Case Report

Adult Granulosa Cell Tumor: A Small Mass Producing Troublesome Morbidity To A Woman

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Abstract:

Granulosa cell tumors are sex-cord stromal tumor ofovary, a rare neoplasmaccounting for approximately 3-5% of all ovarian malignancies. Hormone producing tumor, a total of 95% of all GCTs are adult type and of large size. A majority of women present with abdominal mass and diagnosis made on histopathology. While small size symptoms producing Granulosa cell tumors are rare and it's a rare virilizing tumor of adolescents. Adult Granulosa cell tumor is a clinically and molecularly unique subtype of ovarian cancer. The present case study reports on a case of a small size Granulosa cell tumor producing postmenopausal bleeding in 56-year-old woman.

Key words: Adult Granulosa cell tumors, ovarian carcinoma, FOXL2 C134W mutation

INTRODUCTION:

Granulosa cell tumors (GCTs) are sex-cord stromal tumor of ovaryaccounting for approximately 3-5% of all ovarian malignancies with a relatively favorable prognosis. A total of 95% of all GCTs are adult typeand 5% are juvenile type. Majority of patients are diagnosed in stage I due to the enlarge size and irregular vaginal bleeding[1,2,3].

Granulosa cell tumorpredominantly produce estrogen and androgens and these hormones are responsible for patient's symptoms like irregular vaginal bleeding, postmenopausal bleeding and hirsiutism[4]. Viralization is the prominent feature of juvenile type of Granulosa cell tumors[5]. Adolescent girls become muscular, develop excessive and male pattern body hairs, breast atrophy, and irregular vaginal bleeding. Surgical management based on stage of tumor as well as age of the patient. Premenarchal and reproductive age women with early stage disease are often managed with unilateral salpingo-oophorectomy and appropriate surgical staging in an attempt to preserve fertility. In postmenopausal women and those who have completed child bearing, surgery consists of a total abdominal hysterectomy and bilateral salpingo-oophorectomy, along with standard surgical staging[1].

Case Report:

A 56-year-old female, Nulliparous, married for 14 years, Menopausal for 10 years, presented to Gynae OPD with history of Postmenopausal bleeding on & off for the last 2 years. There is no comorbid, on examination she is of average height and built. On examination: pulse 90b/m, BP, 130/90 mmHg, temperature -98ºF, R/R 12b/m, Chest was clear on auscultation, on abdominal examination abdomen was flabby, No mass palpable, fluid thrill and shifting dullness was negative, gut sounds were audible. On Speculum examination cervix was swollen, nebothian cysts present. On bimanual examination: N/S uterus, Fornixes. On Laboratory investigations, Blood group O +, Hb%- 13 g/dl, RBs 95mg%, HepBsAg – Negative, Anti HCV antibodies- Negative.

On Ultrasound uterus- A/V, N/S, endometrium thick 1.1cm, both ovaries were normal in size. One year back her endometrial sampling was done for the same complaint and histopathology report showed that focal complex hyperplasia with endometrial polyp. She has been prescribed multiple medications from many doctors but she got temporary relief. We have planned total abdominal hysterectomy and bilateral salpingo-oophorectomy for her. Work up has been completed; fitness for general anesthesia has been taken. After taking written informed consent her total abdominal hysterectomy and bilateral salpingo-oophorectomy done and sample contain uterus, both fallopian tubes and both ovaries. Patient remains stable after operation and recovery was speedy. Histopathology report showedcervix- chronic cervicitis, Endometrium- disordered proliferative with fixation artifacts, right ovary – unremarkable, left ovary- adult Granulosa cell tumor measuring 1.5 X 1.0 cm. On immunohistochemistry: Calretinin – positive, Inhibin- positive, Ki 67- Negative. As the whole tumor removed with surgery and there was no evidence of tumor spread beyond ovary so she is not a candidate for chemotherapy or radiotherapy.

