A Rare Case Report of Postmenopausal Virilization: Ovarian Steroid Cell Tumor

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Abstract- Ovarian steroid cell tumors are rare, life-threatening neoplasms that make about 0.1% of all primary ovarian tumors. They frequently present in premenopausal women with the manifestation of virilization. We report a 58-year-old postmenopausal woman that referred to our clinic with clinical manifestation of virilization. Laboratory findings showed markedly elevated serum testosterone level and ultrasound showed 2 follicles with 7 mm diameters in the left ovary. She treated by bilateral salpingo-oophorectomy and synchronous hysterectomy. Histological pathology confirmed a benign steroid cell tumor. The presentation of new-onset and rapid progressive hyperandrogenism is rare in postmenopausal women. In diagnosis, we must consider adrenal and ovarian malignancies. Stromal luteoma is a rare benign ovarian tumor, Which is treated with surgical treatment.

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Introduction

The assessment of hyperandrogenism in the postmenopausal state is usually not taken into consideration because of the lack of association with menstrual disturbances and ascribed of changes in hair patterns as part of the normal aging process. A detailed history is crucial to differentiate progressive hirsutism from true virilization (1). Stromal luteoma is a rare benign ovarian tumor and originated from the stromal sex cords (2). Luteoma stromal tumors demonstrate with hirsutism, acne, androgenic alopecia, male pattern baldness, clitoromegaly, Deepening voice, masculinized features secondary to the production of androgens (3). It is often challenging to detect androgen-secreting ovarian tumors because the size of these tumors often is less than 3cm and routinely not detectable in gynecology examination and radiological imaging (3). We describe a case of a postmenopausal woman with clinical manifestation of virilization, and there were no obvious abnormalities in diagnostic imaging.

Case Report

A 58-year-old postmenopausal woman was referred to our clinic with a history of severe hirsutism, Deepening voice, hair loss (male pattern baldness), and weight loss from one year ago. She had a history of obsessive-compulsive disorder (OCD), and she received citalopram, fluoxetine, and diazepam. She had no symptoms of headaches, galactorrhea, visual change, and she had no history of hormone replacement therapy. In physical examination, she had frontal alopecia, acne, masculinized features, and severe hirsutism with coarse black hair on chest, inner thighs, face, and back (Ferriman Gallwey score> 25). Laboratory findings showed total testosterone: 3.8 (Nl: 0.1-0.8 ng/ml), DHEAS: 91 (Nl: 18-205 ug/d), LH: 20 (Nl> 20 mIU/ml), FSH: 44 (Nl> 20 mIU/ml), prolactin: 2.7 (Nl: 2-28 ng/ml) TSH: 0.6 (Nl: 0.5-4.5 mlu/ml). The pregnancy test was negative, and serum cortisol suppressed an overnight test. Abdominopelvic ultrasound showed normal adrenal glands and 2 tiny follicles with 7mm diameters in the left ovary. There were no pathological findings in the Abdominopelvic CT scan. Finally, the patient underwent total hysterectomy with bilateral salpingo-oophorectomy.

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On gross exam, except for right ovary, which on sectioning revealed a circumscribed unencapsulated nodular lesion with a dark yellowish-brown solid cut surface measuring 1.5 cm in greatest dimension located within the ovarian stroma, no other significant pathologic condition was identified. Microscopic examination of the mentioned lesion showed sheets of polygonal cells with abundant pale to eosinophilic or granular cytoplasm with round uniform centrally located nuclei making nodules. Tumoral stroma was sparse and included delicate connective tissue supporting a prominent capillary network. No Reinke crystal was seen (Figure 1). Also, no apparent mitosis or necrosis was observed. Hyperthecosis was present in surrounding ovarian stroma. The tumor cells were positive for inhibin and synaptophysin and negative for CK and S100. Ki67 index showed about 1-2 % proliferative activity (Figure 2). The tumor was diagnosed as a steroid cell tumor, so-called stromal luteoma. Histologic features suggestive of malignancy were absent in our patient. After a 3-month patient's clinical symptoms improved and testosterone level returned to normal in a regular follow-up.

