



Case Report

## Retiform Variant of Sertoli - Leydig Cell Tumor, a Rare Ovarian Neoplasm; Special Emphasis on Differential Diagnosis

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### ABSTRACT

A case of retiform variant of Sertoli-Leydig cell tumour (SLCT) of ovary was encountered in a 16 year old girl with a history of menstrual abnormalities.

There are marked differences in the frequency of ovarian neoplasms in the first three decades compared with later years, with a much higher percentage of germ cell and sex-cord stromal tumors, and fewer surface epithelial neoplasms and great rarity of metastatic malignancies.

Sertoli-Leydig cell tumors are rare sex-cord stromal tumours that account for less than 0.2 % of all ovarian neoplasms, but comprise 4% of ovarian tumours in females under 20 years. SLCTs are classified into five major classes: well differentiated, of intermediate differentiation, poorly differentiated, heterologous and retiform. Other variants of SLCT are commoner in the third decade (about 75%). The retiform variant accounts for about 10 % of SLCTs and is most frequent in the second decade. It is, therefore, important in the differential diagnosis of ovarian tumors at this age.

Because of its age of presentation, endocrinal disturbances and peculiar morphology, many tumorous and non-tumorous conditions enter in the differential. The presence of heterologous elements in some of these further complicates diagnosis. This article is an attempt to describe the morphological characteristics, review the literature and discuss the salient points in differential diagnosis, including the role of immunohistochemistry.

**Key words:** Ovarian Retiform Sertoli – Leydig cell tumor, Neoplasm.

### INTRODUCTION

There are marked differences in the frequency of ovarian neoplasms in the first three decades compared with later years, with a much higher percentage of germ cell and sex-cord stromal tumors, and fewer surface epithelial neoplasms, and great rarity of metastatic malignancies. <sup>[1]</sup>

Sertoli-Leydig cell tumors (SLCT) are rare sex-cord stromal tumors that account for less than 0.2 % of ovarian

neoplasms in total but comprise 4% of ovarian tumors in females under 20 years. SLCTs are classified into five major classes: well differentiated, of intermediate differentiation, poorly differentiated, heterologous and retiform.

The retiform variant accounts for about 10 % of SLCTs. Other variants of SLCT are commoner in the third decade (about 75%), the retiform variant is most frequent in the second. This tumour is,

therefore, important in the differential diagnosis of ovarian tumors at this age. [2]

Because of its age of presentation, associated endocrinal disturbances and peculiar morphology, many tumorous and non-tumorous conditions enter in the differential. The presence of heterologous elements in some of these further complicates diagnosis. This article is an attempt to describe the morphological characteristics, review the literature and discuss the salient points in differential diagnosis, including the role of immunohistochemistry.

### CASE REPORT

16 yrs unmarried girl presented in the Gynecology department of our institution with a history of amenorrhoea of five months duration with previous history of irregular menses since one year. She was found to have an abdominal lump which was discovered on ultrasound examination to be a right sided ovarian mass of mixed echogenicity with small amount of free fluid in the peritoneal cavity.

Oophrectomy was carried out and the surgical specimen received in the Pathology department was an ovarian cyst 10 x10 x6cm. Cut section of the mass was partly solid, firm cream coloured and partly multiloculated cystic.

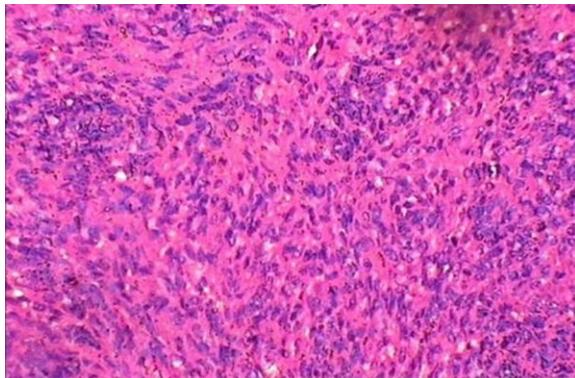


Figure 1. Solid area- Spindle cell fascicles. (Hematoxylin and Eosin, x100).

