

Case Report

An Ovarian Steroid Cell Tumor with High Levels of CA-125 in Sanglah General Hospital: A Rare Case Report

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Abstract: *Background:* Ovarian steroid cell tumors are rare tumors of the ovary characterized by steroid cell proliferation. These sex-hormone secreting tumors raise many differential diagnoses related to hyperandrogenism. Although most of these tumors are benign and slow-growing, approximately 25 – 43% of cases are clinically malignant. *Case:* We herein report a case of 30 years old woman with ovarian steroid cell tumor, not otherwise specified (NOS) with primary infertility. The patient presented with hirsutism and abdominal enlargement due to massive ascites during hospital admission. The blood test result showed significantly increased CA-125. Transabdominal ultrasound revealed a 7.81 x 4.94 cm tumor of the left adnexa. The patient underwent left salpingo-oophorectomy and responded well to the surgery. *Conclusion:* This case report presents a unique case of ovarian steroid cell tumor, NOS with findings of massive ascites, hirsutism, and a high level of CA-125. The findings were never associated with this type of tumor. The steroid cell tumor and its ascites could mechanically irritate the mesothelium that causing overexpression of CA-125. Surgery remains as the first-line treatment of this case. Adjuvant chemotherapy should be done based on the histologic type of the tumor and its surgical stage. Tumor marker decreased after surgery was done and patient remains alive and free of disease after a period of 2 years.

Keywords: Adnexal Mass, CA-125, Hirsutism

1. Introduction

Ovarian steroid cell tumors are uncommon sex-hormone secreting tumors characterized by a steroid cell proliferation. It is a rare type of sex cord-stromal tumours of the ovary. There are less than 0.1% cases of ovarian steroid cell tumours out of all ovarian tumour types [1]. Ovarian steroid cell tumour are classified into three subtypes: stromal luteoma, Leydig cell tumour, and steroid cell tumour not otherwise specified (NOS). This case report describes the case of a 30-year-old woman with an ovarian steroid cell tumor, NOS (not otherwise specified), of the ovary. [2, 3] This is a rare tumor of the ovary which raises differential diagnoses with many disorders causing hyperandrogenism. These tumors should be considered a cause of isosexual precocious puberty in children and virilization in adults, such

as hirsutism, temporal balding, and amenorrhea [3]. In literature, only a few cases of steroid cell tumors, NOS, have been described. A very interesting element of this case is that the patient presented with massive ascites and hirsutism, accompanied by a high level of CA-125, which is never associated with this type of tumor. The Patient had a complete response to surgery which was her only treatment.

2. Case Illustration

A woman, 30 years old, came with a complaint of an enlarged stomach since 6 months ago, accompanied by growing facial hairs. There were no complaints of abdominal pain and shortness of breath. There were no complaints about weight loss or vaginal discharge. The patient has been married for 7 years but does not have children. Menstrual history is

said to be regular with a cycle of 28 days and a menstrual length of 7 days with a volume of 60 ml per day.

On physical examination, there was positive undulation. On inspection of vulvovaginal, there was no visible abnormality. Upon pelvic examination, a floating uterine corpus impression was found and the parametrium adnexa was difficult to evaluate. Transabdominal ultrasound revealed an anteverted uterus with an endometrial thickness of 0.50 cm, hypoechoic mass with a size of 7.81 x 4.94 cm which derives from the left adnexa was seen along with a solid tumor accompanied by massive ascites. Abdominal CT scan shows a solid mass with a well-defined cyst component with a lobulated edge on the left adnexa. Chest X-rays showed no abnormalities. The abdominal ultrasound did not show any metastatic nodules in the liver and para aorta no mass in the cervix and uterus were seen.

Tumor marker examination showed increased CA-125 (437.5 U/mL), normal CA-19.9 (<0.60 U/ml), normal AFP (1.04 IU/mL), and normal CEA (2.50 ng/mL). Pap smear test revealed reactive cellular changes associated with inflammation. The patient was assessed with suspected solid ovarian tumors with massive ascites and primary infertility. A left salpingo-oophorectomy was performed. At the time of the surgery, the uterus was normal, the right ovary tube was normal, a well-defined solid mass measuring 7x7 cm with a flat surface was discovered. The mass was mobile, originated from the left adnexa, and attached to the left tube.



