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JUVENILE GRANULOSA CELL OVARIAN TUMOR PRESENTING AS SECONDARY AMENORRHEA IN A ADOLESCENT GIRL : A RARE CASE REPORT

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ABSTRACT

Granulosa cell tumors are rare, functional sex cord-gonadal stromal tumors. There are two subtypes of granulosa cell tumor-the more common adult granulosa cell tumor and the rare subtype juvenile granulosa cell tumor. Juvenile granulosa cell tumors have varied clinical presentation due to hormone production by the tumor cells. A 15-year-old unmarried female presented with secondary amenorrhea, abdominal lump, and lower abdominal pain. There were no signs of hirsutism, and the pregnancy test was negative. Ultrasonography and computed tomography revealed a large left ovarian cyst. The patient underwent exploratory laparotomy, surgical staging, and left salpingo-oophorectomy. FIGO surgical stage of tumor was stage 1A. Histopathological examination revealed juvenile granulosa cell ovarian tumor. The patient resumed her menstrual cycle shortly after the surgery. Follow up was done with serum inhibin levels and intermittent imaging. Our index case had a purely cystic lesion and presenting with secondary amenorrhea, which are uncommon for this tumor. Juvenile granulosa cell tumor, when diagnosed at an early stage, carries an excellent prognosis. The clinical suspicion of granulosa cell tumor should be kept in mind whenever a child or young woman presents with signs and symptoms of hormonal excess along with a large unilateral adnexal mass. Significantly elevated serum estradiol levels, in the absence of pregnancy, are indicative of an estrogen-secreting tumor. Early diagnosis facilitates complete resection of tumor and preservation of female reproductive potential, which is a prime concern in this age group.

KEYWORDS

sex cord, salpingo-oophorectomy, adnexal mass, inhibin, estradiol

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INTRODUCTION

Granulosa cell tumors (GCTs) are rare functional sex cord-gonadal stromal tumors.1 They derived from sex cord-stromal cells, encompassing only 2% of all the ovarian tumors.2 They have an overall incidence varying from 0.4 to 1.7 cases per 100,000 women.3 They are sub classified based on clinical presentation and histology into juvenile granulosa cell tumor (JGCT) comprising 5% of GCTs and an adult subtype GCT found in perimenopausal women accounting for 95% of cases of GCT.[4]

The exact pathogenesis of juvenile granulosa cell tumors remains unknown, and several cellular & molecular alterations may be implicated in the development of this tumor. It is believed that they originate from early ovarian mesenchyme as they are composed of granulosa cells, theca cells, and fibroblasts in different degrees.

Granulosa cell tumors may have diverse clinical presentations attributed to hormone production; estrogen may cause precocious pseudopuberty in prepubertal girls while steroids lead to virilization.5 More serious effects of estrogen excess can occur in various end organs such as the uterus resulting in endometrial hyperplasia, endometrial adenocarcinomas, and increased risk of breast cancers.

Surgery is the prime modality of treatment, while chemotherapy is reserved for patients with advanced-stage or unresectable recurrent disease. Juvenile granulosa cell tumor, when diagnosed at an early stage, carries an excellent prognosis.6 Most tumors are sporadic in origin, unilateral, and FIGO stage 1 at the time of diagnosis. Syndromic associations are known. The prognosis ofpatient is directly related to the FIGO stage of tumor at the time of diagnosis.

We herewith report an interesting case of juvenile granulosa cell tumor in a young teenage girl.

CASE REPORT

A 15 years old unmarried female presented with amenorrhea, swelling, and pain lower abdomen.She had attained menarche at the age of 11 years,following which her menstrual cycle was regular (5 to 6 days menstruation, every 28 to 30 days), but the patient became amenorrhoeic for the past eight months. There was no history of sexual contact, contraceptive/drug use, headache, change in appetite, or weight gain. She also noticed a bulge over her lower abdomen one month back, which gradually increased in size. Pain over the lower abdomen was present for fifteen days, it was insidious in onset, continuous, dull aching, mild in intensity, non-radiating, no aggravating factor, no diurnal variation, relieved by intake of analgesics. There was no history of vomiting, loss of appetite, or loss of weight. Bladder and bowel habits were normal.

