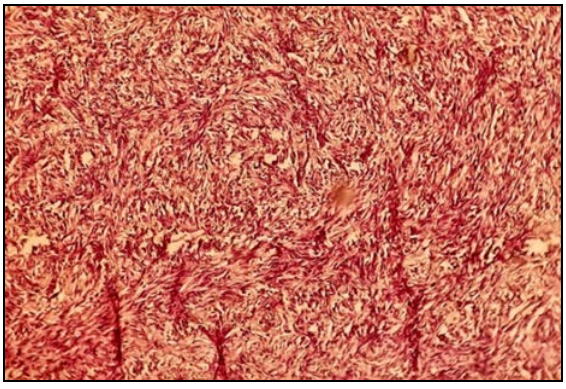


Fig 5: Histo pathological examination revealing mixed sex cord stromal tumor

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