Steroid Cell Tumor of Ovary-A Rare Case Report and Review of Literature

Sir,

Post-menopausal women presenting with features of hyperandrogenism is a diagnostic challenge for clinicians. Various non-tumorous and tumorous causes of ovary and adrenal gland need to be evaluated. When Clinical manifestations of hirsutism are more severe and/or accompanied by virilizing symptoms like male pattern baldness, clitoromegaly, and deepening of voice, a tumorous source of excessive androgen secretion originating from either the adrenals or the ovaries should be excluded.[1,2] Sex cord-stromal tumors of ovary are a group of neoplasms that present with varied clinical manifestations of hormone excess such as hyperestrogenism and hyperandrogenism. They are different from surface epithelial tumors in their clinical presentation, treatment

protocols, and clinical outcomes. Ovarian steroid cell tumors are rare sex cord-stromal tumors of ovary that account for less than 0.1% of all ovarian tumor.[3] Hayes and Scully reported an initial large series of 63 cases in 1987.[4] Steroid cell tumors (NOS) usually present with hyperandrogenic symptoms and increased serum androgen levels. These tumors have a benign clinical course with normalization of hyperandrogenic symptoms after surgical removal.

A 50-year-old woman, a known case of hypertension, presented to Endocrinology opd with excessive facial hair growth and frontal balding since 2 years [Figure 1]. She did not have other virilizing features like clitoromegaly or deepening of voice. Her vitals were normal. Her BMI was 21.4 kg/m^2. There was no significant history of long-term drug usage. She attained menopause 15 years back. Genital examination did not show clitoromegaly and per vaginal examination revealed that uterus was deviated to the left. No obvious mass was felt. Laboratory investigations showed increased serum total testosterone levels-2.71 ng/ml (normal range-0.3-0.9 ng/mL). All other serum markers were within normal ranges-Serum CA19.9 - <2 Units/ml (normal range- <37 Units/ml) carcinoembryonic antigen-2.06 ng/ml (normal range- <3 ng/ml) and CA-125-18.9 Units/ml. (normal range- <35 Units/ml). DHEAS-42.6 µg/dl (normal range-35-430 µg/dl). Serum cortisol-10 µg/dl (normal range-5-25 µg/dl).

Ultrasonography showed well-defined oval hyperechoeic lesion in the right ovary measuring 3.3 × 2.1 × 3 cm. CT showed a well-defined solid enhancing mass lesion in the right ovary measuring 2.8 × 2.4 cm, outer margins well defined. There was no evidence of infiltration into adjacent structures. [Figure 2]. There was no evidence of pelvic lymphnodes. Both adrenal glands were normal.

Total abdominal hysterectomy with bilateral salpingoopherectomy was planned. Intraoperatively right ovary was enlarged measuring approximately 4 × 4 cm. There were no ascites. Total abdominal hysterectomy with bilateral salpingoopherectomy and partial omentectomy was performed.

On gross examination, the right ovary was intact and was measuring-3.5 cm × 3.3 cm × 2.1 cm. Cut section showed a well-circumscribed gray white-toyellow tumor with focal dark brown areas and a rim of compressed normal ovary at the periphery [Figure 3].

Microscopic examination showed a cellular well-circumscribed tumor with cells in nests, sheets separated by stroma, and collagenous bundles. Individual cells were round to polygonal with centrally placed nuclei and prominent nucleoli. Cytoplasm was abundant homogenous pink in some cells and vacuolated to clear in some groups of cells. [Figures 4 and 5] There was no necrosis or mitosis. Reinkes's crystals were not seen.

Immunohistochemistry: The tumor cells were immunoreactive for Inhibin-A, Melan A, Calretinin and Androgen receptor. Tumor cells were immunonegative for chromogranin and SALL4. [Figure 6]. The final diagnosis was confirmed as steroid cell tumor –NOS. Based on the size of the lesion 3.5 cm (<7 cm), absence of necrosis, mitosis, nuclear atypia and hemorrhage the tumor was predicted to behave in a benign fashion.

The patient postoperatively improved and her serum testosterone normalized to-0.9 ng/ml on the second postoperative day. The hyperandrogenic symptom of facial hair disappeared over a period of 3 months after the surgery. The patient is in follow up.

