

## Case Report

## Steroid Cell Tumor of the Ovary: A Rare Case Report

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### Abstract

Sex cord-stromal tumors (SCST) are rare tumors of the ovary that include three main subtypes known as pure stromal tumors, pure sex cord tumors, and mixed sex-cord stromal tumors. This case involves a 25-year-old female who presented to the Gynecology outpatient clinic with a two-year history of amenorrhoea associated with excessive hair growth since menarche. Ultrasonography revealed a solid left ovarian mass. Histopathology confirmed a diagnosis of SCST not otherwise specified with no cytological atypia. In this case report, we describe the process of managing this patient and a brief literature review on the updates regarding the clinical presentation, molecular changes, and management of SCSTs not otherwise specified.

**Keywords:** Sex Cord Stromal Tumor; Mixed Sex Cord Stromal Tumor; Virilization, Androgen Excess; Ovarian Mass; Salpingo-Oophorectomy

**Abbreviations:** ACTH: adrenocorticotrophic hormone; AFP: alpha-fetoprotein; BMI: body mass index; DHEA: dehydroepiandrosterone; FSH: follicle stimulating hormone; hCG: human chorionic gonadotrophin; KHUH: King Hamad University Hospital; LDH: lactate dehydrogenase; LH: luteinizing hormone; MRI: magnetic resonance imaging; NOS: not otherwise specified; SCST: Sex cord-stromal tumors; WHO: World Health Organization.

## 1. Introduction

Ovarian sex-cord-stromal tumors (SCST) are a group of benign and malignant neoplasms that arise from specialized gonadal stroma surrounding oocytes [1]. These include granulosa cells, theca cells, Sertoli cells, Leydig cells, and fibroblasts [2] (Table 1). Morphologically, SCSTs are differentiated by the presence of these cell types, but can also display indifferent features such as fibroblastic, epithelial, presence of other types of stromata, such as cartilage, skeletal muscle, or a mix of cell types [2]. Ovarian SCSTs account for about 7% of all primary malignant ovarian neoplasms [3]. There are three main documented ways that SCSTs can present. Patients with SCSTs can present with non-specific signs and symptoms in the abdomen or pelvis due to the and- exal mass, incidentally on physical examination, or through imaging [1].

Patients can also present with signs of androgen or estrogen excess as some SCSTs are known to produce androgens, estrogens, or other steroid hormones and their precursors [2]. Signs of virilization include oligomenorrhea, amenorrhea, breast atrophy, hirsutism, deepening voice, male pattern baldness,

acne, and clitoral enlargement. Whereas signs of oestrogen excess include precocious puberty, abnormal uterine bleeding, endometrial hyperplasia or carcinoma [1]. Meigs syndrome and Pseudo-Meigs syndrome are also associated with ovarian malignancies or malignancies metastatic to the ovary [2].

If a SCST is suspected, diagnostic work-up can include laboratory investigations such as total testosterone if signs of androgen excess are present, estradiol if there are signs of excess oestrogen, and specific tumor markers such as inhibin A and B and alpha-fetoprotein. Endometrial sampling and trans-vaginal ultrasound imaging can also be performed. However, diagnosing the specific histologic type of ovarian SCST requires examination of a surgical specimen [2]. Lymph node metastases are rare in ovarian SCSTs [5]. Among patients with stage III and stage IV disease, the most common location of regional spread was abdominal, for instance to the diaphragm or omentum [2]. We present a rare case of steroid cell ovarian tumor diagnosed in a 25-year-old female who complained of a two-year history of amenorrhea and excessive hair growth.

### Pure stromal tumors

- Fibroma
- Cellular fibroma
- Thecoma
- Luteinized thecoma associated with sclerosing peritonitis
- Fibrosarcoma
- Sclerosing stromal tumor
- Signet-ring stromal tumor
- Microcystic stromal tumor
- Leydig cell tumor
- Steroid cell tumor

<ul style="list-style-type: none"> <li>• Steroid cell tumor, malignant</li> </ul>
<p><b>Pure sex cord tumors</b></p> <ul style="list-style-type: none"> <li>• Adult granulosa cell tumor</li> <li>• Juvenile granulosa cell tumor</li> <li>• Sertoli cell tumor</li> <li>• Sex cord tumor with annular tubules</li> </ul>
<p><b>Mixed sex cord-stromal tumors</b></p> <ul style="list-style-type: none"> <li>• Sertoli-Leydig cell tumors                             <ul style="list-style-type: none"> <li>○ Well-differentiated</li> <li>○ Moderately differentiated with heterologous elements</li> <li>○ Poorly differentiated with heterologous elements</li> <li>○ Retiform with heterologous elements</li> </ul> </li> <li>• Sex cord-stromal tumors, not otherwise specified</li> </ul>

**Table 1:** The classification of ovarian sex cord-stromal tumors by the World Health Organization (WHO) updated in 2014 from the previous version in 2003 [4].

