Ovarian Sertoli-Leydig Cell Tumour, A Rare Neoplasm: A Case Report

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Abstract: Sertoli-Leydig cell tumours are uncommon tumours comprising less than 0.5% of ovarian neoplasms. It is a sex cord stromal tumour. As the name indicates, Sertoli-Leydig cell tumours are composed of a mixture of variable proportions of cells morphologically resembling male Sertoli and Leydig cells. Most tumours are unilateral and confined to ovaries. And they are seen during the second and third decades of life. These tumours are characterized by the presence of testicular structures that produce androgens. Hence, many patients have symptoms of virilisation depending on the quantity of androgen production. Small subsets of them are hyperestrogenic. The second characteristic feature of this tumour is the degree of differentiation of structure in them. Histologically, these are classified (WHO) as well-differentiated, with intermediate differentiation, poorly differentiated, with heterologous components and retiform type. Prognosis depends upon the degree of tumour differentiation (grading) and tumour extent (staging).

Keywords: Sertoli-Leydig cell tumour, sex cord stromal tumour, ovary, androgens, differentiation

1. Introduction

Ovarian Sertoli-Leydig cell tumours are rare. These constitute less than 0.5% of ovarian tumours [2, 4, 7and8]. The common presenting complaints are due to either mass occupying lesion or hormonal production [3]. They are known to produce various hormones like testosterone and androstenedione. About 1/3 rd cases may present with virilisation [8]. Inactive or even estrogenic tumours have been reported [2, 3]. Age of the patient, stage of the disease and degree of tumour differentiation based on morphology are the most important factors to consider in the management of the case. We are presenting a case of tumour with intermediate differentiation.

2. Case Details

A 23 year old female with previously normal menstrual cycles came with complaints of amenorrhea of 2 years duration. She started developing excessive hair growth over face, arms, abdomen and chest. She also noticed regression of breast and hoarseness of voice since 6 months. On examination, per abdomen was soft and nontender. Per speculum examination showed clitoromegaly, vagina and cervix appeared healthy. Vaginal examination revealed fullness in left fornix and was nontender. Abdominal ultrasonography revealed a left ovarian mass measuring 9.3×7.5×5.6 cm. Investigations showed free testosterone level 5.28ng/ml , FSH <0.66mIU/ml , LH 6.26mIU/ml, sex hormone binding globulin 37.28 , dihydroepiandrosterone 260mcg/dl and 17-hydroxyprogesterone 0.09ng/ml. Renal, liver and thyroid profile were within normal limits. Haematological parameters and coagulation were normal. Patient underwent left oophorectomy. Per operative uterus, bilateral fallopian tubes, right ovary and omentum were healthy. No peritoneal deposits or enlarged pelvic lymph nodes were seen.

Gross evaluation revealed a globular mass measuring 8cm in diameter. Its external surface was smooth with few congested blood vessels; it was partly cystic and partly solid in consistency. Cut surface showed half cystic and half solid area, cystic area drained seromucinous fluid and its wall was smooth. The solid half showed grey yellow and grey white areas with areas of hemorrhage. Paraffin embedded and haematoxylin-eosin stained tissue sections revealed Sertoli like cells which were arranged in groups, sheets and tubules forming cysts at places. These cells were oval-spindle having vesicular nuclei and scant cytoplasm. In the stroma were seen large cells with vacuolated cytoplasm in singles and clusters (Leydig cells). Hence, a diagnosis of Sertoli-Leydig cell tumour with predominant Sertoli cell component was made.

Figure 1: External surface of the left ovarian mass is smooth and glistening.
3. Discussion

Sertoli-Leydig cell tumour (SLCT) of ovary is exceedingly unusual neoplasm that belongs to a group of sex cord-stromal tumour of ovary and accounts for less than 0.5% of all primary neoplasms [5]. This term replaces the old designations arhenoblastoma and androblastoma, and should be considered synonymous with Sertoli-stromal cell tumour. Pure Sertoli cell tumours are also included in this group, but pure Leydig cell tumours are included with lipid cell tumours [12]. It is composed of variable proportions of cells morphologically resembling male Sertoli and Leydig cells [12]. Actual neoplastic component for SLCT is constituted by Sertoli cells [5, 6and 12]. SLCT can affect any age group, ranging from 2 to 75 years of age. But approximately 75% cases are reported during second and third decades of life. Choong CS et al have reported a case of oestrogen secreting Sertoli-Leydig cell tumour in a 12-month-old infant. Less than 10% of cases are reported prior to menarche or following menopause [7]. Predominantly unilateral and confined to ovary, only 2-3% of SLCTs have extra ovarian spread. Reports of SLCTs affecting bilateral ovaries are exceptionally rare and account for only 1.5-2.0% of all the cases [6, 7]. Tumour rupture is documented in 10% of cases. Around 4% of SLCT patients develop ascites [6, 17]. In our patient the tumour was unilateral and with no evidence of pre operative rupture, ascites or extraovarian spread.

SLCTs are graded as well differentiated, with intermediate differentiation, poorly differentiated, with heterologous elements, retiform and pure Sertoli cell tumours based on the degree of tubular differentiation of the Sertoli cell component and the quantity of the primitive gonadal stroma [6,7and 12]. The most common subtypes are intermediate and poorly differentiated. Heterologous components occur in nearly 20% of SLCTs and include glands and cysts lined by intestinal and gastric- type of epithelium, hepatocyte- like cells, retinal tissue, and islands of cartilage, carcinoid tumour, embryonal rhabdomyosarcoma and neuroblastoma [6 and 17].

