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An occult ovarian androgen-secreting steroid cell tumor in a postmenopausal woman with severe clinical and laboratory hyperandrogenism

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Abstract

Ovarian Steroid Cell Tumors (SCTs), are an extremely rare type of sex cord tumors, accounting for less than 0.1% of all ovarian tumors. Testosterone is the most common androgen secreted from this type of tumor and causes clinical androgenic in approximately 50% of cases. These tumors are usually unilateral (94%), and 28% are malignant. A case of a 68-year-old woman who presented with symptoms of hirsutism and alopecia is reported. serum testosterone levels were elevated to 15ng/ml. Systemic imaging done by CT was negative for pathological findings, however gynecologic examination and a transvaginal sonogram revealed a left complex 3 cm ovarian cyst. After a complete work up, the patient underwent a bilateral salpingo-oophorectomy (along with subtotal hysterectomy and sacrocolpopexy secondary to uterine prolapse). Histopathologic examination revealed a 3 cm benign serous cystadenoma, and an adjacent 0.8 cm solid steroid producing tumor. The following report aims to broaden the current and scarce knowledge of this type of rare ovarian tumor.

Conclusions: Steroid cell tumors may be presented as an occult ovarian lesion. In the case of significant androgenic symptoms with no evidence of other possible lesion an occult ovarian tumor should be suspected, and bilateral salpingo-oophorectomy should be considered especially in postmenopausal patients.

Keywords: Steroid cell tumor, ovary, androgen secreting cell tumor, hyperandrogenism.

CaseReport

A 68-year-old woman presented with an 18-month history of increasing hair growth affecting the face, abdomen, arms, and chest as well as balding. She had a normal menstrual history including menopause at 48 years. Obstetrics history included two vaginal deliveries with no previous surgeries, and no family history of malignancy. Background diseases include controlled hypertension, stable asthma, and asymptomatic non-toxic multinodular goiter. Physical examination revealed facial and anterior chest and arm hirsutism along with male pattern alopecia. Abdominal examination showed no organomegaly, tenderness, or other abnormalities. Vaginal examination disclosed clitoromegaly, along with stage III rectocele and stage II uterine prolapse. The patient's laboratory tests revealed elevated serum concentrations of testosterone to 15 ng/ml. Endocrinology panel was within the normal range, including levels of estradiol, 17-hydroxyprogesterone, dehydroepiandrosterone sulphate (DHEA-S), dehydroepiandrosterone (DHEA), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin. Twenty-four-hour urine cortisol concentration and thyroid function tests were also reported at normal range. Tumor markers (CA125,CEA) fell within normal range. Transvaginal ultrasound (TVS) demonstrated a right ovary of 27 mm x 17 mm with a unilocular hypo-echoic finding of 18 mm x 10 mm consistent with simple cyst and a left ovary of 11 mm x 10 mm with normal consistency. No other abnormalities were demonstrated. Computed tomography (CT) of the abdomen showed normal adrenal glands with no intra- or retroperitoneal lymph node enlargement. A Pelvic scan was not performed. Due to symptomatic pelvic organ prolapse, the patient underwent laparoscopic subtotal abdominal hysterectomy, bilateral salpingo-oophorectomy and sacrocolpopexy.

Laboratory results:

Hormone	Case Report	Normal Range	
Testosterone	15 ng/ml	2-8 ng/mL	Elevated
Estradiol	< 10 pg/mL	0-30 pg/mL	Normal
17-Hydroxyprogesteron	2.17	< 51 ng/dL	Normal
FSH	106.7	26 - 135 IU/L	Normal
LH	41.8	16 - 54.0 IU/L	Normal
24 hours – Urine Cortisol	13 U/24 hours	13-75 U/24 hours	Normal

Pathology report:

Macroscopic examination showed a normal appearing uterus of 11.5 cm x 6.0 cm x 2.5 cm, and left oviduct and ovary of normal size and appearance. The right ovary contained a cyst 2 cm in diameter with clear fluid. Solid yellow-gray nodule 0.8 cm in diameter appeared adjacent to the cyst, a finding that was undetected on preoperative sonographic examinations. Microscopic examination showed ovary with benign serous cystadenoma [Figure 1] and steroid cell tumor measuring 0.8 cm in diameter [Figure 2-3].