Figure 1. Transabdominal ultrasonography.

A cytological evaluation of ascites fluid was obtained with the result of the sample consisted of a small distribution of mononuclear cells, polymorphonuclear, and macrophages, affirming the finding of ascites. The histological section revealed sheets and cords of polygonal neoplastic cells with small round nuclei, an abundant amount of vacuolated eosinophilic cytoplasm, mild atypia, and no mitosis or Reinke's crystals were present. Fat stains were positive. These findings were consistent with a benign ovarian steroid cell tumor, NOS.

After the procedure, the patient is routinely controlled without any complaints. Her facial hairs had disappeared after 2 months post-surgical excision, with the results of the tumor

marker (CA-125) one year postoperatively within normal limits (6.50 U/mL). After this period of time, the patient remains alive and free of disease after a period of 2 years.

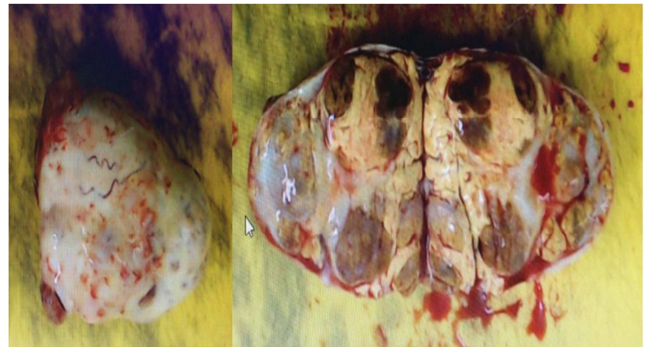


Figure 2. Gross appearance - Cut surface of the left ovary showing solid, yellowish appearance.

3. Discussion

The ovarian steroid cell tumor was known previously as lipid or lipoid cell tumor, though sometimes it has little or no lipid content. Steroid cell tumors derive from adrenal rest cells, ovarian stromal lutein cells, or Leydig cells. Steroid cell tumors have been classified into three subtypes – NOS, Leydig cell tumor, and stromal luteoma [4]. Androgenic manifestations are common in these tumors as they secrete hormones like androstenedione, α -hydroxyprogesterone, and testosterone [5, 6]. Around 56% of patients present with hirsutism and virilization. It also may cause precocious puberty in children, and in adults, it can manifest as oligomenorrhea, acne, increased libido, and deepening of the voice, besides hirsutism [5, 7]. It can also present estrogenic manifestations (6-23%), such as menorrhagia or postmenopausal bleeding. Cushing syndrome occurs in about 6-10% of ovarian steroid cells tumours cases and approximately in 25% of ovarian steroid cells tumours cases lack of endocrine symptoms [1].

In cases where there is unexplained hirsutism, ovarian and adrenal tumor association should be ruled out as there may be occult malignancies. However, there may also be atypical presentations of these tumors, in which they do not show any symptoms of virilization. In these cases, the diagnosis is usually made postoperatively on finding a tumor in the ovary [3]. In this case report, the patient presented with hirsutism and primary infertility which are the symptoms of ovarian steroid cell tumors.

The most important factor to be determined in steroid cell tumours of the ovary is whether the tumour has malignant features or not. Almost all of these tumours are benign. However, there are 25-43% of steroid cell tumours are clinically malignant. About 20% of cases malignant steroid cell tumours with metastasis outside of the ovary [6, 8]. These tumours are growing slowly and the symptoms are usually present for many years before the diagnosis is made. Therefore, these tumours usually can be diagnosed at an early stage. Almost all of these ovarian steroid cells tumours

cases (94%) are unilateral, large-sized at time of diagnosis, solid, and well-circumscribed. [8, 9]. The most common color of the cut surface is yellow, but it can be different depends on the lipid content. Histopathology examinations remains as gold standard to diagnosed this tumours. Hayes and Scully identified five pathologic features that are highly associated with malignancy: tumor diameters of >7 cm related with 78% malignancy, two or more mitosis per 10 high-power fields related with 92% malignancy, necrosis related with 86% malignancy, haemorrhage associated with 77% malignancy, and grade 2 or 3 nuclear atypia associated with 64% malignancy. Steroid cell tumor, NOS should be differentiated from other steroid cell tumors such as stromal luteoma and Leydig cell tumor. Stromal luteoma is most commonly located in the ovarian stroma, and it frequently occurs in association with stromal hyperthecosis. Another feature which helps in diagnosing this tumor is the presence of degenerative pseudovascular spaces containing red blood cells [7, 10].

