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RARE CASE OF OVARIAN STEROID CELL TUMOR NOT OTHERWISE SPECIFIED IN A POSTMENOPAUSAL WOMAN

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Abstract

Ovarian steroid cell tumors, not otherwise specified (NOS), are rare ovarian sex cord–stromal tumors with malignant potential. They represent less than 0.1% of all ovarian neoplasms. Little is known about this tumor, it is rare, and only a small number of case reports are available in the literature.

This type of tumor can produce testosterone, leading to hyperandrogenism, virilization and amenorrhea. Postmenopausal occurrences are rare. We present a 60-year-old woman with onset of virilization, worsening alopecia and excessive growth of hair on abdominal and genital parts of the body. She has elevated levels of adrenal androgens. Radiologic studies were consistent with left sided ovarian changes. A diagnostic and therapeutic bilateral salpingo-oophorectomy confirmed steroid cell tumor NOS in both ovaries.

Post-operatively, the patient had complete resolution of her symptoms and normalization of testosterone levels.

Keywords: ovarian steroid cell tumor, ovarian neoplasma, hyperandrogenism, virilization.

Introduction

Ovarian steroid cell tumors (SCTs) are characterized by cells with abundant intracellular lipids that are similar to adrenocortical cells. They account for 0.1-0.2% of all ovarian tumors, and the majority of them show virilization [1].

There are three subtypes: Leydig cell tumor, stromal luteoma, and steroid cell tumor, not otherwise specified (NOS). Steroid cell tumor, not otherwise specified, accounts for approximately 60% of steroid cell tumors, of which 25-45% clinically malignant [1,2].

Aproximately half of the steroid cell tumor NOS are associated with androgenic changes. Tumors causing virilization are often small [1,3].

The majority of steroid cell tumors are benign or with low-grade behavior. The specificity of this type of tumors is that pathologically benign tumors can behave in a clinically malignant fashion. Steroid cell tumors often present as unilateral solid tumors, but sometimes they can present as cystic tumors. Steroid cell tumor (NOS) can turn up at any age (mean, 42 years).

Case report

We present a 60-year-old with past history of hysterectomy at 46 years of age due to benign condition. Several months before she appeared in the office, she noticed partial hair loss that gradually became more intense, deapening of the voice, excessive hair growth on lower back part of the body, low abdomen upfront and genital region. On examination she has elevated serum testosterone levels 39.8 nmol/L (ref. < 2.10 nmol/l), DHEA-S 2.56 mcg/ml (ref <2.5), androstenedion>9.1 ng/ml (ref <3.5), FSH 77.2 mIU/ml, LH 68.1 mIU/ml, Estradiol <5 pg/ml, Prolactin 4.17 ng/ml, cortisol 398,7 nmol/l renal and liver functions were within normal limits. A negative dexamethasone suppression test ruled out Cushing syndrome. CEA, CA 15-3 CA 125 were within normal limits.

Abdominal and pelvic ultrasound showed increased left ovary (40×30mm), no follicules seen, and tumor formation with diameter 25 mm with parenchymal echogenicity rounded by echogenic hallo,

and normal right (21x15 mm) ovary. No ascites or other abnormalities were present. Computed tomography (CT) of abdomen with iv contrast, demonstrated oval ovarian mass in left ovary (30 mm), with excessive hyperdensity inside, surrounded by hypointense nodular wall(Figure 1). No ascites in abdominal cavity was found and no enlarged lymph nodes in retroperitoneal, iliac and inguinal space were detected. With clinical and biochemical suspicion of testosterone producing ovarian tumor, patient was advised a surgery.

