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Case Report

Pathology Section

Ovarian Sertoli-Leydig Cell Tumour with Heterologus Elements Masquerading as Mucinous Tumour on Frozen Section: A Case Report

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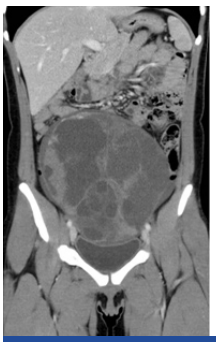
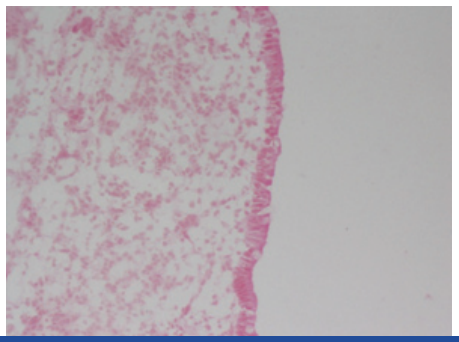
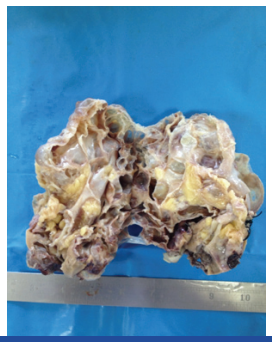
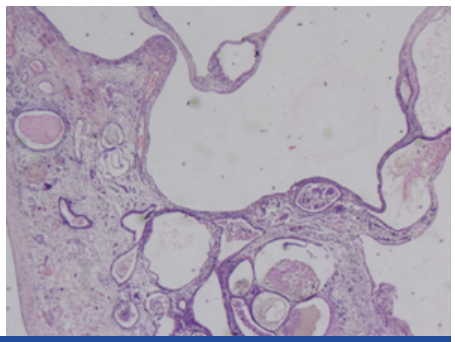
ABSTRACT

Sertoli-Leydig cell tumour (SLCT) is an extremely rare ovarian neoplasm. This tumour is characterized by excessive proliferation of normal testicular structures sertoli and leydig cells. These cells are seen in varying proportions and exhibit varying degrees of differentiation. We report a case of primary ovarian SLCT with heterologus elements in a 17-year-old girl which was misdiagnosed on frozen section as mucinous cystic neoplasm. We discuss the clinicopathologic features of SLCT along with the unusual features seen in this case.

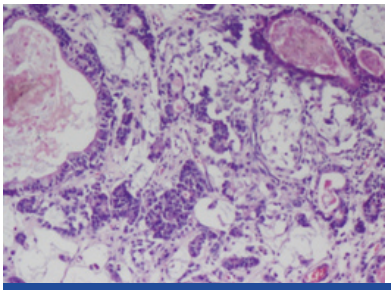
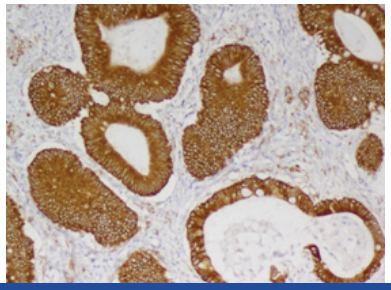
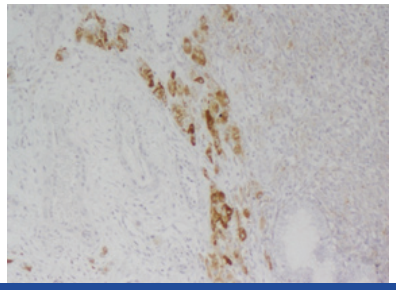
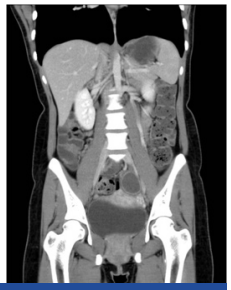
Keywords: Ovarian neoplasms, Sertoli cell, Sex cord-stromal