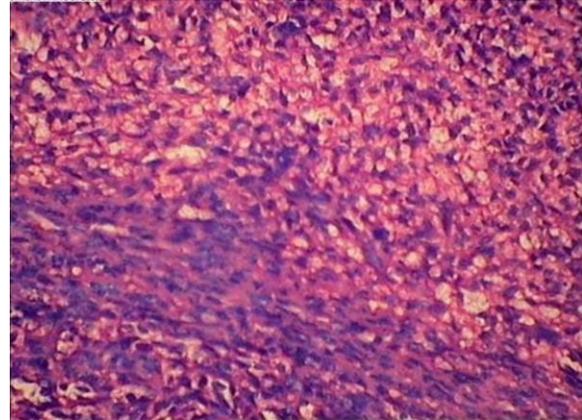


Figure 2. Solid area- Vacuolated and spindle cells. (Hematoxylin and Eosin, x 400).

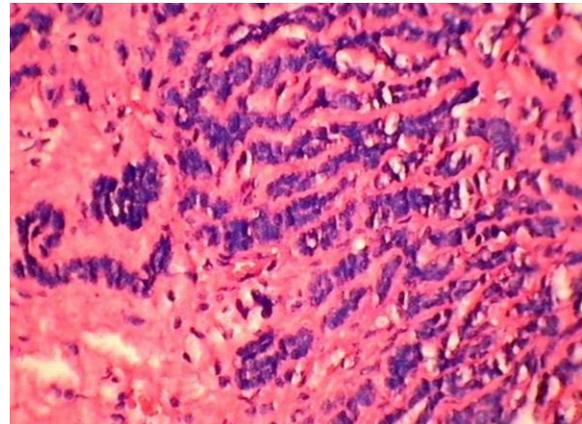


Figure 3. Cords, slit like tubules of immature sertoli cells. (Hematoxylin and Eosin, x400).

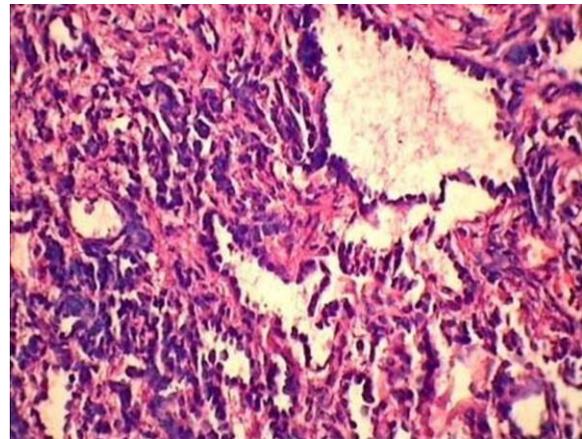


Figure 4. Larger tubules – single layered, low cuboidal lining. (Hematoxylin and Eosin, x400).

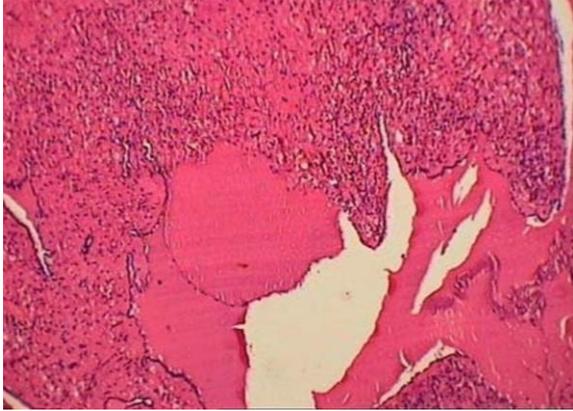


Figure 5. Cystic area – edema, tubules, Cysts with eosinophilic material (Hematoxylin and Eosin, x100)

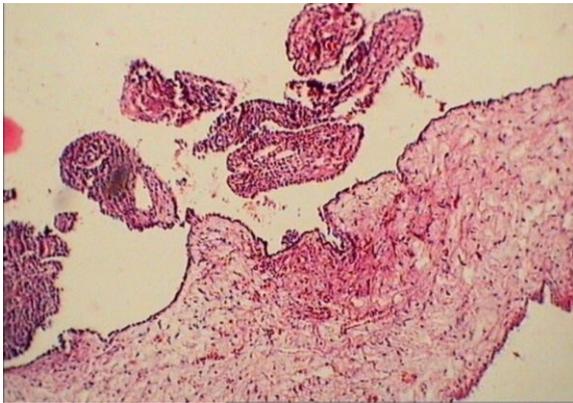


Figure 6. Cystic area- blunt papillae, edematous stroma. (Hematoxylin and Eosin, x100)

