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Granulosa Cell Tumor as Incidental Finding in a Female after Menopause- A Rare Case Report.

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ABSTRACT:
[1]Sex cord stromal-tumors of the ovary are rare and comprise several cancer subtypes of varying histopathological traits and clinical presentation. [2]These tumors encompass 5% of the total neoplasms of the ovary. It mostly affects women in the age group around fifties. The patients usually present with a mass in the adnexa, or haemoperitoneum, endometrial hyperplasia or adenocarcinoma. They can show fluctuating clinical presentations due to their oestrogenic activity ranging from precocious puberty to menorrhagia to postmenopausal bleeding.[3] Differentiation in sex cords or in stroma is noted in these ovarian tumors. The more common types are granulosa cell tumors, fibrothecomas and sertoli-leydig cell tumors.[4] As these tumors are small and very infrequent, they are often diagnosed by histopathology following surgical removal.[5] As these tumors are mostly benign with a comparatively good outcome, a broad impression of differential diagnosis and detailed understanding of clinical and pathological findings along with ancillary studies if needed is important for correct diagnosis and appropriate treatment.[6] Serum tumor markers may be important in making a diagnosis before surgical intervention and monitoring. Extensive knowledge of the molecular pathogenesis of these ovarian tumors will pave the way for novel therapeutics.
We present a rare clinical case of incidental finding of theca granulosa cell tumor of the ovary with a predominant spindle cell morphology in a postmenopausal female who presented with postmenopausal bleeding and abdominal pain. Most of these tumors are diagnosed with gross and microscopic features. However, the existence of variable clinical and histological presentations make the use of immunohistochemistry crucial in their diagnosis. As most of these tumors are of low grade and are associated with endometrial hyperplasia and endometrial adenocarcinoma, prompt diagnosis is essential for better management.

Key words: therapeutics, tumor, molecular, histopathological, postmenopausal, immunohistochemistry.

I. INTRODUCTION

[4]Ovarian sex cord stromal tumors are rare tumors in contrast to epithelial neoplasms. [5]These tumors arise from different cells of the ovary and can present with varied clinical symptoms.[6] These tumors are mostly unilateral affecting only one ovary, may reach upto 15 cm in greatest dimension. They may be solid, firm, and may range from being lobulated to soft and friable, often with hemorrhage and necrosis.

[7]The WHO classification (2014) of sex cord stromal tumors were regrouped into pure stromal tumors which comprises fibroma, cellular fibroma and fibrosarcoma, pure sex cord tumors including adult and juvenile granulosa cell tumors and mixed sex cord stromal tumors-sertoli leydig cell tumors. [8]These tumors have a wide variety of histological picture based on the cell type. They may be formed of glands as seen in sertoli cell tumors or composed of spindly cells as seen in fibromas. As most of these tumors are very uncommon with a variable presentation diagnosis may be difficult. Apart from regular histological findings, ancillary methods like Immunohistochemistry may be needed to come to an exact diagnosis. Inhibin has been the most useful marker to report SCSTs until now. Recently, studies have shown that staining with calretinin which is mainly used for diagnosis of mesothelioma is also useful in the diagnosis of SCSTs of the ovary.
[9]Theca cell tumors are not as common as granulosa cell tumors. Theca cells are estrogenic in 50% of cases. These tumors can also contain luteinised cells with calcification. They may produce peritoneal and intestinal fibroids. They are

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more common in post menopausal women and are oestrogenic.

II.CASE REPORT

A 59 year old female came with complaints of abdominal pain and postmenopausal bleeding for 3 days. She attained menopause when she was 55 years old. P/s revealed minimal brownish discharge from os. USG abdomen done- uterus 7.9x4x5.2 cms; endometrium- 12.7 mm, small left ovarian cyst with internal septation seen.

Endometrial sampling and cervical biopsy were done revealing early adenocarcinoma endometrium and chronic cervicitis.

Total abdominal hysterectomy with bilateral salphingo-oopherectomy was done. We received an already cut open uterus specimen which measured 8.5x7.5x3 cm. Endometrial cavity measuring 4 cm in length. Cut section revealed a endometrial polyp measuring 1 cm in diameter. Endometrial thickness was 2.3 cm. Cervical canal was 2.5 cm in length. Right ovary measured 4.5x2.5x1.5 cm with attached fallopian tube with fimbrial end measuring 4.5 cm in length. Cut section of right ovary showed a ill-defined whitish yellow nodule measuring 1.5x1 cm. Left ovary measured 2.5x1.5x0.8 cm with attached fallopian tube with fimbrial end measuring 3.5 cm in length. Cut section of left ovary and both tubes were unremarkable.

Histopathology, sections studied from cervix showed papillary endocervicitis. Endometrium showed endometrial hyperplasia with early malignant transformation. No invasion into myometrium made out. Left ovary and attached fallopian tube appeared normal. Right ovary revealed a follicular cyst and a well defined nodule formed of nodules & whorls of proliferating plump granulosa and theca cells with few areas of calcification and nest of plump cells with round vesicular nucleus and few foci of polygonal cells. IHC with calretinin and inhibin were done which were both positive and a diagnosis of theca granulosa cell tumor was given.