**2. Case Report**

A 25-year-old female presented to the outpatient Gynecology clinic at King Hamad University Hospital (KHUH), a tertiary teaching hospital with a history of amenorrhea for two years associated with hirsutism, deepening of the voice, and acne. She reached menarche at 14 years of age and had irregular periods ever since until the onset of amenorrhea in the last two years before presentation. The patient did not have any present comorbidities, medical history, or family history of malignancy. Surgical history revealed a left knee ligament repair and she identifies as bisexual.

On general examination, the patient’s height was 165cm and weight was 96kg with a body mass index (BMI) of 35.3. She exhibited central obesity and male-pattern baldness (Figures 1-4). She had a score of higher than 15 on the Ferriman-Gallwey scale for hirsutism, indicating moderate or severe hirsutism

(Figures 5 and 6). According to the Tanner Staging, breasts were classified as Stage 3 and pubic hair was classified as Stage 2 (Figure 1). Abdominal palpation revealed a non-tender, mobile, palpable pelvi-abdominal mass estimated of less than 12 weeks in gestational size. Perineal examination revealed clitoromegaly. Pelvic ultrasonography revealed an echogenic mass located in the left ovary measuring 5x6 cm in diameter. The patient’s right ovary and uterus were normal. A further magnetic resonance imaging (MRI) of the pelvis confirmed the presence of a heterogeneous lobulated mass measuring 60x53x45mm in the left ovary. Table 2 demonstrates the patient’s hormone profile, which revealed an elevated serum testosterone level and low luteinizing hormone (LH). Lactate dehydrogenase (LDH) was 238.4 U/L, total human chorionic gonadotrophin (hCG) was 0 mIU/mL, while various cancer biomarkers were normal, as shown on Table 3. The patient underwent a left salpingo-oophorectomy where the left ovary was

noted to be replaced by a solid, cystic, yellowish mass with an intact capsule. On gross examination of the specimen, the left ovary was enlarged, measuring 6x5cm (Figure 7). On closer inspection, the mass had a firm solid yellowish appearance and was vaguely nodular without any foci of hemorrhage and necrosis (Figures 8 and 9). Microscopically, the tumor was circumscribed, composed of sheets and clusters of oval, polygonal, and round cells with granular to mostly clear, abundant cytoplasm. No Reinke

crystals, nuclear atypia or mitotic activity were seen. The fallopian tube was unremarkable and with no evidence of malignancy. The patient's postoperative serum test-osterone decreased from 559ng/dl to 77 ng/dl within 24 hours of surgery. Chromosomal analysis was also performed and showed a normal female karyotype, 46XX. The patient had a smooth post-operative recovery. Follow-up revealed that the patient was no longer amenorrheic but resumed her previous history of irregular menses.



**Figures 1:** Tanner Stage 3 Breasts and Central Obesity.



**Figures 2:** Tanner Stage 3 Breasts and Central Obesity.



**Figures 3:** Tanner Stage 3 Breasts and Central Obesity.



**Figure 4:** Male-Pattern Baldness on the Patient.



**Figure 5:** Hirsutism on the Patient.



**Figure 6:** Hirsutism on the Patient.



**Figure 7:** Gross appearance of the left ovarian mass prior to resection.



**Figures 8:** A more magnified appearance of the left ovarian mass.



**Figures 9:** A more magnified appearance of the left ovarian mass.

Hormone	Value	Normal Range
Serum testosterone	559 ng/dl	15-70 ng/dl
17 Hydroxy-progesterone	3.96 nmol/L	< 6.06 nmol/L
Adrenocorticotrophic hormone (ACTH)	23.7 pg/mL	9-52 pg/mL
Dehydroepiandrosterone (DHEA) Sulphate	71.0 µg/dL	65 to 380 µg/dL
Follicle Stimulating Hormone (FSH)	6.98 IU/L	1.5 to 12.4 IU/L
Luteinizing Hormone (LH)	1.75 IU/L	5 to 25 IU/L
Prolactin	7.8 ng/ml	< 25 ng/mL

**Table 2:** The patient's hormone profile.

Laboratory Test	Value	Normal Range
CA-125	10.6 U/mL	< 35 U/mL
CA-153	5.7 U/ml	<30 U/mL
CA19-9	10.67 U/mL	< 37 U/mL
Alpha Fetoprotein (AFP)	0.8 ng/mL	< 20 ng/mL

