Case Report

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Cystic Granulosa Cell Tumor of Ovary: An Incidental Finding in a 50 years Old Lady.

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ABSTRACT

Granulosa cell tumours (GCTs) are rare ovarian sex cord stromal tumours. GCTs usually are oestrogen producing neoplasms and hence consequently, symptoms related to hyperestrogenism are common at the time of diagnosis. Here we document a case of cystic GCT that was incidentally discovered on histopathological examination. An abdominal hysterectomy was done for abnormal uterine bleeding in a 50 years old lady, clinically was thought to be due to uterine fibroid. A unilateral oophorectomy was also done due to a small cyst in the left ovary, which on histopathological examination revealed cystic granulosa cell tumour in the ovary. Equipped with this knowledge, a better clinical correlation with the presenting symptoms could be made in future by clinicians and pathologists. The final diagnosis may change the prognosis and also the future treatment plan.

Keywords: *Cystic granulosa cell tumour, Hormone producing neoplasms of ovary, Histomorphological features of granulosa cell tumour.*

Introduction

Adult granulosa cell tumour (GCT) is a rare ovarian malignancy accounting for 1-2% of all tumours and 95% of germ cell tumours originating from sex cord-stromal cells. [1].GCT can occur at any age but most commonly presents during the peri-menopausal or early postmenopausal period with median age of diagnosis between 50 and 54 years in most cases.[2] It is the most common hormone-producing ovarian tumour which, usually produce oestrogen and leads to symptoms and signs of oestrogen excess. Endometrial hyperplasia and adenocarcinoma of uterus reported in 50 % and 15% of the cases of GCT respectively in peri-menopausal and postmenopausal women. However, dysfunctional uterine bleeding (DUB) and irregular menstruation are frequently seen in women of reproductive age.[3]

Case Report

A 50- year- old lady came with complaints of irregular and excessive menstrual bleeding since 6 months associated with on and off pain, more during active bleeding. General physical examination was normal except mild palor. All her hematological parameters were within normal range except for mild decrease in hemoglobin (9.8 gm %). Her biochemical parameters were also within normal range including CEA which was 12.5 ng/ml. A diagnostic endometrial biopsy was done and the histopathology report revealed benign cystic hyperplasia endometrium. The signs of hyper estrogen were in the form of irregular and excessive menstrual bleeding, which was confirmed on histopathological examination of hysterectomy specimen.

Ultrasound abdomen and pelvis was done, which revealed a mass in the uterus measuring 1.8 cm in diameter and left cystic ovary measuring 5 x 4 x 3 cm. A provisional clinical diagnosis of abnormal uterine bleeding was made probably due to fibroid in uterus. Later on total hysterectomy with removal of left ovary and both fallopian tubes was performed.

The hysterectomy specimen measuring 13 x 8 x 5 cm in size was received. The endometrial canal measured 5cm in length. On cut surface of uterus, a well circumscribed mass was identified measuring 2 cm. in diameter. Left ovary measured 5 x 4 x 2 cm (Fig 1a) and cut surface revealed a small cyst measuring 1.5cm in diameter (Fig 1b), which was filled with brownish fluid. The cut surface presented yellowish solid areas speckled with few hemorrhagic patches. Both the fallopian tubes were normal in appearance.

Microscopic examination of H&E stained paraffin sections revealed simple endometrial hyperplasia and adenomyosis uterus. An interstitial leiomyoma was embedded in the myometrium. Sections of cervix revealed chronic cervicitis with Nabothian follicles.

Several sections of the left ovary were examined, which revealed that part of the ovary was replaced by granulosa cell tumor and partly it was normal in architecture. The ovarian cyst wall was composed of proliferated granulosa cells (Fig 2a). The cells were arranged in follicular and trabecular forms (Fig 2b) with classical Call-Exner bodies and coffee bean nuclei (Fig2c) in another area.

Immuno-histochemistry (IHC) for granulosa cell tumor was carried out in one section (Fig 3a). The tumor cells were arranged in diffuse pattern. The IHC with inhibin antibody showed diffuse positivity (Fig 3b) whereas it was negative for antibody against epithelial membrane antigen (Fig 3c).