Secondary sexual characteristics were well developed. Clinical examination did not reveal any signs of hirsutism, acne, hypothyroidism, or hyperprolactinemia. On per abdomen examination, there was a mass of size 22 to 24 weeksarising from pelvis, non-tender, cystic in consistency with restricted mobility; lower border of mass could not be reached.

The urine pregnancy test was negative. Complete hemogram, liver and renal function tests were within the normal range. No derangement was seen in thyroid hormone and serum prolactin levels. Tumour markers were not elevated (CEA 1.4 ng/ml, CA-125 19.1 U/ml, beta hCG 0.1 mIU/ml). However, serum lactate dehydrogenase was slightly elevated (568 U/l).

Ultrasonography revealed a large pelvic cyst (? ovarian cyst) of size10.6x9.6 cm (Fig 1), extending to the abdomen with non-visualized left ovary, normal right ovary, and retroverted uterus. On CT scan, a well-defined cystic lesion measuring 13.5x13.7x10 cm was seen in the pelvis, which appeared to be arising from the left ovary, and the left ovary was not separately visualized. There was no evidence of internal calcifications or solid components in the cyst. The first possibility of the left ovary's serous cystadenoma was kept, and the patient was planned for laparotomy.

The patient underwent exploratory laparotomy with surgical staging, left salpingo-oophorectomy, and omental & peritoneal biopsy. On opening the abdomen, there was no free fluid in the abdomen; peritoneal washings were taken and send for cytology examination. There was a large left ovarian cyst of size 20x15 cm, with a smooth

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surface and no papillary excrescences(Fig 2). The right ovary, bilateral fallopian tubes, and uterus were grossly normal.There were no enlarged lymph nodes, metastatic deposits, or disseminated lesions in the intraperitoneal organs or omentum. Left salpingo-oophorectomy was performed without a breach in the capsule of tumor. Surgical staging of the tumor on laparotomy was FIGO(International Federation of Gynecology and Obstetrics) Stage 1A.

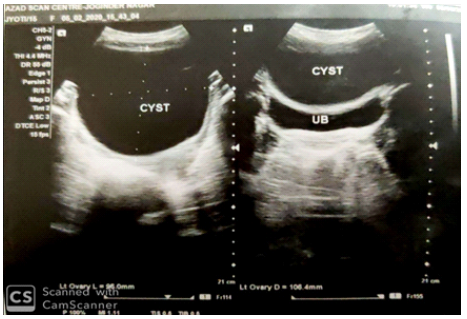

Figure 1:Ultrasonography revealed a completely anechoeic lesion suggestive of a purely cystic consistency. Note the absence of sepatae.

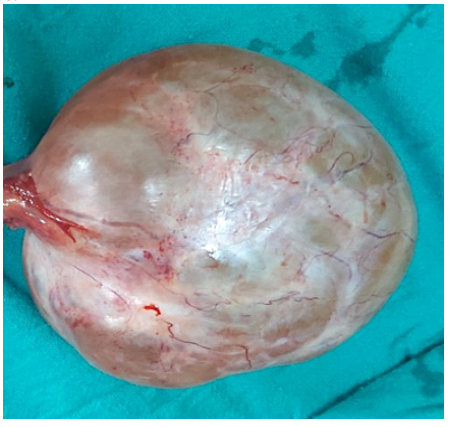

Figure 2: Gross salpingoopherectomy specimen showning left cystically enlarged ovary with smooth surface without any papillary excrescences

Cut section of the left ovarian cyst revealed a simple uniloculated cyst with hemorrhagic fluid. No solid areas were identified within the cyst. Cytology of peritoneal washing turned out to be negative for malignant cells. Histopathological examination of the ovarian cyst was showed features consistent with juvenile granulosa cell tumor (Fig 3A,B,C). The fallopian tube, peritoneum, and omental biopsy specimen were free from tumor invasion.

After receiving the histopathological report, follow-up of the patient was done with serial inhibin A levels (baseline postoperative value: 7.90 pg/ml) and intermittent imaging. At 3 month follow up her USG and Inhibin level were normal.

