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JUVENILE GRANULOSA CELL TUMOUR IN A SEVEN YEAR OLD GIRL PRESENTING AS PRECOCIOUS PUBERTY

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ABSTRACT

Granulose cell tumours (GCTs) are a group of gynecological malignancy that occurs rarely, especially in children. Isosexual precocious puberty in prepubertal girls has several etiologies. Juvenile granulose cell tumour (JGCT) is one of the rarest causes that only accounts for 1% of all ovarian cancers. We report a 7 year old girl with abdominal pain as well as isosexual precocity, who presented as premature thelarche and vaginal bleeding. Abdominal ultrasound revealed a mass in the right adnexa. Tumour markers were within normal range. She underwent an exploratory laparotomy for tumour resection and right salpingo-oophorectomy. Histopathology reported a juvenile granulosa cell tumour of the ovary. Postoperatively, she experienced a cessation of vaginal bleeding and regression of breast enlargement. She has since been followed up for one year with serial ultrasound scans confirming that early stage disease has good prognosis.

KEYWORDS: Granulosa Cell Tumor, Juvenile, Precocious Puberty, Sex Cord Stromal Tumor

INTRODUCTION

Ovarian JGCT is a rare sex cord-stromal tumour [1]. It accounts for only 4-5% of ovarian tumours of children [2]. Scully (1977) described distinctive histological features of these granulosa cell tumours occurring predominantly in the young age group and adopted the term Juvenile Granulosa Cell Tumours(JGCT) in contrast to the conventional granulosa cell tumours of adulthood [3]. A similar incidence has been reported for this group of tumour throughout the world [4]. There are a group of cells in juvenile granulosa cell tumours (JGCT) with ability to secret steroid hormones, similar to the steroid hormone-secreting cells [5]. Clinically, these patients typically present with signs of hyperestrogenism—precocious puberty due to excessive estrogen production. Common symptoms include abdominal swelling, abdominal pain, abnormal uterine bleeding, appearance of acne, breast enlargement and occasional facial, axillary and or pubic hair appearance [4, 6]. Juvenile granulosa cell tumour, a subtype of ovarian stromal cell tumours, has a favourable prognosis if diagnosed at early stage. Recurrences are uncommon and typically occur within the first year [7]. The prognosis of the JGCT is excellent after salpingo-oophorectomy in patients who have only ovarian involvement [8]. Other modalities of treatment, however, range from surgical removal of the tumour to chemotherapy, radiotherapy and hormonal treatments [4, 9]. There are limited data

on these other therapies as most cases are cured with surgery alone and probably the rarity of these tumours may be responsible for the paucity of reports on other therapies.

CASE REPORT

A 7 year old girl who presented with recurrent abdominal pain with abdominal swelling of 3 weeks duration and bleeding per vaginam of 2 weeks duration. Complaints dated back to 3 weeks prior to presentation when patient started experiencing abdominal pain located in the suprapubic region and subsequently involved the lower abdominal quadrant. Pain was of sudden onset, colicky in nature, non-radiating with no known aggravating factor but fairly relieved with analgesia. Mother also noticed the presence of an abdominal mass around the umbilicus which was firm and painful when touched.

Two weeks before presentation, patient started bleeding per vaginam which was bright red, scanty and continuous which warranted use of sanitary pad but no associated passage of blood clots. She had no prior history of bleeding disorders, or bleeding from other orifices, trauma, abnormal vaginal discharge, or sexual assault. However, patient's complaints were preceded by breasts enlargement and presence of pubic hair for about 6 months.

Examination revealed bilateral breast enlargement (Tanner's Stage 3) [Figure 1]. No galactorrhoea or peripheral lymphadenopathy. The abdomen was distended with palpable abdominopelvic mass occupying the right lower abdominal quadrants, tender, firm and smooth. There was ascites demonstrable by shifting dullness. Vaginal examination revealed pubic hair (Tanner's Stage 3) [Figure 2]. There was blood smear on the vulva but no active bleeding at presentation.

A clinical assessment of most likely juvenile ovarian tumour to rule out malignant component was made. Abdominopelvic scan revealed a fairly rounded heterogeneous mass with some cystic component in the right adnexa measuring 9.6cm X 8.1cm. There was ascites. The liver, spleen and both kidneys were normal. Chest radiography showed no abnormality. Assay for β-HCG, AFP and CA-125 were within normal. Inhibin could not be done.

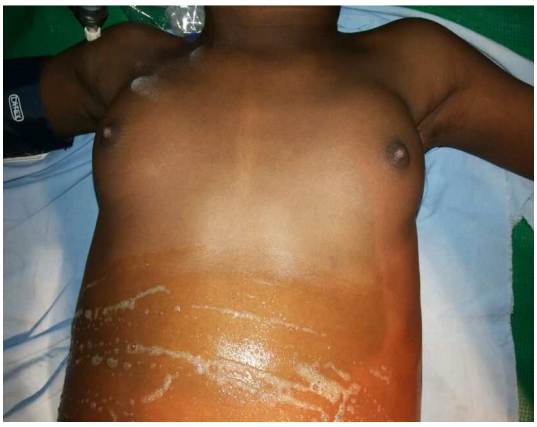

Figure 1: Showing Bilateral Breast Enlargement

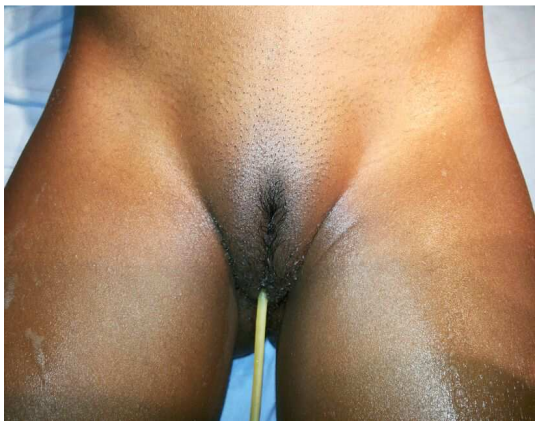

Figure 2: Presence of Pubic Hair Which was Shaved Just Before Surgery (Urethral Catheter In-Situ on the Operation Table)