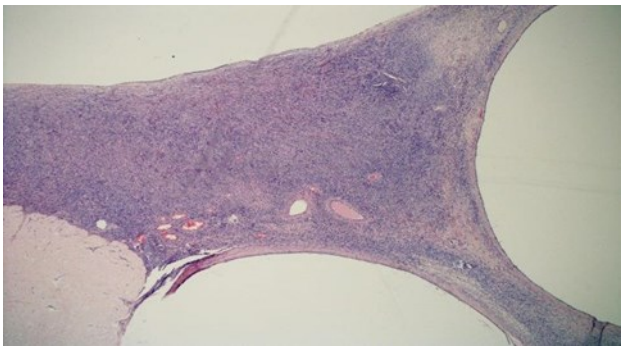


Figure 1: Serous cystadenoma (H& E, original magnification×10)

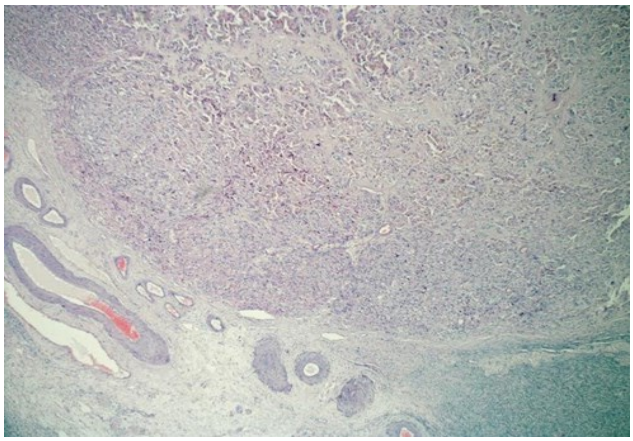


Figure 2: Steroid cell tumor (H&E, original magnification×40). Well circumscribed tumor nodule.

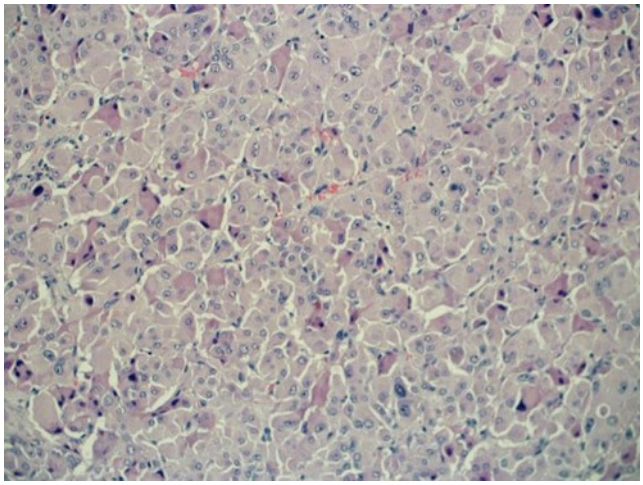


Figure 3: Microscopic findings of steroid cell tumor (H&E, original magnification×200).
Tumor cells with abundant eosinophilic cytoplasm, round nuclei and prominent nucleoli.

Her symptoms regressed during the second postoperative month and the serum testosterone level normalized within 2 weeks. The patient is followed up closely and regularly with measurements of hormone levels and pelvic ultrasound

Discussion

Ovarian steroid cell tumors, a subtype of sex-cord stromal tumors (SCT), are rare type of ovarian tumors accounting for only 0.1% of all ovarian tumors.

When classifying SCT, three subtypes exist: the most common is SCT NOS (60%), and the remaining cases are either stromal luteoma tumors or Leydig cell tumors. **(1-3)**.

Ovarian SCTs, NOS, are usually benign and unilateral and may occur at any age, however, they generally arise at younger ages compared with other SCTs, with an average age of 43 years at diagnosis. **(4, 5)** Several clinical features include abdominal pain, distention, and bloating. However, the more frequent presentations are those associated with hormonal activity. **(6)** Physical and hormonal androgenic features may be observed in over 50% of these cases. These clinical changes include hirsutism, hair loss, amenorrhea or oligomenorrhea. Despite the clinical signs of hormonal imbalance, 10-25% of SCT have laboratory hormone levels in the normal range. **(4, 6)** The majority of SCTs have benign or low-grade behavior. Contrarily, benign SCT demonstrate a clinically malignant presentation. **(7)** About 20% of patients develop metastatic lesions usually within the peritoneal cavity and rarely at distant sites. **(4)**.

Unfortunately, SCT has no screening test (neither tumor marker or imaging technique) that can contribute to preoperative diagnosis. The first step in evaluating androgen excess is measuring blood levels of both androgen and DHEA-S. **(8)** In order to differentiate between androgen-secreting tumors and non-neoplastic lesions, serum testosterone levels can be helpful. Testosterone levels above 200 ng/dL frequently point to androgen secreting tumors. **(9)** Specifically, testosterone levels above 200 ng/dL that coincide with normal levels of LH, FSH, DHEA-S and 17-hydroxyprogesterone levels indicate a viriliz-

ing ovarian tumor. **(10)** TVS and CT or alternatively Magnetic Resonance Imaging (MRI) are useful radiologic imaging techniques for detecting both ovary and adrenal gland tumors **(11),** while tumor markers, alpha fetoprotein (AFP) and CA-125, may facilitate the differential diagnosis of ovarian malignancy. **(10)** Nonetheless, in order to confirm a definitive diagnosis, an excised biopsy is usually needed.