DISCUSSION

Granulosa cell tumors are estrogen secreting tumors that arise from granulosa cells. They are thought to be tumors of low malignant potential, mostly following a benign course, perhaps due to the early stage at diagnosis. Early diagnosis is attributed to the signs and symptoms of hormonal excess produced by the tumor. Juvenile granulosa cell tumors have a favorable prognosis if diagnosed at an early stage.[6]

Juvenile granulosa cell tumor usually occurs in prepubertal girls and females under the age of 30 years. Although the classical presentation of JGCT is precocious "pseudopuberty" and an abdominal mass7, there are many diverse reported signs and symptoms in literature, including virilization, massive ascites, primary amenorrhea, acute abdomen, Meigs syndrome, galactorrhea7, and secondary amenorrhea8. Limited data is available since it is a rare disease. Our index case presented with secondary amenorrhea and a palpable adnexal mass.

During the initial evaluation, estimation of serum estradiol levels, whichare uniformly elevated in JGCTs,7 was missed in our patient. Granulosa cell tumors generally present as solid masses with varying amounts of hemorrhage and necrosis responsible for the cystic components; purely cystic presentation, as seen in our patient, is quite rare.9 There were no radiological features suggestive of malignant ovarian masses including thick, irregular walls and septae, papillary projections, and solid, echogenic foci, in our index case.[10]

Surgical staging remains the mainstay of diagnosis. The overall goal of surgery is to evaluate the extent of disease, completely resect the tumor, and spare all uninvolved reproductive organs if feasible. The preservation of reproductive potential is a high priority.

Ultimately histological confirmation supplements the surgical staging of the tumor. Typical histologic findings include immature nuclei, absent nuclear grooves, and absent Call Exner Bodies.4 Follicles have irregular size and shape. Neoplastic cells have ample eosinophilic cytoplasm, polymorphic nuclei, and mitotic figures.

The majority of the patients at the time of diagnosis are at FIGO surgical stage 1A, requiring only salpingo-oophorectomy as treatment and regular follow up. JGCT diagnosed at this stage carries an excellent prognosis in most cases. Adjuvant chemotherapy with a cisplatin-based regimen is warranted if the tumor is FIGO stage Ic, II, III or has a high mitotic rate. Our index case was at stage 1A of ovarian tumor, and following salpingo-oophorectomy, her symptoms were resolved, and the normal menstrual cycle was restored.

Most granulosa cell tumors secrete inhibin, which has been used as a granulosa cell-specific tumor marker11; it has a role in patients' follow-up. Ultrasonography is also used for the follow up of patients. Recurrence of the tumor is rare but may occur during the first three years after diagnosis. It is less likely in Stage I JGCTs after surgery, though late recurrences can occur even in stage I patients, necessitating long-term follow-up.When tumor reoccurrence occurs, it tends to have a lethal outcome[5].

CONCLUSION

Juvenile cell granuloma may be an unusual cause of secondary amenorrhea in adolescents once traditional causes have been eliminated. Recognition of the diverse signs and symptoms of abnormal hormone production in children and young women presenting with an adnexal mass and consideration of juvenile granulosa cell tumors in the differential diagnosis can allow for early identification, timely surgical intervention, and excellent prognosis with preservation of reproductive potential for the patient.

CONFLICT OF INTEREST

Authors has no conflict of interest to declare

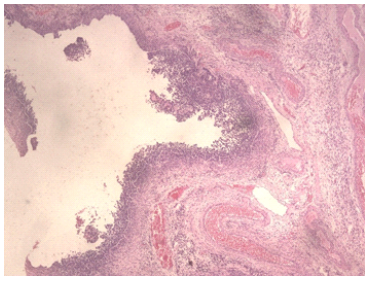

Figure 3A Micrograph of JGCT in 5x magnification: A cyst lined by tumor cells is seen.

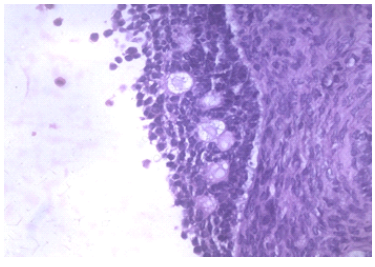

Figure 3B
Micrograph of JGCT in40x magnification:Granulosa cells are

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present in sheets; the tumor cells have rounded, hyperchromatic nuclei.

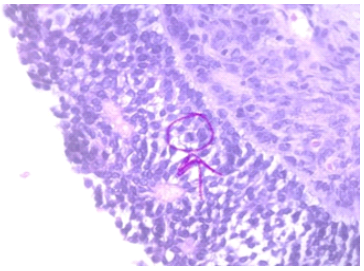

Figure 3C Micrograph of JGCT 40x magnification: Granulosa cells with a mitotic figure.

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