

## Bilateral ovarian sex-cord stromal tumors and review of literature

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### Abstract

Sex cord stromal tumors (SCST) are rare, accounting for only 5-10% of all ovarian tumors, with bilateral tumors representing an exceedingly small percentage. We report a case of a SCST, unclassified, involving one ovary, while the other ovary was affected by a sclerosing stromal tumor. A 19 year-old female, presented with history of pelvic pain. A CT (Computerized tomography) scan identified a 16 cm multi-cystic mass arising from the right adnexal region. Microscopically, the right adnexal mass showed an admixture of patterns of stromal overgrowth and increased cellularity present in diffuse areas resembling different sex cord cells with sporadic mitotic activity, consistent with SCST, unclassified. A wedge biopsy of the left ovary revealed features of a sclerosing stromal tumor, to include alternating cellular/hypocellular areas within an edematous background. The diagnosis of a unclassified SCST should be considered when a tumor does not fulfill the morphologic features of a well-characterized sex cord stromal tumors. While bilateral involvement by two varieties of a SCST is very uncommon, it could be explained by the fact that all ovarian sex cord-stromal tumors are derived from the developing primitive gonadal stroma. Consequently, such tumors can develop along a testicular or ovarian differentiation pathway. Importantly, prognosis is evaluated based on the identification of atypical histological features within individual cases. Surgical excision with close clinical follow-up remains the standard approach.

**Keywords:** sex cord stromal tumor; unclassified; sclerosing stromal tumor; bilateral; surgical excision.

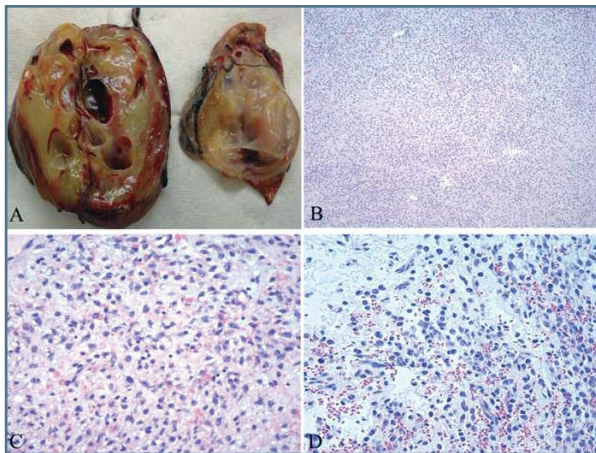
### INTRODUCTION

Unclassified sex cord-stromal tumors are a rare type of sex cord-stromal tumors. This diagnosis should be considered when a tumor does not meet the morphologic features of a well-characterized sex cord stromal tumors. We report a rare case of sex cord stromal tumor, unclassified in one ovary and sclerosing stromal tumor within the other ovary.

### CASE REPORT

A 19 year-old female presented with a two month history of pelvic pain. The patient's prior medical history was unremarkable. Clinical examination revealed a distended abdomen with a palpable mass. The clinical impression was concerning for malignancy. A CT scan of the abdomen and pelvis revealed a septated, multicystic mass apparently arising from adnexal region inferiorly, and deforming deviating uterus. Tumor markers including CEA (carcinoembryonic antigen), AFP (al-

pha-fetoprotein), and HCG (Human Chorionic Gonadotropin) were within normal range, while CA 125 was mildly elevated. The patient underwent an exploratory laparotomy with removal of the mass, plus pelvic washings and biopsies. Intra-operatively there was a large multi-cystic solid mass involving the right adnexa (Figure 1A), while the left ovary was only mildly enlarged, firm and indurated, consistent with either a fibrotic process or edema. There were a few dense adhesions on the posterior cul-de-sac, which were removed. The resected mass from the right ovary and wedge biopsy from the left ovary, omentum, posterior cul-de-sac and pelvic walls was sent to the pathology. Grossly, the right ovary consisted of a 15.2 cm cystic mass weighing 1438 grams, with a tan grey cut surface. Microscopically, it showed an admixture of patterns of stromal overgrowth and increased cellularity present in diffuse areas resembling different sex cord cells (granulosa or Sertoli) with sporadic mitotic activity (Figures 1B, 1C, and 1D). An immunohistochemical panel was performed to include inhibin, calretinin, ER (estrogen), PR (progesterone) and cyto-

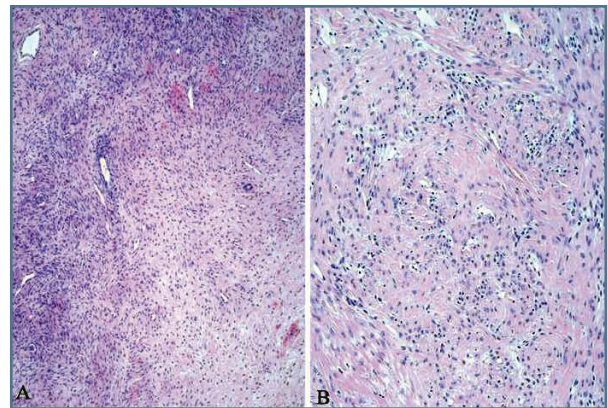


**FIGURE 1 (A-D):** (A) Multi-cystic large mass, showing tan to yellow cut surface, gross appearance. (B) Low power view of the right adnexal mass showing areas with stromal overgrowth & increase cellularity (sex cord stromal tumor, unclassified), (C) High power view showing abundant vacuolated or eosinophilic cytoplasm (sex cord stromal tumor, unclassified). (D) High power view showing cells with atypia and mitosis (sex cord stromal tumor, unclassified).