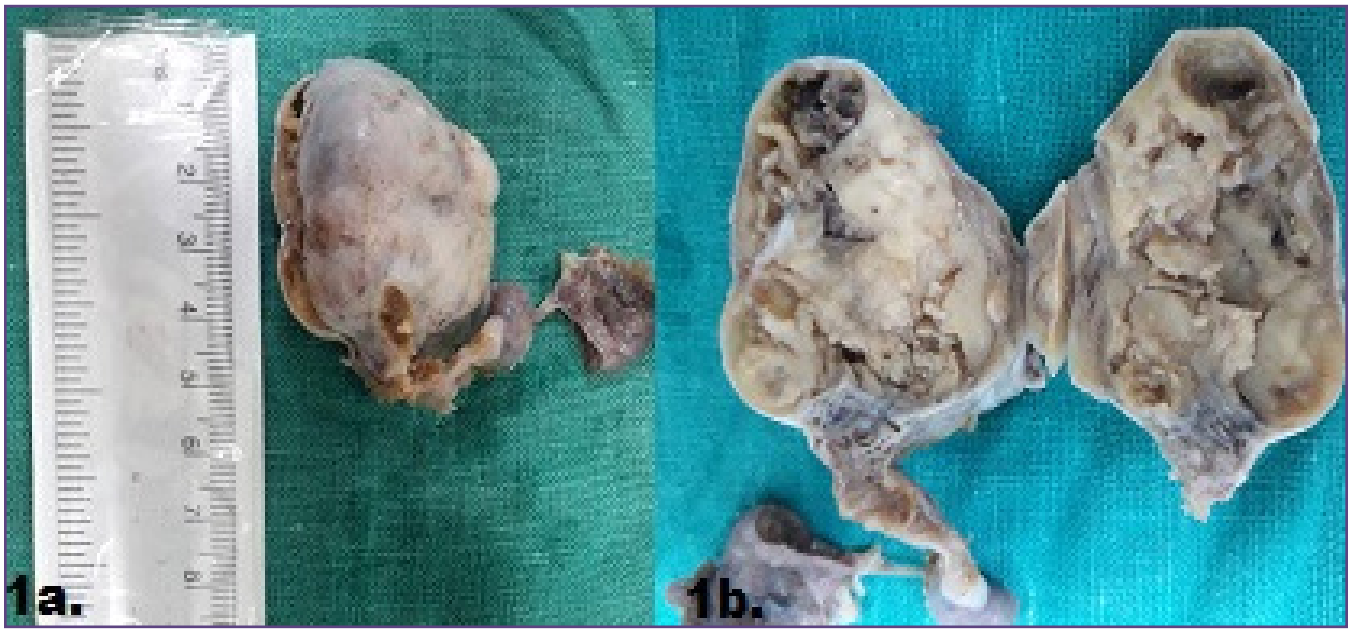

Fig. 1: Gross left ovary (a)Outer surface is smooth. (b). Cut surface showed a cyst measuring 1.5cm in diameter.

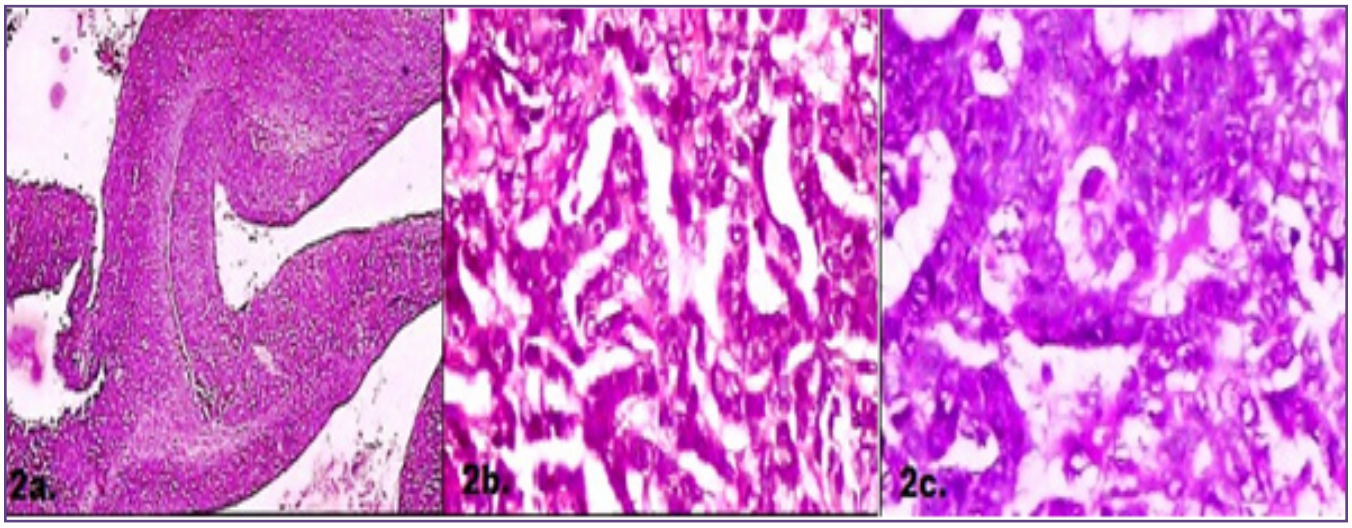

Fig. 2: (a)The cyst wall is lined by granulosa tumor cells (H:E X 10). (b). Tumor cells are arranged in follicular and acinar patterns (H:E X 40).(c). Call-Exner bodies and coffee bean nucleiare present (H:E X80).