Grossly, these tumors are most often solid, and have a well circumscribed appearance. They are relatively large, having a mean diameter of 8.4 cm. Occasionally they are lobulated, and macroscopically have a yellow-orange hue if the tumor contains large amounts of lipid. If the tumor is lacking in lipids, its appearance will be red to brown. However if the tumor contains large amounts of cytoplasmic lipochrome pigment, the tumor will appear brown to black in color. In some cases necrosis, lipid degeneration and hemorrhage can be seen grossly. **(4, 12 ,13)** In our case the macroscopic analysis revealed an unusual small, 0.8 cm in diameter, solid yellow-gray nodule.

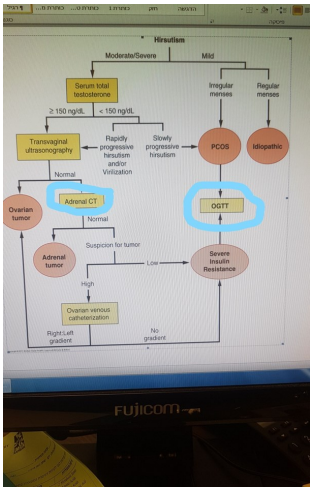
The definitive diagnosis is based on histological characteristics which include polygonal to round cells with unequivocal cell borders, along with recognizable Reinke's crystals seen in cytoplasm of increased volume. **(1)** Another feature occasionally seen is large clusters of cells of cells, seldom in a columnar pattern. Cytoplasm spans from a eosinophilic appearance to a vacuolated appearance, and occasionally nuclei contain prominent nucleoli. (4) Scattered tumor cells may be seen in the edematous or even myxoid stroma. The stroma may become calcified with an increased quantity of psammoma bodies. (4, 12, 13) A specific pattern of immunohistochemistry staining defines tumor cells: the cells stain for inhibit and vimentin (75%), anti-hymon cytokeratin (46 %), and AE1/AE3 (37%) . (1) The most important characteristic of malignancy in these tumor cells are: over 2 mitoses per 10 high-power fields, cell size exceeding 7 cm, necrosis, hemorrhage and lastly Grade 2 or Grade 3 nuclear atypia. **(4)** In our patient the microscopic evaluation revealed tumor cells with abundant eosinophilic cytoplasm, round nuclei and prominent nucleoli [Figure 3], that is consistent with SCT.

Because of their rarity, no conventional treatment has been established for SCTs NOS. However, since these tumors are considered to be sex cord stromal tumors, the primary treatment is surgery. **(4)** In older women, and when future fertility is not an issue, total abdominal hysterectomy and bilateral salpingo-oophorectomy should be considered. Whereas in young women, unilateral salpingo-oophorectomy is a reasonable choice if histology shows no malignant features, since the frequency of bilateral occurrence is only 6%. Follow-up is mandatory and includes regular physical examination and measurement of serum testosterone levels. CT imaging is reserved to cases where the follow-up reveals pathologic findings in the physical examination or elevated serum testosterone level. **(14)** If preoperative increased testosterone does not change after surgery, gonadotropin releasing hormone agonists may be utilized. **(15)** Optimal management of malignant SCT NOS steroid cell tumors is surgical resection, while adjuvant chemotherapy and radiation therapy should be considered. **(4)** However, as signs and symptoms lead to early diagnosis and as recurrence or metastasis is ra-

re, the therapeutic value of chemotherapy and radiotherapy is controversial. **(15)** Higher malignant potential with poor prognosis is associated with a higher disease stage, larger tumor size, gross necrosis, or hemorrhage. Recurrence or metastases are also associated with poor prognosis due to insufficient research on additional treatment options. **(4).**

Conclusion

Steroid cell tumors are rare, and androgenic symptoms with increased testosterone levels are important suspicious signs of a functional ovarian tumor. We reported a case of SCT presented with hirsutism and alopecia in which preoperative evaluation did not reveal the source of the suspected androgen secreting tumor. However, postoperative histo-pathology examination revealed a 0.8 cm steroid secreting tumor in the right ovary. Interestingly, although the imaging studies failed to find either adrenal or ovarian tumor, a thorough histopathologic examination and high suspicions facilitated the diagnosis of the culprit SCT tumor. Despite the small size of the tumor, significant symptoms were presented. This emphasizes that an awareness of this entity along with a full and comprehensive endocrinologic, gynecologic, and histopathologic evaluation are essential for the diagnosis of SCTs.



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