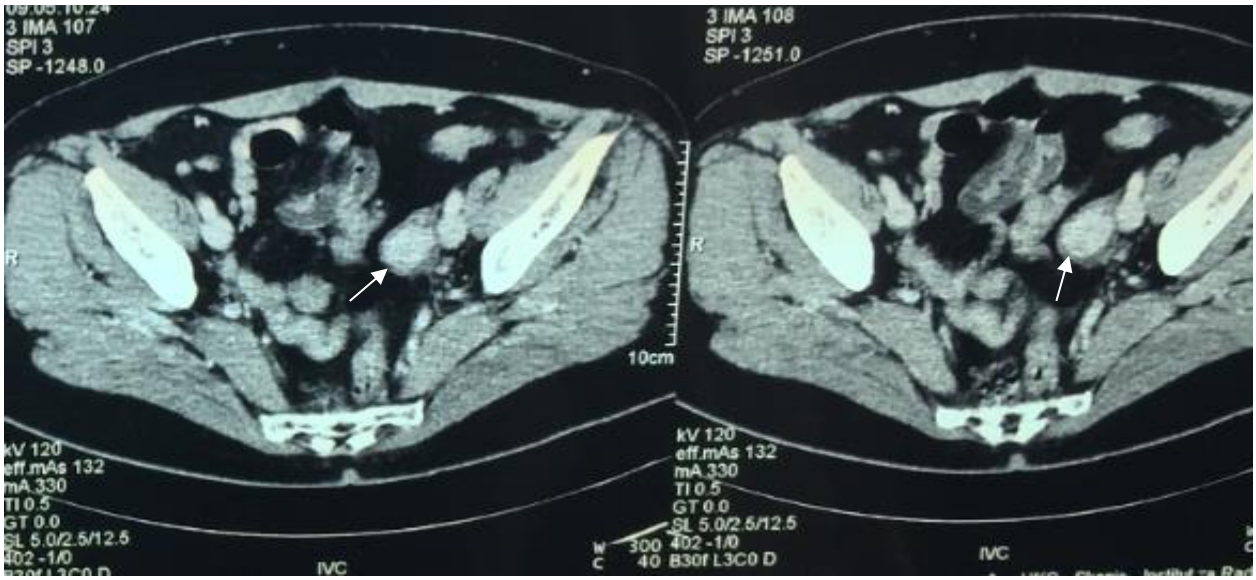


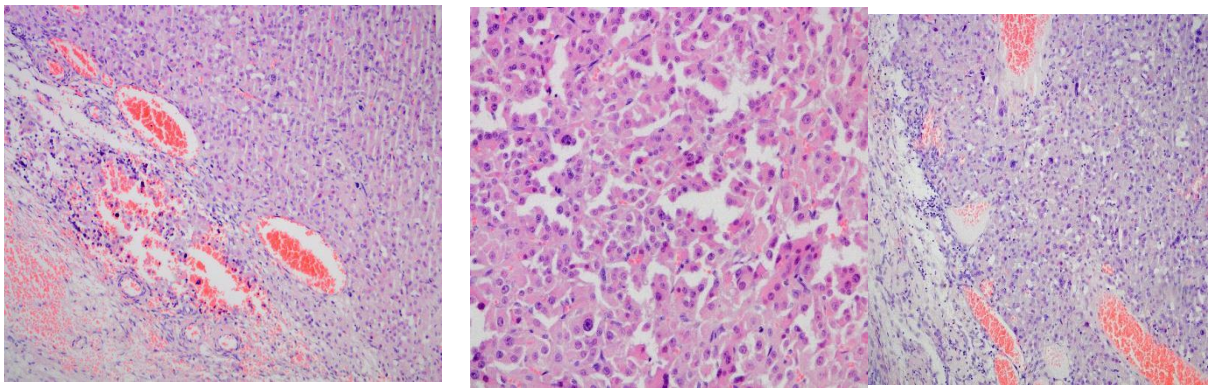
Figure 1. Pelvic CT scan with depiction of the tumor (arrows).

A laparotomy was undertaken and bilateral salpingo-oophorectomy was performed.

Final histopathological report:

Both uterine tubs were normal.

Left ovary dimension was 3x3x2.5 sm with two different cell populations. The first population consisted of big oval cells with large and light coloured cytoplasm. The second population was dominant and had oval polygonal cells with eosinophilic granulated cytoplasm and nuclear atypia of moderate to high level. The mytotic activity was low with only one mythosis per 10 fields on big magnifier (40) x power field. There were emboli built of neoplastic cells in vascular spaces. Hemorhage and necrotic parts were also found (Figure 2 a,b,c).