CASE REPORT

A 17-year-old girl with previously normal menstrual cycles visited gynecology out patient department of a tertiary care hospital with complains of amenorrhea of 18 months duration, hirsutism for 12 months and abdominal distension since 4 months. Six months after developing amenorrhea, she started developing excessive hair growth on the face, arms, abdomen and chest. She also noticed reduction in the size of breast and hoarseness of voice. Cushingoid features were absent. On per abdomen examination, a mass measuring 22x15 cm was palpated in bilateral lumbar, umbilical and iliac fossa. Investigations showed total testosterone 502.42ng/dl (N 14-76 ng/dl) and AFP 290.7ng/ml (N 0-9ng/ml). Levels of CEA, CA19.9, CA125, serum beta HCG, serum cortisol were normal. Renal, liver and thyroid profile were within normal limits. Haematological parameters and coagulation were normal. CT abdomen confirmed solid multicystic lesion arising from right adnexa measuring 17.5x16.4x8.8cm [Table/Fig-1]. Patient underwent right Salpingo-oopherectomy. Per operative uterus, bilateral fallopian tubes, left ovary and omentum were healthy. No peritoneal deposits or enlarged pelvic lymph nodes were seen. Ovarian mass was sent for frozen section and reported as mucinous cystic neoplasm [Table/Fig-2]. Peritoneal wash did not show any malignant cells. On histopathology, an enlarged ovarian mass with attached tube weighing 500 gm and measuring 15x11x5cm was received. Cut section showed mucoid filled multiloculated cysts and grey yellow solid areas [Table/Fig-3]. Microscopy revealed a tumour composed of solid and cystic areas with interspersed tubules of sertoli cells, nests of spindle shaped primitive gonadal stroma and clusters of leydig cells. It also showed cysts lined by mucinous epithelium with focal intestinal differentiation showing goblet cells [Table/Fig-4,5]. IHC showed cytokeratin positivity in epithelial and cystic component and inhibin positivity in leydig cells [Table/Fig-6,7]. Diagnosis of

[Table/Fig-1]: CT abdomen, large multicystic lesion **[Table/Fig-2]:** Mucinous epithelium on frozen section Rapid H&E, X100 **[Table/Fig-3]:** Multiloculated cysts and yellow solid areas **[Table/Fig-4]:** Predominant multicystic mucinous areas H&E, X200

[Table/Fig-5]: Mucinous epithelium with intestinal metaplasia, Sertoli cell tubules and Leydig cell clusters H&E, X100 **[Table/Fig-6]:** Cytokeratin positivity in epithelial component, X100 **[Table/Fig-7]:** Inhibin positivity in Leydig cells, X100 **[Table/Fig-8]:** CT abdomen, Postsurgery- no residual tumour/recurrence

SLCT with intermediate grade and heterologus elements was given. Postoperative serum testosterone and AFP reduced to 0.1ng/ml(N 0.2-1.2ng/ml) and 74.8ng/ml (N 0-9ng/ml) respectively. Patient was referred to oncology for further management. Postoperative CT abdomen and pelvis was done and showed no evidence of residual tumour or recurrence [Table/Fig-8]. Patient is on regular follow up since one year. During last follow up serum testosterone, AFP levels and ultrasound were normal.

DISCUSSION

Sertoli-Leydig cell tumour (SLCT) is a rare sex cord-stromal tumour of ovary accounting for less than 0.5% of all primary ovarian neoplasms [1]. Earlier designated as arrhenoblastomas and androblastomas, SLCTs are characterized by proliferation of neoplastic Sertoli and Leydig cells exhibiting varying degrees of differentiation. Actual neoplastic component for SLCT is constituted by Sertoli cells [1,2]. SLCTs can affect any age group but approximately 75% cases are reported during second and third decades of life. Less than 10% of cases are reported prior to menarche or following menopause. Predominantly unilateral and confined to the 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 [1]. Tumour rupture is documented in 10% of cases. Around 4% of SLCT patients develop ascites [3]. In our patient the tumour was unilateral and with no evidence of pre operative rupture, ascites or extraovarian spread.

SLCTs are graded as well, moderately and poorly differentiated, and with heterologous elements based on the degree of tubular differentiation of the Sertoli cell component and the quantity of the primitive gonadal stroma [1-3]. 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 or gastric-type epithelium, hepatocyte-like cells, retinal tissue, islands of cartilage, carcinoid tumour, embryonal rhabdomyosarcoma and neuroblastoma [3].