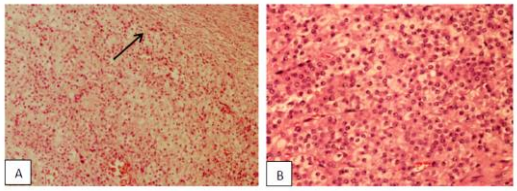

Figure 1. A.well demarcated proliferation of polygonal tumor cells (H and E).B.Sheets of pale to eosinophilic tumor cells with round centrally located nuclei

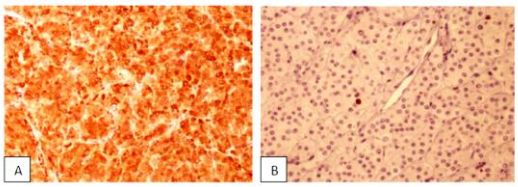

Figure 2. A. Tumor cells were positive for inhibin. B. Ki67 staining shows low proliferative activity

Discussion

The presentation of new-onset and rapid progressive hyperandrogenism is rare in postmenopausal women, and it is usually associated with ovarian or adrenal tumors (4). Ovarian tumors are divided into 3 groups, include epithelial tumors, sex cord-stromal, and germ cell tumors. Steroid cell tumors are rare and make about 0.1% of primary ovarian tumors. Steroid cell tumors produce steroid hormones with estrogen and/or androgenic effects. Approximately 56-77% of patients with steroid cell tumors have androgenic finding such as virilization, 6-7% of patients have hypercortisolism, and 25% of patients haven't any clinical manifestation (5). Hyperandrogenism associated with increased LDL and triglyceride levels, a decrease in HDL, increase insulin resistance, hypertension, and fluid retention (3).

The WHO classification of sex-cord stromal tumors has recently been revised (6,7). Based on, these tumors have been regrouped into following clinicopathologic entities: Pure stromal tumors, pure sex-cord tumors, and mixed sex-cord stromal tumors. Steroid cell tumors are defined as ovarian neoplasms composed of cells resembling steroid secreting cells without Reinke crystals. Based on the new classification, these tumors are categorized in to "steroid cell tumor" and "steroid cell tumor, malignant." Stromal luteoma, which was used to designate small steroid cell tumors confined to the ovarian cortex, has been discarded (6).

Based on gross pathology findings, Leydig cell tumors are usually located in the ovarian hilum, whereas stromal luteoma (steroid cell tumor) is mainly localized in the stroma (8) as presented in our case.

Also, in the microscopic exam, Leydig cell tumors contain steroid cells, including Reinke crystalloids (8), which were absent in our case.

Other histological differential diagnoses include malignant melanoma or metastatic clear cell carcinoma such as Renal Cell Carcinoma. Both were excluded based on negative immunohistochemistry results for S100, HMB45 for the former, and CK for the latter. Histologic features suggestive of malignancy including 2 or more than 2 mitoses per 10 HPF, necrosis, diameter more than 7 cm, hemorrhage, or grade 2-3 nuclear atypia were absent in our case (9,10). Ovarian secreting tumors have increased serum testosterone and normal DHEAS level. Therefore total testosterone concentrations are the best laboratory test for diagnosis and follow up in postmenopausal women with hyperandrogenism (11). Testosterone levels above 1.5-2 ng/ml should increase the suspicion of malignancy. Sielert *et al*., report an Androgen-producing steroid cell ovarian tumor in a young woman which her testosterone level was 4.85 ng/ml, and it had reached 0.32 ng/ml at the post-operative visit 13 days after surgery (5). In the first step in a patient with hyperandrogenism and an elevated serum testosterone level, an ultrasound should be performed. Diagnostic measures should be continued if negative ultrasound is detected (12,13). It is known that pathologically benign stromal cell tumors can behave in a clinically malignant fashion (9,10). So, the careful

correlation between clinical findings and histopathological features should be considered, and regular follow up of the patient should be stressed upon in order to detect any possible recurrence or even metastasis of the tumor (10). This case is significant because of the rarity of ovarian steroid cell tumor, and there were no obvious abnormalities in diagnostic imaging.

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