Image 1: cut section of Right ovary.

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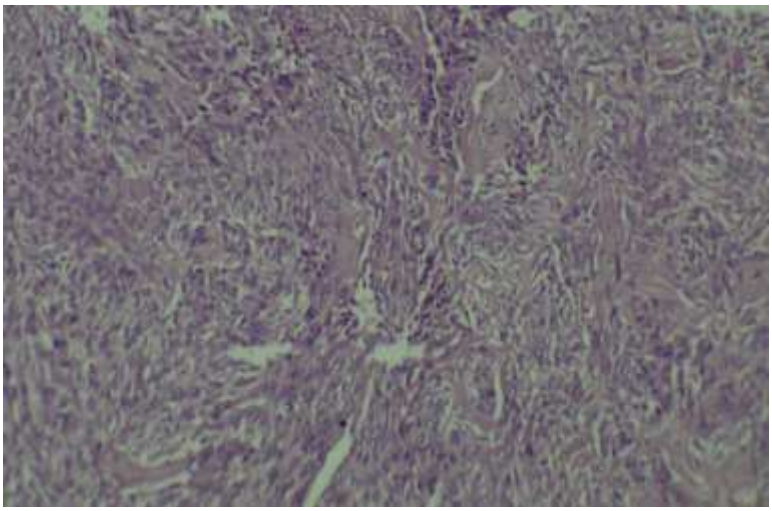

Image 2: H&E section of ovary under low power.

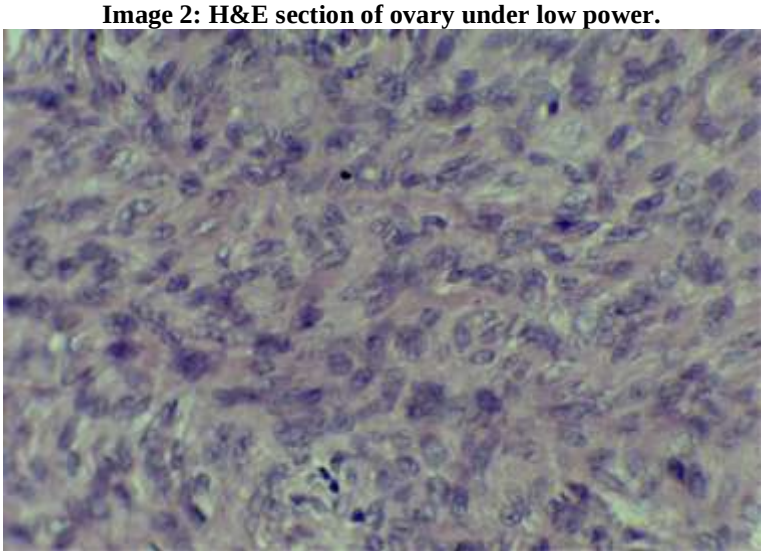

Image 3: H&E section of ovary under 45x.

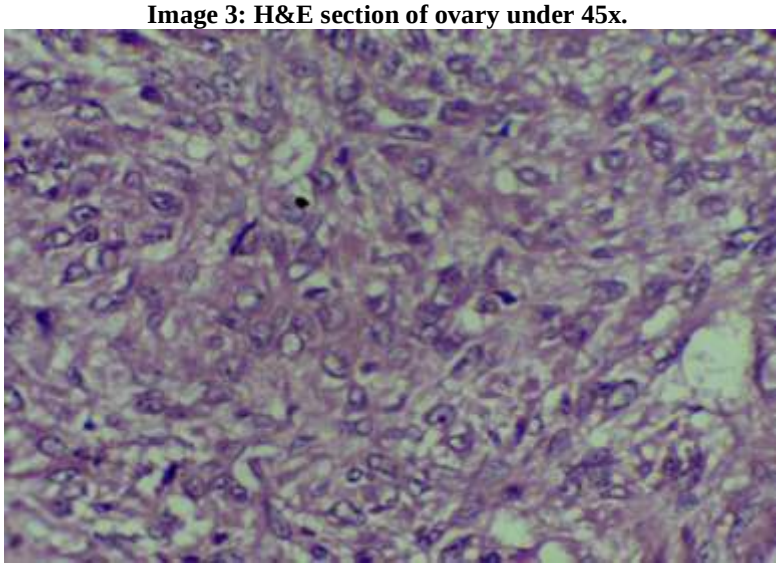

Image 4: H&E section of ovary under 45x.