Hyperandrogenic symptoms in postmenopausal women have a wide spectrum of causes that need to be worked up in a systematic manner. It includes tumorous and non-tumorous causes. Non-tumorous causes include poly cystic ovarian syndrome, ovarian hyperthecosis, congenital adrenal hyperplasia, Cushing's syndrome, and iatrogenic steroid excess. Tumorous hyperandrosteronism is suspected when the testosterone levels are more than 1.0-1.4 ng/ml and is usually associated with abrupt onset and rapid evolution of symptoms.[5] Androgen secreting adrenal adenomas and carcinomas are rare causes of tumorous hyperandrogenism. Ovarian sex cord-stromal tumors are infrequent and represent approximately 7% of all primary ovarian tumors. The majority tend to present as a low-grade disease that usually follows a nonaggressive clinical course in comparison to surface epithelial tumors. Ovarian sex cord-stromal tumors are comprised of a variety of tumors with a propensity to produce androgens and display a wide range of clinical manifestations. Tumors formed from ovarian cells (e.g., granulosa cells and theca cells) are often hyperestrogenic, whereas those comprising testicular cell types (e.g., Sertoli and Leydig cells) are usually hyperandrogenic. However, many tumors are nonfunctioning, and those comprising female cells may produce androgens and vice-versa.[6] Steroid cell tumors are grouped under pure stromal tumors of the sexcord stromal tumors group according to the latest classification. Steroid cell tumors are defined as tumors composed of steroid hormone-producing cells. These tumors are rare and account for less than 0.1% of all ovarian tumors. The term steroid cell tumor has been used, because it reflects both the morphological features of the neoplastic cells and their tendency to secrete steroid hormones. They have been divided in to 3 subtypes according to their cell of origin-Stromal luteoma, Leydig cell tumor and steroid cell tumor NOS of which the latter is the most common variant accounting for 56% of steroid tumors.

Steroid cell tumor NOS usually occurs in adults with an average age at diagnosis of 43 yrs. Majority of the patients present with virilizing symptoms, amenorrhea and lower abdominal pain. In our patient serum, Testosterone level was elevated preoperatively and normalized postoperatively. Steroid cell tumors NOS are unilateral and appear as large tumors (average size, 8.4 cm) that vary from solid masses to multilocular cystic masses with nodular walls.

Radiologically these tumors are circumscribed and confined to one ovary.

On gross examination steroid cell tumors are well circumscribed with yellow areas indicating high lipid content. Microscopically the tumor cells are arranged in nests and sheets with intervening fibrovascular tissue. Individual cells have clear to pink cytoplasm depicting the steroid content. Reinkes crystals are not identified.[7] Most of the tumors are benign. Hayes and Scully identified the following features that are associated with malignancy [Table 1].