keratin. However, the immunohistochemical staining pattern was equivocal with inhibin negative within the tumor cells, focal calretinin staining and negative for cytokeratin and progesterone. Based on the histological and immunohistochemical staining pattern the lesion was considered as a sex cord stromal tumor, unclassified. A wedge biopsy of the left ovary revealed features of a sclerosing stromal tumor, to include alternating cellular/hypocellular areas within an edematous background (Figures 2A and 2B).

## DISCUSSION

Less than 10% of sex cord stromal tumors are difficult to categorize, thus being classified as sex cord stromal tumor, unclassified type. Bilateral involvement of the ovary by the sex cord stromal tumor is unusual. The unclassified group includes neoplasms in which a predominant feature of testicular or ovarian differentiation is not clearly identifiable. The boundary lines of tumors of ovarian and testicular cell type are not clear because analysis of intermediate morphologic patterns and closely comparable cell types inevitably are subjective. Categorizing as unclassified group of sex cord stromal tumor is not satisfying since one cannot direct clinicians to a particular series of such cases. In fact, so-



**FIGURE 2 (A-B):** (A) Low power view of left ovarian biopsy showing hypocellular and hypercellular areas and characteristic vascular network (sclerosing stromal tumor). (B) High power view showing spindle cell & luteinized cells (sclerosing stromal tumor).

me ovarian tumors simply do not have morphologic characteristics that enable them to be readily categorized as granulosa cell, Sertoli-Leydig cell, or as any recognized form of pure stromal tumor.

Most sex cord-stromal tumors (granulosa-stromal cell tumor) comprise of ovarian cell types but some (sertoli-stromal tumors) contain cells of only testicular type. When the neoplastic cells are immature and their morphologic appearance is intermediate between those of testicular and ovarian type and immunohistochemical staining pattern is equivocal, it may be challenging to determine whether the tumor fits in the granulosa-stromal or sertoli-stromal cell category; such tumors are categorized in unclassified type. There are several variations in the morphology of sex cord tumors as considered above and the mere awareness of them is required to making the correct diagnosis. Extensive sampling is necessary to uncover diagnostic foci.

Cecchetto G. et al evaluated 23 documented sex cord stromal tumor cases. Of these 23 cases only 2 were sclerosing stromal tumor and none of them were in the unclassified category<sup>1</sup>. Microscopically they can show a mixture of stromal growth with areas of diffuse cellularity, cellular atypia and variable mitotic activity. The immunohistochemical findings include positive staining for calretinin and inhibin<sup>2</sup> but overall staining pattern is usually inconclusive. The unclassified sex cord-stromal tumor behaves like other sex cord stromal tumors with intermediate differentiation<sup>3</sup>. The differential diagnosis includes granulosa stromal cell tumors and sertoli-stromal tumors. Morphologic fea-

tures and immunohistochemical staining pattern are helpful in separating each type. Management of unclassified type is similar to other granulosa or Sertoli-Leydig cell tumors, which is surgical resection<sup>4</sup>. Prognosis depends on the stage of the tumor. Sex cord stromal tumors, unclassified have good prognosis, when they are only limited to the ovaries. The 5-year survival rate for early stage sertoli-stromal tumor is around 92%<sup>5</sup>.

Careful evaluation and extensive sampling is required for cases difficult to classify in any specific sex cord stromal tumor category. Complete surgical resection is necessary for the tumors that are categorized in the sex cord stromal tumors unclassified type. Close and regular follow up is important for the early detection of re-occurrence. Our patient underwent chemotherapy afterwards and she is doing well with no recurrence after one year follow-up.

## REFERENCES

1. Cecchetto G, Ferrari A, Bernini G, Alaggio R, Collini P, Virgone C, et al. Sex cord stromal tumors of the ovary in children: a clinicopathological report from the Italian TREP project. *Pediatr Blood Cancer* 2011; 56:1062-67.
2. Young RH. Sex cord-stromal tumors of the ovary and testis: their similarities and differences with consideration of selected problems. *Mod Pathol* 2005; 18:S81-98.
3. Simpson JL, Michael H, Roth LM. Unclassified sex cord-stromal tumors of the ovary: a report of eight cases. *Arch Pathol Lab Med* 1998; 122:52-5.
4. Seidman JD. Unclassified ovarian gonadal stromal tumors. A clinicopathologic study of 32 cases. *Am J Surg Pathol* 1996; 20:699-706.
5. Sigismondi C, Gadducci A, Lorusso D, Candiani M, Breda E, Raspagliesi F, et al. Ovarian Sertoli- Leydig cell tumors. A retrospective MITO study. *Gynecol Oncol* 2012;125:673-6.