Steroid cell tumor not otherwise specified of bilateral ovaries: A rare cause of post menopausal virilization

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ABSTRACT
Steroid cell tumors of the ovaries are rare sex-hormone secreting tumors which are usually benign and unilateral. One previous study has estimated the tumors to be bilateral in 6% of patients. We report a case of post menopausal virilization where tumor histology revealed steroid cell tumor not otherwise specified with benign characteristics. The presence of tumor in bilateral ovaries made this case unique.

Key words: Post menopausal, steroid cell tumor not otherwise specified, virilization

INTRODUCTION
Steroid cell tumors of the ovary are rare hormone secreting tumors characterized by a steroid cell proliferation, of which there are three subgroups: Steroid cell tumor not otherwise specified (NOS), Stromal luteoma and Leydig cell tumor. Steroid cell tumors account for less than 0.1% of all tumors of the ovary,[1] and of the three subtypes steroid cell tumor (NOS) is the most common. Steroid cell tumors NOS are usually benign and unilateral. They may present as post menopausal virilization and have been reported in patients ranging in age from two and half years to 80 years.[2] Although, there are many case reports on steroid cell tumor (NOS) of the ovary, reports of bilateral tumors are very rare, and one clinic pathological study had revealed the tumors to be bilateral in 6% of patients.[2]

CASE REPORT
A 54-year-old gravida two, para two post menopausal woman presented with a 6 month history of progressively worsening facial hair growth and receding hairline. She required daily shaving and was troubled by the excessive loss of scalp hair. There was no history of bleeding per vagina, abdominal pain, or distension. On examination, she had hirsutism with a Ferriman-Gallwey score of 13/36. She had greasy skin and although post-menopausal she had non-atrophic breasts. Pelvic examination revealed clitoromegaly. There were no striae, acne, and bruising or proximal muscle weakness.

Hormonal assessment revealed an inappropriately high serum follicle-stimulating hormone (FSH) level of 1.1 mIU/mL (post menopause >30 mIU/mL), serum luteinizing hormone (LH) level of 3.2 mIU/mL (post menopause >30 mIU/mL), and a serum testosterone level of 7.31 ng/ml (normal 0.4-0.76 ng/mL). Additionally, she had a serum dehydroepiandrosterone sulfate (DHEA-S) level of <15 µg/dL (normal 35-430 µg/dL) and a serum testosterone after dexamethasone suppression of 6.32 ng/ml (not suppressed). The hormone profile demonstrated normal values for serum prolactin,
cortisol, thyroid-stimulating hormone, and human chorionic gonadotrophin. Tumor marker CA-125 was 0.55 u/ml (1.9-16.3). Other hematological and biochemical parameters were normal. Imaging by transvaginal ultrasound and computed tomography of abdomen and pelvis revealed no ovarian masses. Thus, ovarian venous sampling was carried out under radiological guidance, but the left ovarian vein cannulation was technically difficult and the procedure was relatively unsuccessful except for revealing that the right ovary was a source of testosterone in this patient [Table 1].

The patient, therefore, underwent hysterectomy and bilateral salpingo-oophorectomy. During the laparotomy, straw-colored ascitic fluid was evacuated but found to be negative for malignant cells. The right ovary was slightly enlarged (4 × 1.5 × 1.3 cm) showing a slightly elongated, nodular appearance. Left ovary was normal in appearance (3 × 1.6 × 1.4 cm) [Figure 1]. The cut surface of both ovaries showed multiple white spots. There were no peritoneal lesions. Microscopic sections of both ovaries revealed infiltrating islands and cords of tumor cells exhibiting round to oval nuclei and abundant eosinophilic cytoplasm [Figures 2 and 3]. There were no features to suggest malignant behavior such as nuclear atypia, hemorrhage, necrosis or increased mitotic activity. Reinke’s crystals were not observed. Immunohistochemically, tumor showed intense reactivity to alpha inhibin. Brown-colored pigment was also noted in the cytoplasm [Figure 4]. The final diagnosis was bilateral ovarian steroid cell tumor NOS. Histologically, the tumor

Table 1: Results ovarian venous sampling for serum testosterone and estradiol

| Testosterone ng/mL (0-0.8) | Right ovarian vein | Left ovarian vein | Femoral vein |
|----------------------------|--------------------|-------------------|-------------|
| 3.08                       | 1.88               | 1.83              |
| Oestradiol pg/mL (0-30)    | 59                 | 21                | 14          |
| Cortisol (nmol/L)          | 95                 | 92                | 157         |
| Tes: Cortisol ratio (normalized) | 0.032 | 0.020 | 0.011 |
| Ovarian/peripheral testosterone ratio | (0.032/0.011) | ≥2.9       |

Figure 1: Macroscopic appearance of resected specimen

Figure 2: Infiltrating tumor of the left ovary (H and E, x40)

Figure 3: Islands of tumor cells in the right ovary (H and E, x40)

Figure 4: Tumor cells are strongly positive for alpha inhibin (H and E, x40)
exhibited benign characteristics. Tumor was confined to both ovaries whereas bilateral tubes and parametrical tissue were normal. Sections of the uterus revealed inactive endometrium with adenomyosis.

By 3 weeks post surgery, her serum testosterone had returned to normal range: 0.38 ng/mL and the clinical signs of hyperandrogenism resolved. She currently remains asymptomatic with normal testosterone levels and imaging at 6 months and 12 months after surgery.

**DISCUSSION**

Steroid cell tumor NOS is usually composed of solid aggregates of cells with occasional nests or trabeculae. Tumor cells are polygonal in shape with granular eosinophilic cytoplasm and sometimes show vacuolated cytoplasm. Cytoplasmic lipofusin pigment may also be identified as a brown cytoplasmic pigment seen in this case. Steroid cell tumors NOS are differentiated from Leydig cell tumors because of their lack of cytoplasmic Reinke crystals which are eosinophilic rod shaped inclusions.[3]

The feature that makes this case unique is the presence of tumor cells in bilateral ovaries. Although, there were tumor cell clusters in both ovaries, there was no evidence of capsular extension in either ovary. It could be argued that the second ovary may well be harboring the deposits of the malignant tumor in the 1st ovary. Hayes and Scully reported on certain histopathological features which correlate highly with clinically malignant behavior. These being two or more mitotic figures per 10 high power fields, necrosis, a diameter ≥7 cms, hemorrhage, and grade 2-3 atypia.[3] None were present in this tumor. The complete resolution of serum testosterone to normal levels following removal of ovaries was also against the possibility of malignant ovarian deposits.

Despite several reports of steroid cell tumor NOS leading to a wide variety of clinical presentations, there has been very few cases reported on tumor occurring in bilateral ovaries. In the clinico-pathological analysis of 63 cases of steroid cell tumor NOS by Hayes and Scully, they reported that in 6% of patients the tumors were bilateral.[2] In another clinic pathological study of eight patients, they have not described patients having bilateral tumors.[3] The exact pathophysiology for bilateral occurrence is not very clear at this stage and warrants future evaluation. Although the tumors were pathologically benign steroid tumor NOS, as there have been reports of benign tumors with malignant behavior,[4] careful follow up was carried out in this patient and at 1 year, there were no indication of metastasis.

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