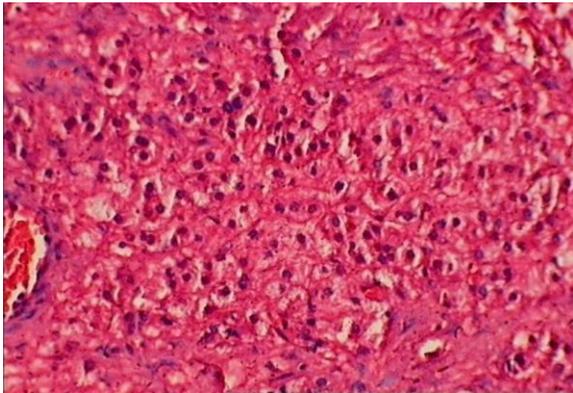


Figure 7. Leydig cell groups. (Hematoxylin and Eosin, x400)

Microscopic examination of the sections from solid areas showed cellular spindle cell fascicles (Figure 1). Cells showed moderate amount of cytoplasm and central oval to spindle nucleus (Figure 2). Also seen were cells with abundant pale vacuolated cytoplasm.

Sections from cystic areas showed a loose edematous tissue with an irregular network of elongated, mostly slit like tubules (Figure 3) and some larger tubules with a wide lumen were also seen (Figure 4). The tubular lining was seen to be single layered low cuboidal, with scanty cytoplasm and round regular nuclei. Cysts with eosinophilic hyaline material (Figure 5) and blunt papillae with an edematous stroma were prominent (Figure 6).

Interspersed between these cords were groups of large cells with abundant granular cytoplasm (Figure 7). These are Leydig cell groups. It is important to identify these for a correct diagnosis. Based on the clinical, endocrinal and histopathological features the diagnosis of retiform variant of SLCT was entertained.

## DISCUSSION

The usual patient is a young girl in the second decade but younger and older patients have been reported. They present with a mass lesion and endocrine abnormalities, usually androgenic. [3] These cases may present with virilization, masculinization, oligomenorrhoea or amenorrhoea. Clinically this variant is less often associated with endocrinal disturbances than other variants of SLCT, having these signs and symptoms only about 20% of the time. This is important to remember because androgenic manifestations point to a diagnosis of SLCT in a young person; conversely absence of these features may lead to the diagnosis being overlooked.

Estrogenic effects have also been reported, for example precocious puberty in a 12 month old infant. [4] Androgenic manifestations are more common with tumors of lesser differentiation. [5]

### *Morphological characteristics*

Grossly retiform tumors are often soft and spongy, cystic with edematous

intraluminal excrescences. These tumors are so named because they are characterised, microscopically, by growth patterns that simulate those of the rete testis. The basic pattern is an irregular network of elongated, often slit-like tubules and cysts which often contain papillae. The papillae may be short and rounded or blunt, often containing hyalinised cores, or larger with fibrous or edematous cores. Cysts may be markedly dilated with eosinophilic secretion, imparting a struma-like appearance in some cases. The tubules are usually lined by a single layer of cuboidal epithelial cells with round to oval nuclei, although stratification is conspicuous sometimes. The cytoplasm is typically scanty and mitotic activity variable. Similar cells typically line the papillae and cysts, but the lining of large cysts may be flattened.

The stromal component varies from moderately cellular fibrous tissue (which is focally hyalinised) to a very cellular immature mesenchymal tissue which, frequently has a sarcomatous appearance.<sup>[1]</sup> A case has been reported with marked hyalinization, calcification and ossification.<sup>[6]</sup> Calcifying Sertoli cell tumors have been reported in the testis, but this is the first one reported in the ovary.

**Heterologous component:**

These are common in tumors of intermediate and poor differentiation, as well as in the retiform variant. The commonest component (about 90% of cases) is gastrointestinal type mucinous epithelium. Mathur et al report one such case with extensive mucinous element.<sup>[7]</sup>

Mesenchymal components are seen in tumors with sarcomatous background.<sup>[1]</sup> Kataria et al report a case of a 14 year old girl showing 50-60 % smooth muscle component in a retiform SLCT.<sup>[8]</sup>

**Differential diagnosis**

Sertoli-Leydig cell tumors (SLCT) are sex cord-stromal tumors which exhibit testicular differentiation. The morphological appearance of the parenchymal and stromal component of these tumors varies widely. This, along with variable amounts of heterologous component and clinically variable endocrinal manifestations, leads to wide differential diagnostic possibilities.