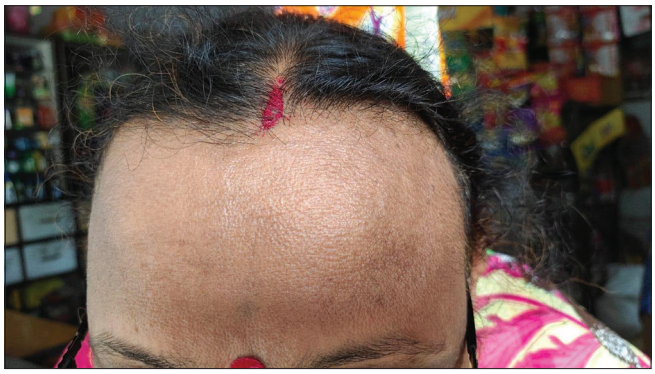

Figure 1: Frontal balding

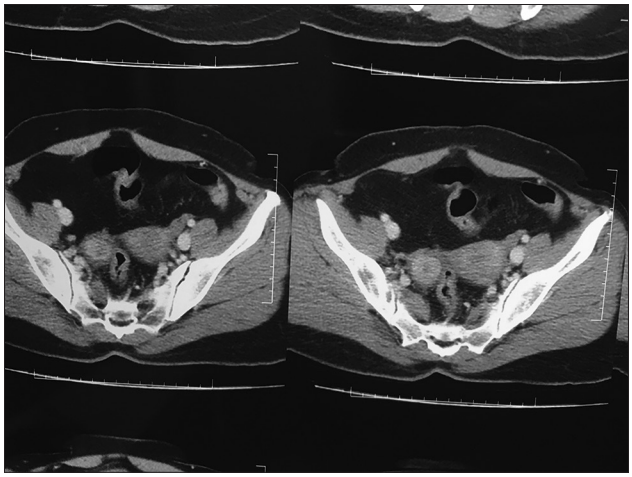

Figure 2: CT-showing right ovarian tumor

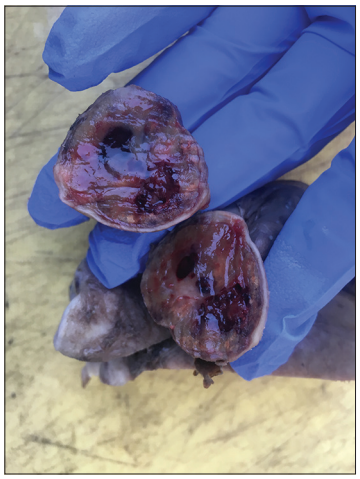

Figure 3: Gross –C/S showing grey white tumor

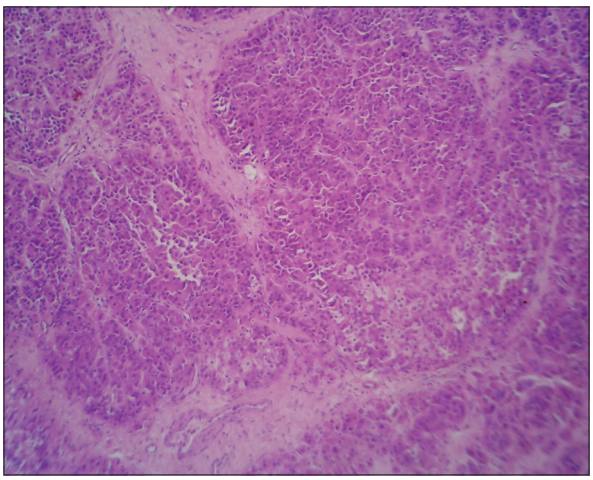

Figure 4: Low power showing tumor sheets

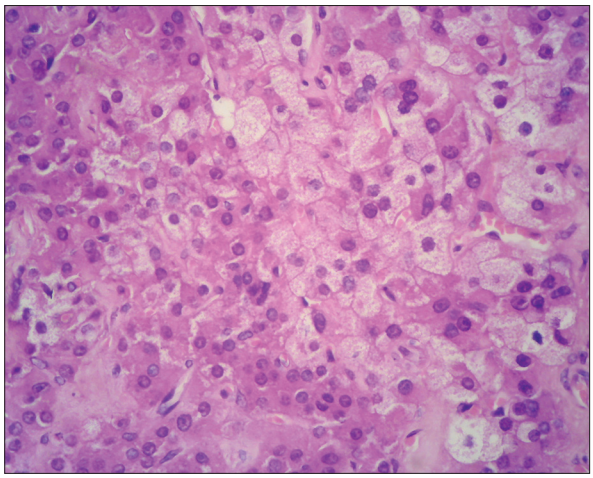

Figure 5: High power showing lipoidal cells and cells with abundant cytoplasm

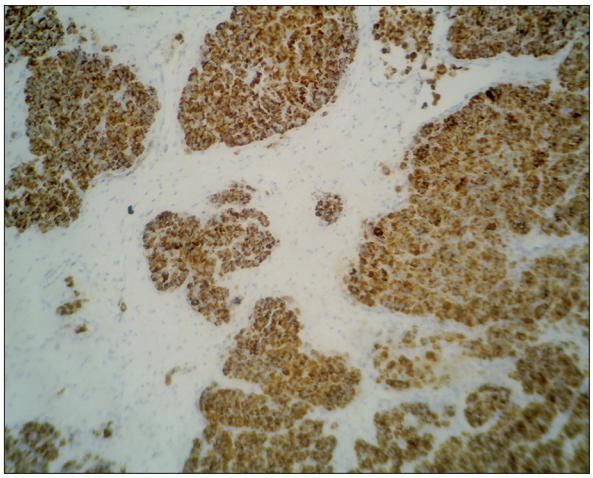

Figure 6: IHC-Melan A positive

Table 1: Predictive pathological characteristics of malignancy for ovarian steroid cell tumors, NOS

Microscopic features	% chance of malignancy
A. Two or more mitosis/hpf	92%
B. Necrosis	86%
C. Size of 7 cms or larger	78%
D. Hemorrhages	77%
E. Grade 2/3 nuclear atypia	64%

Since our case did not show any of the above characteristics, the tumor was predicted to behave in a benign fashion.