**Table 3:** Cancer biomarker values.

### 3. Discussion

The incidence of SCSTs not otherwise specified (NOS) is highest in women particularly in their third and fourth decades but postmenopausal women or children may also be susceptible [6, 7]. Hayes and Scully studied 63 cases of SCSTs not otherwise specified and found that the NOS type constituted 56% of steroid cell tumor cases. In addition, androgen excess was present in 56% of cases, and malignancy was found in 43% [8]. This is consistent with our case as the patient presented with signs of virilization, which included hirsutism, deepening of the voice, and acne. The majority of SCSTs not otherwise specified occur as unilateral, well-circumscribed, solid and/or cystic masses that can measure from 1.2 up to 45cm. The colour of the mass may range from yellow to orange to red or brown depending upon the lipid content and areas of necrosis or

haemorrhage [6]. The tumor in our case was a firm yellowish mass without any foci of haemorrhage and necrosis. Certain characteristics are correlated with adverse behaviour of this tumor. These include older age at the time of presentation, tumor exceeding a size of 7cm, mitosis more than 2/10HPFs, grade two to three nuclear atypia, necrosis, and haemorrhage [6]. None of these characteristics were present in our patient, which supports their histologically benign diagnosis.

Ovarian SCSTs not otherwise specified have a highly varied morphology and can be differentiated from other types of SCSTs by the presence of monomorphic, round to polygonal cells arranged in nests. Clear, vacuolated, or eosinophilic cytoplasm can be observed within the cells and they often have well-defined cell borders. In addition, the nuclei are round



with the presence of a fine chromatin pattern and subtle mitotic figures. It is important to note that this appearance leads to a differential diagnosis that also includes lutein cells, Leydig cells, and adrenal cortical cells. The subtype of SCSTs not otherwise specified, is designated when a tumor of the steroid cell type has an unidentifiable origin and does not contain Reinke crystals [7]. Treatment should be based on the specific histological picture, surgical staging, and patient's desire to preserve fertility [6]. Surgery is the treatment of choice for SCSTs as the majority of patients present with stage I disease. In post-menopausal women, a total abdominal hysterectomy with bilateral salpingo-oophorectomy is recommended, whereas in women of childbearing age, a unilateral salpingo-oophorectomy can be pursued [3]. Surgery can be performed alone or in conjunction with the above-mentioned treatment options. In our case, the patient successfully underwent a unilateral salpingo-oophorectomy and experienced clinical improvement. Due to the scarcity of published studies with long-term follow up, regular monitoring of the patient needs to be achieved over several years to ensure that no recurrence or malignant transformation occurs.

Chemotherapy and hormonal therapy are only considered in advanced or recurrent disease. The listed options for chemotherapy include bleomycin, etoposide, and cisplatin, cisplatin with etoposide, and carboplatin with paclitaxel. It is interesting to note that postoperative chemotherapy has been shown not to be associated with improved prognosis or disease-free survival. Hormonal therapy has been mainly been developed to target recurrent granulosa cell tumors. In literature, aromatase inhibitors were shown to have a higher response rate when compared with other hormonal therapies, namely gonadotropin

releasing hormone agonists, steroidal progestins, and selective oestrogen receptor modulators). The use of targeted therapy such as tyrosine kinase inhibitors as well as inhibitors of apoptosis proteins have also been explored in instances of recurrent granulosa cell tumors [3]. Recent molecular advancements have established a link between genetic aberrations in adult and juvenile granulosa cell tumors, Sertoli-Leydig cell tumors, and *FOXL2*, *DICER1* mutations. Previous immunohistochemical markers such as  $\alpha$ -inhibin, calretinin, and SF-1 only helped to establish cell lineage [9]. Mayer et al also published a case of SCST not otherwise specified, where a *FOXL2* C134W mutation was confirmed as well as mutations in *TP53* (V172F) and *TERT* promoter (-124C>T) region [10]. By identifying these mutations, there is a potential to improve the classification, prognosis, and treatment strategies of SCSTs.

In conclusion, this case highlights a very rare ovarian tumor in a woman of childbearing age. Symptoms of androgen excess, particularly in cases of virilization, should be carefully worked up using appropriate imaging and evaluation. Androgen-producing tumors should be included in the differential diagnosis to ensure the correct diagnosis and treatment. In addition, more cases need to be published to further the work done regarding genetic mutations and to establish the long-term outcomes of SCSTs.

### Declarations

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### Conflicts of interest

The authors declare that they have no conflicts of interest.

### Informed consent

The patient featured in this case study provided written informed consent for publication of this case and associated photos.

### Ethical approval

This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration. This case report received ethical approval by the Institutional Review Board (IRB) at King Hamad University Hospital (KHUH).

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