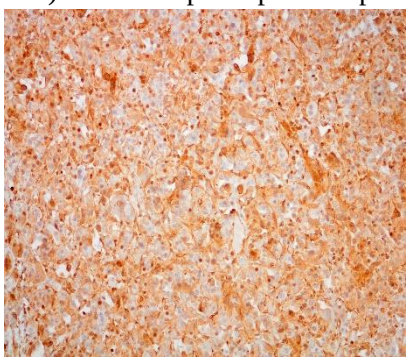
a. **b.**

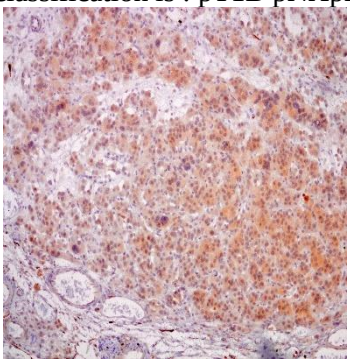
Figure 2. a) Diffuse sheets of large polygonal cells, hematoxilin and eosin stain (magnification x 50) b) polygonal cells with granular eosinophilic cytoplasm (magnification x200).

Right ovary with dimensions 3 x 2.5 x 2 sm also had neoplasm in cortical part (0.5 sm in diameter) with same morphological characteristics as described in the left ovary.

The cells (Figure 3) revealed positive staining for Inhibin, Vimentin, CD68, Desmin and S100 protein, and negative staining for HMB45, Alpha fetoprotein, EMA and pancytokeratin. Proliferative Ki67 marker was positive in 7% of the cells.

Morphological and imunochistochemical characteristics of the tumor suggest final diagnosis-Ovarian steroid cell tumor, not otherwise specifie. Pathologic features which indicates malignancy, are: three of five (necrosis, nuclear atipia and hemmorhagi). The rest two parameters were not found (the size of the tumor is less than 7 sm , and number of mythotic fitures per 10 high power fields is less than two). The final post operative pTNM classification is : pT1B pNXpMX G2 NG3.





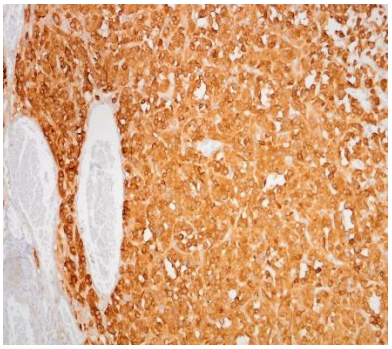
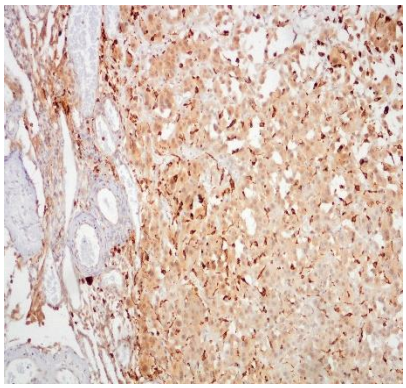


Figure 3. Vimentin positive cells. S 100 positive cells. Inhibin positive cells.



CD 68 positive cells.

Discussion

Hayes and Scully [4] reported an initial large series of 63 cases in 1987. The controversy exists about the malignant potential of these lesions. Clement and Young [1], in 2000, has been working on the limitations of histopathology, providing a definitive classification of the steroid cell as benign or malignant, because it is still unclear why some benign-looking tumors had a malignant clinical outcome. Hayes and Scully reviewed 63 cases with 18 patients who had clinically malignant tumors.

The best pathologic features that correlates with behavior were the presence of two or more mitotic figures per 10 high-power fields (92% malignant); necrosis (86% malignant); a diameter of 7 cm or greater (78% malignant); hemorrhage (77% malignant); and grade 2 or 3 nuclear atypia (64% malignant) .

Therefore, well-differentiated adrenal cortical tumors are difficult to predict, but these patologic features provide a high possibility of suspicion (3). Unfortunately, the clinical presentation is not

sufficient to distinguish benign from malignant ovarian SCTs. Malignant ovarian SCTs occur at any age, with average reported of 43 years [4].

In the pediatric age, SCTs can be misdiagnosed and mixed with nonclassical congenital adrenal hyperplasia; in reproductive age, they can be misdiagnosed as polycystic ovary syndrome or late-onset congenital adrenal hyperplasia, especially if presented with oligomenorrhea or hirsutism. Patients may have variable clinical manifestation; from completely asymptomatic to hormonally active The commonest presenting symptom in all age groups is virilization is [4].