Steroid cell tumors NOS differentiated from Leydig cell tumors, stromal luteoma, luteinized granulosa cell tumors, clear cell carcinomas, and metastatic renal cell carcinomas by its specific histopathological features. Inhibin, Calretinin, Melan –A are confirmatory Immunohistochemistry markers. Our case showed immunoreactivity to the above markers.

The management of these tumors is based on the histological picture, surgical staging and patient's desire to preserve fertility. Surgical resection is the treatment of choice for localized and benign disease. In young females who wish to preserve fertility, unilateral salpingo-oophorectomy can be performed. In older, post-menopausal women, total abdominal hysterectomy with bilateral salpingo-oopherectomy is preferred.[8] As our patient was post-menopausal, total abdominal hysterectomy with bilateral salpingo opherectomy was done. Serum testosterone levels normalized in our patient post-surgically. As our patient was postmenopausal dual energy x-ray absorptiometry scan was done which showed osteoporosis. (T-score -2.8 at spine -3 at Left Femur and -2.7 at Right Femur). Patient was given calcium, Vitamin D and residronate 35 mg weekly.

Clinical evaluation of symptoms, high index of suspicion aided with biochemical and radiological investigations will lead to proper diagnosis of cause for hyperandrogenism in postmenopausal women. Once the tumorous etiology is established, histopathological examination and immunohistochemistry will confirm the diagnosis. Surgical resection results in complete cure in benign androgen-producing ovarian tumors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Pallavi S. Pitale, Aditya A. Shrikhande, Padmaja S. Achanta[1]

Departments of Internal Medicine and Endocrinology and [1]Pathology, Dew Medicare and Trinity Hospital Nagpur, Maharashtra, India

Address for correspondence: Dr. Padmaja S. Achanta, Consultant Pathologist, Dew Medicare and Trinity Hospital, No-80 and 81, Hindustan Colony, Wardha Road, Nagpur - 440 013, Maharashtra, India.
E-mail: achantapadmaja@yahoo.com

References

1. Rothman MS, Wierman ME. How should postmenopausal androgen excess be evaluated? Clin Endocrinol (Oxf) 2011;75:160-4.
2. Alpanes M, Gonzalez-Casbas JM, Sanchez J, Pian H, Escobar-Morreale HF. Management of postmenopausal virilization. J Clin Endocrinol Metab 2012;97:2584-8.
3. Young RH, Clement PB, Scully RE. Sex-cord stromal, steroid cell and germ cell tumours of the ovary. In: Mills SE, Carter D, Greenson JK, Oberman HA, Reuter V, Stoler MH, editors. Sternberg's Diagnostic Surgical Pathology. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004, p. 2579-615.
4. Hayes MC, Scully RE. Ovarian steroid cell tumors (not otherwise specified). A clinicopathological analysis of 63 cases. Am J Surg Pathol 1987;11:835-45.
5. Markopoulos MC, Kassi E, Alexandraki K, Mastorakos G, Kaltsas G. Hyperandrogenism after menopause. Eur J Endocrinol 2015;172:79-91.
6. Pratt J. Sex cord and stromal tumors. In: Pratt J, editor. Pathology of Ovary. 1st ed. Philadelphia: Saunders; 2004, p. 197-226.
7. Paraskevas M, Scully RE. Hilus cell tumor of the ovary. A clinicopathological analysis of 12 reinke crystal-positive and nine crystal-negative cases. Int J Gynecol Pathol 1989;8:299-310.
8. Mehdi G, Ansari HA, Sherwani RK, Rahman K, Akhtar N. Ovarian steroid cell tumour: Correlation of histopathology with clinicopathologic features. Patholog Res Int 2011;2:987895.

Submitted: 16-May-2021 **Published:** 12-Jan-2022
Accepted: 29-Nov-2021

Access this article online

Quick Response Code:

Website: www.ijem.in

DOI: 10.4103/ijem.ijem_205_21

How to cite this article: Pitale PS, Shrikhande AA, Achanta PS. Steroid cell tumor of ovary-A rare case report and review of literature. Indian J Endocr Metab 2021;25:466-9.