Our case had raised AFP levels. With limited literature available, approximately 75% of AFP producing SLCTs is seen in patients less than 30 years of age. AFP production is associated with Leydig cells, Sertoli cells and heterologous hepatocytic cells. Levels should regress immediately after surgery. The exact histogenesis and clinical prognosis of these tumours need further substantiation [4]. SLCTs with heterologous elements were thought to have a teratomatous origin but could not be explained as neither Sertoli nor Leydig cells are identified in ovarian teratomas. An alternative hypothesis is endodermal neometaplasia within a tumour of mesodermal origin [5]. Endodermal components including gastrointestinal epithelium most frequently appear as heterologous elements. Even AFP production by SLCT may be a result of functional neometaplasia to some endodermal components [6].

Clinical features are due to either hormonal production or mass occupying lesion. Only 30% patients present with symptoms of virilization. Usual presentation is non specific abdominal symptoms due to ovarian mass more so observed in SLCTs with heterologus elements [3,7]. However, our patient presented with hirsuitism, hoarseness of voice, breast atrophy, increased testosterone levels and amenorrhea due to androgen excess. 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 [1]. Unusual manifestations like associated Peutz-Jeghers syndrome, splenic metastasis and peritoneal implants are documented in the literature [2].

Imaging studies especially sonography are the preferred modality for the initial assessment of ovarian SLCTs. Other imaging modalities such as CT, MRI and positron imaging tomography (PET) scans can be used for better characterization, identifying extraovarian disease or metastasis [7]. Grossly, SLCTs are well-encapsulated, solid or cystic, lobulated, and yellow-gray masses ranging between 5-15 cm in size. SLCTs with heterologous elements are more frequently cystic as seen in our case and larger in size compared to pure SLCT [5]. On histology, they show proliferating tubules lined by Sertoli cells and intervening nests of Leydig cells in interstitial stroma. Mitotic figures are infrequent [1,3]. Our case also showed mucinous epithelial lining cysts as heterologus elements. On IHC, SLCTs stain positive for inhibin and calretinin, and are negative for epithelial membrane antigen (EMA). In addition, they also stain positive for WT-1 and CD56 [1].

SLCTs have diverse morphologic patterns. Presence of heterologus elements further add to the diagnostic dilemma. When mucinous type intestinal epithelium is present, as in our case, possibility of mature cystic teratoma and mucinous cystic neoplasm are to be considered. Mature cystic teratomas are typically composed of a variety of tissues arising from all three germ layers. SLCTs may have heterogenous elements but typically to a much lesser degree. The clusters of Leydig cells may be confused with heterologous hepatocytes but IHC can resolve the dilemma [3]. As in our case intestinal type epithelium as heterologus component may be present so extensively that it would mask the Sertoli-Leydig cell component and lead to a misdiagnosis of mucinous cystic neoplasm of ovary. Also the presence of yellow gray tissue favors SLCT with heterologus elements over mucinous neoplasm. One should remember that history of virilization is only suggestive and not conclusive for SLCTs as mucinous cystic neoplasms may also be masculinizing due of the presence of lutein cells in their stroma [5]. Hence, an extensive search for SLCT component should be made for apparent mucinous cystic neoplasm with history of hirsutism. These diverse patterns along with frozen section artefacts not only pose diagnostic challenges but can also lead to an errorneous diagnosis as seen in our case. We sampled predominantly the heterologus component for intra operative consultation which led to the misdiagnosis as mucinous cystic neoplasm. However, on paraffin blocks heterologus mucinous component constituted around eighty percent of the entire tumour. Virk et al., have reported a case of mucinous adenocarcinoma as heterologous element in an ovarian SLCT [8]. In our case, the mucinous epithelium was benign.

Management of ovarian SLCTs lacks standardized protocols. However, fertility sparing surgical resection is the mainstay of management [1,3]. Postoperative chemotherapy is considered for patients with poor prognostic factors. Prognosis depends on the degree of tumour differentiation and extent. Moderately and poorly differentiated SLCTs are associated with 11% and 59% of malignant potential respectively and have an overall 5-year survival rate of 80% [1]. Long-term follow-up is advised in all patients. Our patient is on regular follow up.

CONCLUSION

SLCT 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 and limited experience of the pathologists for this entity, establishing the diagnosis may be difficult especially when associated with heterologus elements and during intra operative consultations.

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