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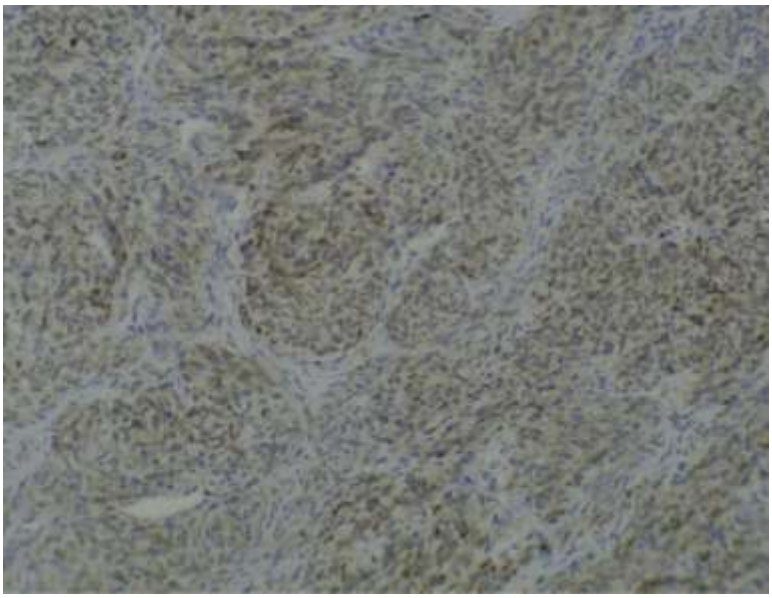

Image 5: IHC of ovary using Inhibin- positive.

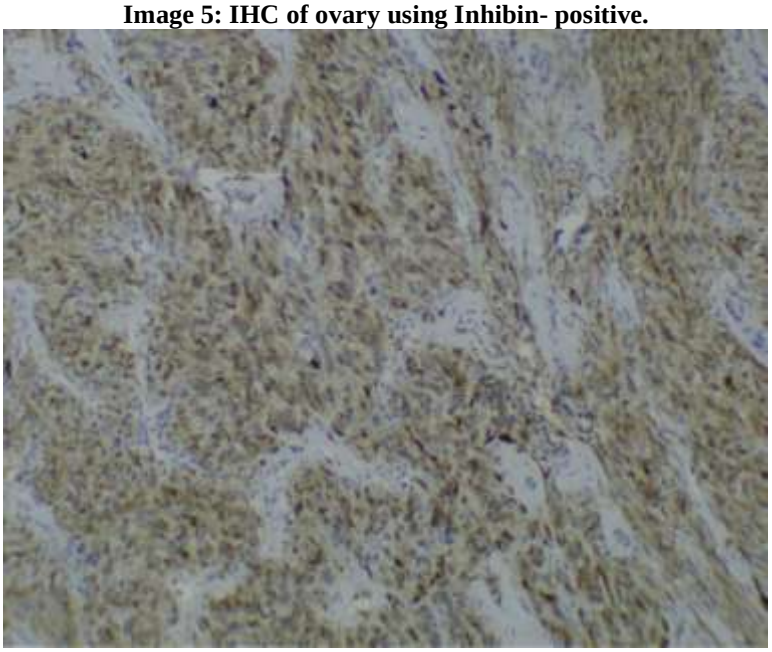

Image 6: IHC of ovary using Calretinin- positive.

IV.DISCUSSION

[10]Ovarian Sex cord stromal tumors comprise several morphologically distinct neoplasms which are uncommon. Inspite of being rare, these tumors present with so many differentials.

[11]Jiang et al., mentioned that in some histopathological subtypes of ovarian SCSTs in radiological study, the echo of the entire ovary is the same and the lesions are not detectable. Diagnosis in such cases is ultimately based on pathology in conjunction with the clinical symptoms of the patient, radiological features, and serum hormones.

[6]Ann et al., studied and found that levels of inhibin, estradiol, testosterone and AFP may be needed if the patient is suspected to have a ovarian SCST. Granulosa cell tumors may show high levels of inhibin and estradial owing to the estrogenic effect. High levels of testosterone may be associated with Sertoli-leydig cell tumors.

[12]Rathore et al, postulated that FOXL2 was 100% sensitive and specific for all cases of sex cord stromal tumors in their study. However, there

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is no clearcut range of sensitivity and specificity studied for calretinin and inhibin in SCSTs. Numerous studies have confirmed the role of FOXL2 in diagnosing ovarian adult granulosa cell tumors with no clear literature when compared to inhibin and calretinin in the diagnosis of the same.

[13]Agarwal et al, in his case study proposed that granulosa cell tumors of the ovary are unpredictable and if the tumor size is small, it may be clinically missed. The tumor often secretes estrogens and the patient presents with the hormone-related symptoms. Endometrial pathology has to be sorted out thoroughly to rule out endometrial hyperplasia or endometrial carcinoma. This helps in early detection, intervention and better management for the wellbeing of the patient.

[14]Schumer et al, studied the granulosa cell tumors of ovary and has concluded that long term follow up with clinical evaluation and estimation of serum tumor markers such as estradiol and inhibin timewise is needed as GCTs may recur several years after diagnosis and treatment.

V.CONCLUSION

We, hereby present a interestingly rare case of estrogenic granulosa cell tumor of ovary in a postmenopausal woman with endometrial hyperplasia and early malignant transformation which was confirmed by biopsy following total abdominal hysterectomy. Immunohistochemistry with inhibin and calretinin confirmed the diagnosis. The ovarian tumor was diagnosed incidentally which has caused endometrial hyperplasia and early malignant change. The patient is currently being followed up and symptom free.

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