The two main theories of the histogenesis of Sertoli-Leydig cell tumours suggest that they arise either from the gonadal mesenchyme of the ovary or from remnants in the hilum [1and12].
Clinical features are due to either hormonal production or mass occupying lesion. Only 30% patients present with symptoms of virilisation. Usual presentation is non-specific abdominal symptoms due to ovarian mass more so observed in SLCTs with heterologous elements [6, 17]. Rarely patient presenting with features of excess of estrogen production like precocious puberty, abnormal uterine or vaginal bleeding, menstrual abnormalities, breast engorgement and endometrial hyperplasia have been documented [3, 9]. Unusual manifestations like associated Peutz-Jeghers syndrome, splenic metastasis and peritoneal implants are documented in the literature [5].

Imaging studies especially sonography are the preferred modality for the initial assessment of ovarian SLCTs. Other imaging modalities such as CT, MRI and PET scans can be used for better characterization, identifying extraovarian disease or metastasis [6].

Grossly, SLCTs are frequently unilateral, well-encapsulated, solid, firm, lobulated, and yellow grey masses of roughly 7cm in diameter on average. Cut surface exhibits varying degrees of greasy/fleshy consistency, straw-coloured fluid, necrosis, haemorrhage and cystic spaces separated by fibrous septae [7].

Microscopically, SLCTs are classically made up of uncontrolled proliferation of varying degrees of differentiation of tubules lined by Sertoli cells and intervening nests of Leydig cells. Well and moderately differentiated SLCTs are the most frequently encountered histological variants. Leydig cells are typically found in clusters in interstitial stroma and typically exhibit polygonal cells with well-defined margins, centric nuclei, prominent nucleoli, and eosinophilic cytoplasm. Sertoli cells typically form tubular structures lined by single or multiple layers of cuboidal-columnar cells with well-bounded margins, oval dark (basal) nuclei, inconspicuous nucleoli and eosinophilic or vacuolated cytoplasm. Mitotic figures are extremely rare. Poorly differentiated SLCTs represent a considerable diagnostic challenge owing to the huge range of microscopic/histopathological diversity. The classical arrangement of tubules lined by Sertoli cells and intervening nests of Leydig cells is greatly minimal, very occasional and most difficult to identify.

The sex-cord neoplastic cells exhibit poor differentiation with high nuclear atypia, increased nuclear to cytoplasmic ratio, coarse chromatin and extremely abundant mitotic figures can be misleading and easily mistaken for a diagnosis of undifferentiated sarcoma.[7]. One of the interesting facts about this tumour is that only Sertoli cells compose the malignant part of the tumour [12].

Immunohistochemically, almost all SLCTs, stain positive for inhibin and calretinin, and negative for epithelial membrane antigen (EMA). In addition it has been shown that SLCTs stain positive for WT-1 and CD56 (7). A collective profile of hematoxylin and eosin (H&E) stains in addition to immunohistochemical studies are expected to yield the most accurate definitive diagnosis of SLCTs [7]. SLCTs have many patterns and thus the differential diagnosis is quite wide. The general differential diagnosis for all SLCTs should include granulosa cell tumour, moderately to poorly differentiated endometrioid carcinoma and female adenexal tumor of probable woffian origin (FATWAO). In cases of SLCTs of intermediate differentiation with heterologous elements of mucinous type intestinal epithelium, however, the differential diagnosis should be expanded to include mature cystic teratoma and mucinous cystadenoma [17].

Management of ovarian SLCTs remains challenging owing to lack of standardized management protocol guide-lines. Surgical resection represents the mainstay of management of ovarian SLCTs. Fortunately, the vast majority of SLCTs are largely diagnosed during reproductive age, frequently unilateral, mostly confined to ovary and nearly 90% classified as stage I at the time of clinical diagnosis. Therefore, fertility-sparing surgery (unilateral salpingo-oophorectomy) can be considered in all patients with well-differentiated ovarian SLCTs. Patients desiring fertility and exhibiting moderately or poorly differentiated ovarian SLCTs can be considered for unilateral salpingo-oophorectomy plus standard staging surgery (omentectomy, appendectomy and pelvic lymphadenectomy). The need for pelvic lymphadenectomy is still debatable.

Owing to rarity of ovarian SLCTs, limited number of documented case reports/series and lack of randomized clinical trials, effectiveness of post-operative chemotherapy remains questionable and requires further evaluation. Generally, postoperative chemotherapy is considered for patients with poor prognostic factors such as: advanced disease stage, moderate to poor tumour grading, high mitotic profile, existence of heterologous elements and tumour rupture. The first-line and most frequently used chemotherapeutical regimen is bleomycin, etoposide and cisplatin (BEP) [7].

To determine the prognosis of a patient, stage of the tumour is very important. Stage Ia is found in 80% of tumours, tumour rupture or involvement of external surface of ovary in 12% and ascitis in 4%. Spread beyond the ovary within the pelvis or upper abdomen is found in 25%. Poorly differentiated were more often ruptured or presented at a higher stage. Well differentiated tumours were usually 0-1% malignant, intermediate 11%, poorly differentiated 59%, heterologous 19% and retiform 25% [8].

4. Conclusion

Sertoli-Leydig cell tumour is a rare ovarian sex cord stromal tumour of reproductive age group with limited number of documented cases in literature. In view of the rarity, diverse morphologic features establishing the diagnosis may be difficult especially when associated with heterologous elements.

References