Leydig cell tumor is usually present in the hilar location. The tumor cells show cytoplasmic Reinke crystals, and it is usually associated with Leydig's cell hyperplasia. Pregnancy luteoma may sometimes microscopically resemble a steroid cell tumor. It is most commonly multifocal and occurs bilaterally in approximately one-third of the patients. It usually regresses after pregnancy [11]. In the present case, features such as stromal hyperthecosis, pseudovascular spaces, or Reinke crystals were absent to suggest the possibility of stromal luteoma and Leydig's cell tumor, and hence, this case was concluded as steroid cell tumor-NOS. Immunohistochemical markers, inhibin, and calretinin are quite useful in differentiating this tumor from other non-sex cord tumors [7, 8]. Even though the size of the tumor was >7 cm, she had a good prognosis as on microscopy, there were no mitotic figures, necrosis, or hemorrhage.

CA-125 is the most well-characterized biomarker for ovarian cancer. CA-125 was raised (>35 U/ml) in 69% of women with malignant ovarian cancers and 32% of women with benign ovarian cancers. CA-125 is expressed by fetal amniotic and coelomic epithelium and in adult tissues derived from the coelomic (mesothelial cells of the pleura, pericardium, and peritoneum) and Mullerian (tubal, endometrial, and endocervical) epithelia. The surface epithelium of normal ovaries does not express CA-125 [12-14]. Currently, CA-125 is still the most widely used tumor biomarker for the detection of ovarian cancer. However, its poor specificity was highlighted in a large number of false-positive results, 80% of the abnormal results in the female audit population undergoing investigation for suspected malignancy/ovarian cancer were not caused by ovarian cancer. Malignancies at other sites, and inflammatory or benign gynecological disease, were the most common causes for a raised CA-125 concentration [15].

The specificity of CA-125 increased with rising concentrations, although there were still five false positives with results over 1000 kU/liter, a recognized occurrence. Elevated levels of CA-125 are strongly associated with serous

tumors compared to mucinous tumors, but a high level of the marker has never been associated with a steroid cell tumor, NOS of the ovary. In this case, the patient had a high level of CA-125 and massive ascites [15-17]. Conjecturally, in our case, the steroid cell tumor and its ascites mechanically irritated the mesothelium, causing overexpression of CA-125.

The treatment of these tumors should be based on the histological picture, surgical staging, and patient's desire to preserve fertility. The first-line treatment is surgery. In the young patients who want to preserve their fertility, unilateral salpingo-oophorectomy is the preferred method of treatment. For women who have completed childbearing, total abdominal hysterectomy with bilateral salpingo-oophorectomy and complete surgical staging is indicated. Adjuvant chemotherapy should be based on the histologic appearance of the tumor and its surgical stage. The majority of steroid cell tumors, NOS are benign, and even in cases of malignancy, recurrences are rare [7, 8, 18]. In this case, a 30 years old patient, with a history of primary infertility and histological features leading to a benign tumor, a left salpingo-oophorectomy was performed. After the procedure, the patient was routinely controlled without any complaints. Her facial hairs had disappeared after 2 months post-surgical excision, with the results of the tumor marker (CA 125) one year postoperatively within normal limits (6.50 U / mL). After this period of time, the patient remains alive and free of disease after a period of 2 years.

4. Summary

Steroid cell tumors, NOS, are usually rare tumors. A proper history and physical examination, in addition to laboratory values and imaging studies, helps in arriving at the diagnosis. Elevated levels of CA-125 has never been associated with a steroid cell tumor, NOS, of the ovary, but in this case, the patient had a high level of CA-125 and massive ascites. The steroid cell tumor and its ascites could mechanically irritate the mesothelium that causing overexpression of CA-125. Disease management should be decided based on the tumor pathology, surgical staging, and the desire for preserving fertility. The primary treatment is the surgical removal of the primary lesion.

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