DISCUSSION:

Granulosa cell tumors are divided into two histological subtypes, classified as adult- type and juvenile - type. The adult subtype representing 95% of all Granulosa cell tumors (GCTs), occur in perimenopausal or postmenopausal women, at a peak age frequency between50 and 55 years[1,2,3]. The symptoms of the tumor occur due to its hormone production: hyperestrogenism in 97-98% of the cases, and hyperandrogenism in 2-3% of the cases. Clinical manifestations of estrogen producing tumor are amenorrhea, dysfunctional

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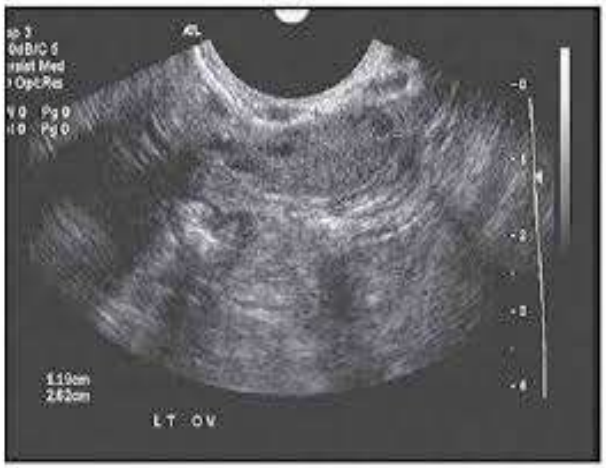
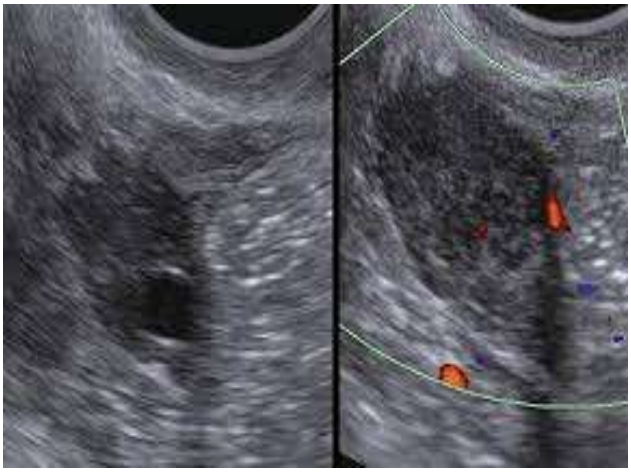


a) Normal size ovary with small cystic area measuring 1X1cm.



b) Doppler ultrasound of ovary showing active blood flow.

uterine bleeding, growth of uterine fibroids and hyperplasia of the endometrium or endometrial cancer. The symptoms and signs of rare virilizing GCTs are primary or secondary amenorrhea, hirsiutism, clitoris hypertrophy, deepening of the voice, muscular development and acne due to elevated testosterone levels[5]. GCts secrete gonadal peptides including Inhibin and Mullerian inhibiting substance (MIS) /anti-Mullerian hormone and synthesize estrogen[6]. Adult – type Granulosa cell tumors are molecularly characterized by a pethogenomic somatic point mutation402C->G(C134W) in the transcription factor FOXL2[7].

Diagnosisis based on laboratory and histopathological findings. Anti-Mullerian hormone and Inhibin-B are currently the most accurate circulating biomarkers[7].

Imunohistochemical data on estrogen and progesterone receptors in ovarian neoplasm is limited, with many reports suggesting that estrogen receptors alpha and progesterone receptor were frequently expressed in adult granulose cell tumors (66% and 98%, respectively) and Sertoli-Leydig cell tumors (79% and 86%, respectively)[8]. Microscopic features of Adult granulose cell tumor is mature follicles with Call-Exner bodies[3,9]. Adult granulosa cell tumor is most commonly detected in stage I, whereupon the prognosis is good. The disease however, recurs in one third of stage I patients and death in half of these[1,10]. Adjuvant chemotherapy, hormonal therapy, and radiotherapy were not associated with survival. Older age, more comorbidities, prior malignancy, higher stage, poor differentiation, larger tumor size, incomplete surgical staging and residual disease at a surgical margin were independently associated with increased hazard of death. Among women with stage I disease, each one centimeter increase in tumor size was associated with 4% increased hazard of death[11,12]. recurrent disease develops in up to 25% of patients, often after a long interval. Early recurring tumors had less Call –Exner bodies, higher mitotic rates and higher degrees of atypia[3,12].

CONCLUSION:

Every patient with postmenopausal bleeding should be investigating for Adult granulosa cell tumor as a small tumor can produce a troublesome morbidity to the patient. Majority of patients with granulosa cell tumors of the ovary present in early stage. Surgery is the primary treatment modality for granulosa cell tumors. Advance stage and presence of residual disease were associated with inferior survival, but only prospective studies can ascertain their definite role.

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