Presentation in postmenopausal women can also be challenging, as such patients do not present with menstrual irregularities. Sometimes, other clinical presentations can be related to glucocorticoid excess. Cortisol has been reported to be produced by 6 to 10% of cases [5-9].

In our case, the virilization brought her to endocrinologist, rather than to gynaecologist. The complete hormonal spectar revealed normal hormonal postmenopausal design, exept total testosterone and androstenedione.

Elevated testosterone and DHEAS are markers of androgen excess. DHEAS has been used as an biomarker of an adrenal source of androgen hypersecretion. In our patient there was high testosteron level, DHEAS on upper limit of normal reference range, and androstenedione, an androgen derived from ovary - extremely high. Knowing that androstenedion is androgen produced in adrenal glands and in ovaries, the focus was thrown on discovering some process in these glands.

Different radiologic modalities have been used for diagnosing and following of these patients; transvaginal ultrasound, CT, and magnetic resonance imaging (MRI).

Typically, these tumors are characterized with a solid component and intermediate signal intensity with homogenously intense enhancement. Rarely, they can be heterogenous with cystic and solid areas. Rarely they are too small, and if this is the case, they can be detected by structural imaging such as radiolabeled steroid scans using aldosterol, iodocholesterol, and Se75. In our patient, the first two methods were sufficient in the diagnosis and follow-up.

Local metastasis has been reported in 20% of cases of ovarian SCTs with peritoneal cavity as the most common area of metastasis. Distant metastasis are very rare and reported in bones [8].

Pelvic recurrence has been reported by Hayes and Scully [4] in 12 patients, despite chemotherapy and external-beam radiation treatment. Indicators of prognosis are tumor size and stage. The standard therapy for malignant ovarian SCTs is surgery.

Staging of tumor and fertility are used to determine the extent of surgical intervention. A patient in reproductive age who has stage 1 disease and desires future fertility can be managed by conservative surgery with unilateral salpingo-oophorectomy.

For postmenopausal patients and younger patients who are not concerned about fertility, total abdominal hysterectomy and bilateral salpingo-oophorectomy is a recommended option [10].

Our patient was postmenopausal, and we decided to recommend a surgery.

In our patient there was only left sided tumor seen before the surgery. Following the reccomendations, we decided to perform complete bilateral salpingo-oophorectomy. Surprisingly, there was tumor in the right ovary with the same patohistological charasteristics which was not preoperatively visualized.

Usually most of these tumors are diagnosed in early stage and do not reccur or metastize, therefore less is known about their response therapy.

It is recommended that patients with ovarian steroid tumors NOS should be menaged surgically, like every other ovarian stromal tumor.

The recommended treatment is completely surgical, i.e. total abdominal hysterectomy and bilateral salpingo-oophorectomy for older postmenopausal woman. Our patient was already without uterus due to hysterectomy done earlier, so the surgery was-bilateral salpingo-oophorectomy. Since our Clinical center has no experience with this rare type of tumors, we asked for second opinion in other two European oncology centers.

Both of them agreed indipendently that there are no well established chemotherapy guidelines for clinical menagement of steroid cell tumors.

This particular tumor was malignant according to patological report, but surgically removed on early stage, and therefore, they suggest regular clinical and laboratory examinations, CT scan or ultrasound periodically. Up-to-date, the patient is on regular check-ups done in 6 months interval, feeling well, with no shown recurrence of the tumor, neither clinically nor biochemically.

Conclusion

This case represents one of the rarest ovarian tumors and therefore difficult to diagnose. Careful history taking, physical examination, laboratory testing and imaging studies are helpful in making the diagnosis.

We recommend that any female patient who has symptoms of hyperandrogenism and biochemical evidence of high testosterone levels, should be investigated systematically in order to determine the origin of high testosterone level (adrenal or ovarian). Prompt discovery followed by surgery play main role in resolution of the simptoms and good prognosis.

The desion for therapy should be strongly individualized, based on tumor histology, surgical staging, and, if the staging of the tumor allows, the desire for fertility preserving. All steroid cell tumors NOS with malignant characteristics should be managed operatively, with life-long follow-up.

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