Differential diagnosis can be discussed under two heads- SLCT with heterologous elements (Table I) and without heterologous elements (Table II).

Table I. Differential diagnosis of SLCT without heterologous element.

Entity	Feature causing diagnostic confusion	Features favouring diagnosis other than SLCT
Endometrioid stromal sarcoma (ESS)	ESS with sex cord like differentiation	Middle age, diffusely arranged small oval to spindle cells with scant cytoplasm. Spiral arterioles seen. Associated endometriosis common
Serous surface epithelial tumor	Cases of SCLT with marked papillary formations, stratification & Solid foci in stroma.	Older age group, No androgenic manifestations. More typical SLCT areas.
Tubular variant of Krukenberg tumour	Tubules and desmoplastic stroma may cause confusion	Bilaterality and evidence of primary lesion.
Massive edema of ovary	May occur in childhood, with menstrual disturbances	Cortical areas selectively spared.
Homologous (MMMT) Malignant Mixed mullerian tumor	Sarcomatoid stroma in poorly differentiated type of SCLT mixed with ill formed epithelial element may cause confusion	Older age group Absence of endocrinal manifestations
Carcinoid tumour	When tubules predominate in well differentiated SLCT	Leydig cell groups absent, carcinoid syndrome, no sex hormonal manifestations.

Table II . Differential diagnosis of SLCT with heterologous element.

Entity	Feature causing diagnostic confusion	Features favouring diagnosis other than SLCT
Teratoma	Epithelial and stromal elements intermixed.	Neural elements, Squamous epithelium and skin appendages common.
Mucinous surface epithelial tumours	When a lot of heterologous mucinous element seen in SLCT and papillary areas present.	Older age group Absence of endocrinal manifestations

### ***Immunological studies in differential diagnosis.***

In the typical case, the distinction between sex cord-stromal and other ovarian neoplasms requires nothing more than routine pathological examination.

In diagnostically challenging cases immunohistochemistry has to be resorted to. Cytokeratin and EMA, traditional epithelial markers, showed overlapping results. [9] Inhibin is a glycoprotein produced by normal ovarian granulosa cells and testicular sertoli cells. Inhibin antibody (IAB) has been found to be a good marker for sex cord differentiation in ovarian tumors. [10] Alpha -inhibin is a very useful marker because granulosa and sex-cord stromal tumors are positive whereas other potential mimickers are usually negative. [11]

Caution should be exercised in the interpretation of alpha-inhibin-positive cells, because a wide variety of primary and metastatic ovarian tumors may contain significant numbers of trapped alpha-inhibin-positive stromal cells. [12] As with other immunohistochemical stains, a panel of stains and comparison with the corresponding haematoxylin and eosin slides is necessary, especially when staining patterns and cellular localization are in question. The antibody will not help to differentiate tumors within the category of SCST. The pattern or the intensity of staining in SCSTs does not predict tumor behavior, although there is a tendency of loss of alpha-inhibin expression in poorly differentiated Sertoli or Sertoli-Leydig cell tumors.

Calretinin has been recently recognized as a more sensitive, but less specific marker for SCSTs and it may be used to recognize an inhibin-negative SCST. [13] However, the value is somewhat limited since occasional neoplasms which enter into the morphological differential diagnosis may be positive. Calretinin should always be used as part of a larger panel.

EMA, inhibin, and chromogranin represent the most helpful triad of immunomarkers serving to exclude two common mimics of Sertoli cell tumors (endometrioid carcinoma [inhibin-, EMA+, chromogranin-] and carcinoid tumor [inhibin-, EMA+, chromogranin+]). [14]

### **CONCLUSION**

Retiform variant of SLCT is a rare ovarian neoplasm with variable endocrinal manifestations, diverse morphology and presence or absence of heterologous elements. The diagnosis may be missed if one is not aware of this entity. In the typical case morphological features, taken in the clinical and endocrinal context, are fairly diagnostic. In the atypical case, however many entities enter in the differential and in these cases alpha-inhibin, calretinin , EMA and chromogranin are some of the immunohistochemical markers which would help in diagnosis.

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