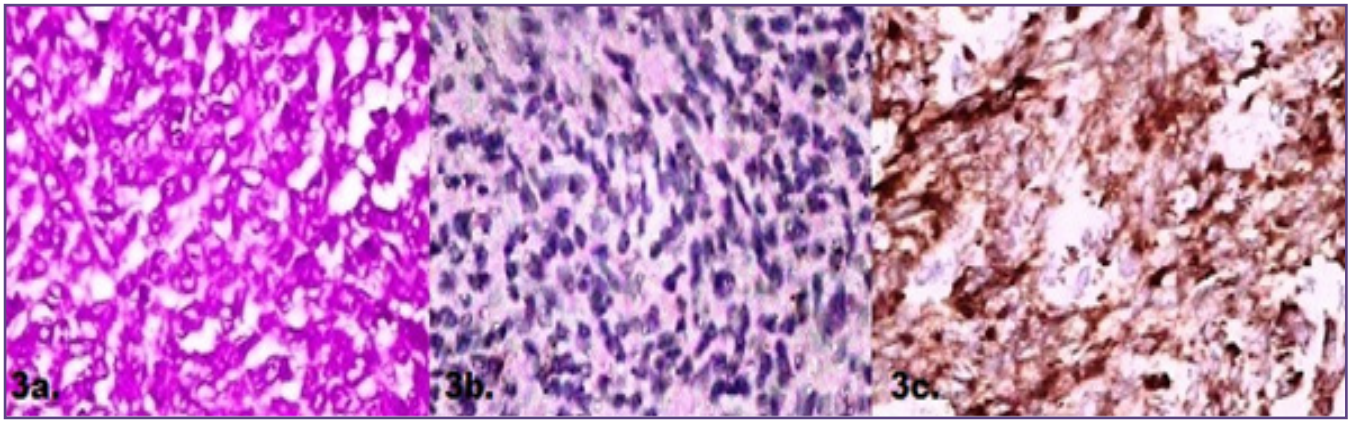

Fig. 3: (a) Diffuse pattern of granulosa cell tumor (H:E X40). (b). Epithelial membrane antigen (EMA X40) negative. (c). Inhibin positive (IH X40).

Discussion

Granulosa cell tumor of ovary was described by Rokintansky in 1855.[4] These are frequently unilateral, bilateral occurrence is reported in less than 5 % of tumors. Hormone production is frequent and approximately 25% to 50% of GCTs are associated with endometrial hyperplasia and 5% to 13% with endometrial carcinoma. Patients may present as dysfunctional uterine bleeding (DUB) as happened in the present case.[5,6] Presence of coexisting benign cystic hyperplasia of the endometrium, fibroid and adenomyosis in this case also substantiates the functional dependence of these pathological changes in the uterus on estrogen as mentioned in the literature.[7]

Imaging findings in adult GCT vary widely and range from solid masses, tumors with varying degree of hemorrhagic or fibrotic changes, to multilocular cystic lesions separated by thin septa and even up to completely cystic tumors. [8] These radiological features were well supported in the present case on histopathological examination i.e. the ovarian tumor was partly solid and partly cystic and also the part of ovary was intact.

Grossly GCT varies from solid, soft or firm to predominantly cystic and sometimes even may resemble mucinous cystadenoma.[8] Majority of these tumors are of substantial size (more than 8 cm) at the time of presentation, averaging 11.9 cm in the Norris series [9], 9.3 cm in the Chua series [10], in contrast to 5 cm only involving a part of the ovary in the present case. It was missed on clinic-radiological examination, but the diagnosis was established on histopathological examination alone.

A variety of histological patterns, are described in the literature, which include micro-follicular, trabecular, solid, tubular, diffuse and water silk type. The preset case too presented varied histomorphological features i.e. diffuse, cystic, tubular, micro-follicular with classical Call-Exner bodies and coffee bean appearance of the nuclei. Differential diagnoses include undifferentiated carcinoma ovary, adenocarcinoma, cellular fibroma, cellular thecoma and carcinoid etc. Call-Exner bodies, nuclear grooving and coffee bean nuclei are pathognomonic diagnostic features of GCT. These diagnostic features were very well appreciable in our case.

Immunohistochemistry (IHC), GCT shows positivity for Inhibin and Calretinin; variable positivity with S100; negativity for epithelial markers such as Cytokeratin(CK) and Epithelial membrane antigen(EMA). Inhibin positivity and EMA negativity supported the diagnosis of Granulosa Cell Tumour in the present case.

Conclusion

Granulosa cell tumors of the ovary are rare ovarian neoplasms, and cystic granulosa cell tumor is still rare. It is a unique ovarian neoplasm with an indolent, albeit unpredictable presentation. If the tumor size is small it may be clinically missed, as happened in the present case. The tumor often secretes estrogens and the patient presents with the hormone-related symptoms. Diligent endometrial pathology has to be sorted to rule out endometrial carcinoma, which helps in its early detection, better management for patient's wellbeing.

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