She underwent an exploratory laparotomy for tumour resection and right salpingo-oophorectomy. There was massive ascitic fluid about 1.5litre and a solid right ovarian tumour about 16cm X 10cm X 12cm in dimension. The right tube was grossly enlarged, oedematous and densely adhered to the right ovarian mass [Figure 3]. The left tube and ovary

appeared normal. The uterus was normal for age. The hepatic, diaphragmatic, omental, bowel surfaces as well as pelvic side walls were examined and free of metastasis grossly.

Histopathology confirmed the diagnosis of juvenile granulosa cell tumour without malignant potential. She had since been followed up in clinic over one year with remission of breast enlargement [Figure 4], no further bleeding per vaginam and no re-growth of pubic hair. Abdominopelvic scan revealed normal left adnexa and uterus.

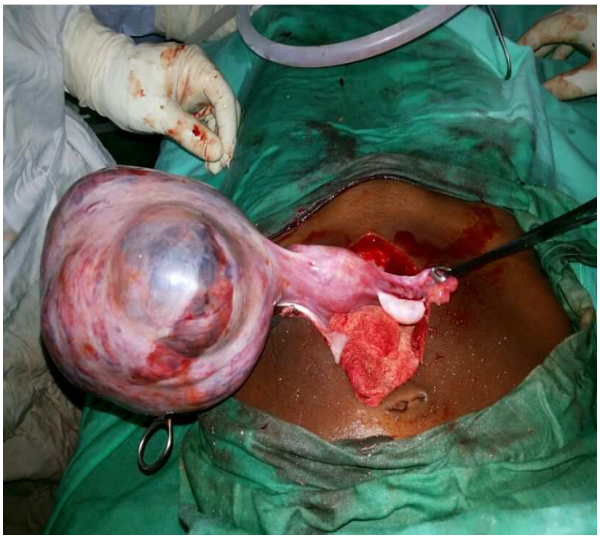

Figure 3: During Surgery, Showing the Huge Ovarian Mass, Normal Uterus and Left Appendages

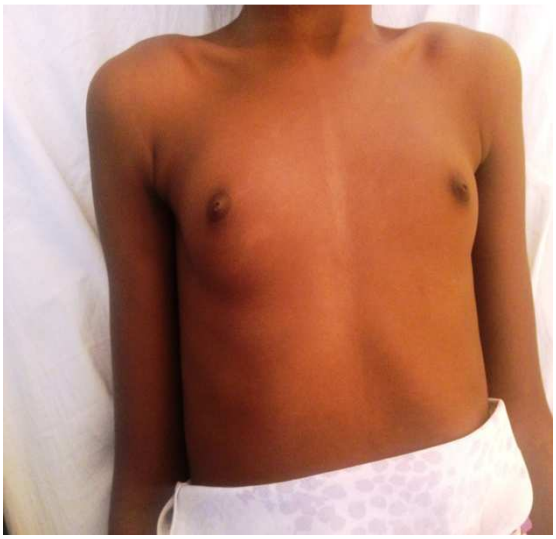

Figure 4: Breast Regression During Follow-Up Clinic

DISCUSSION

Malignant ovarian tumours are rare in children [2] and represent only 1% of all paediatric malignant tumours [3]. Most of these are germ cell tumours [4, 5]. Granulosa cell tumours (GCT) are divided into juvenile GCT and adult GCT based on clinical presentation and histology. Less than 5% of all ovarian GCTs occur prepubertally [2, 3, 6]. In 70–90% of cases, GCTs in the young female present with isosexual precocity [3, 7, 8]. Compared to juvenile GCT, only 1% of all cases of sexual precocity in prepubertal girls are due to granulosa-theca cell tumours (GTCT), an even rarer entity due to the theca component [10].

Rapid onset of precocious puberty is indicative of an ovarian tumour [10]. Indeed, clinical suspicion, hormonal investigations, and imaging will result in correct diagnosis in most circumstances. Clinical manifestations of an ovarian GCT may also include abdominal swelling, pain, or a palpable mass. Juvenile GCT is usually large (averaging 12 cm) and in most cases is limited to one ovary at the time of diagnosis [4, 11, 12]. Ascites is present in 10% of patients [6, 10]. In the case presented, it is worthy of note that all these features were present and the presence of breast enlargement and bleeding par vaginam alongside a huge pelvic mass aided the suspicion of the diagnosis. In a retrospective review of 40 cases of ovarian juvenile granulosa cell tumors, Plantaz et al found the first signs and symptoms were abdominal pain (52%) and endocrine symptoms (48%) [13]. At diagnosis, 94% had abdominal signs such as increased abdominal girth and palpable tumour. Sixty-eight percent had endocrine signs of precocious puberty. All girls diagnosed on the basis of precocious puberty were FIGO stage 1A [13] and so also was the case presented.

The primary treatment of juvenile GCT and GTCT is surgical [2, 4, 5, 6, 8, 10, 12-15]. The extent of surgery must be carefully evaluated to preserve fertility and hormone function and unilateral oophorectomy is the first choice for treatment; there is no role for simple ovarian cystectomy [12, 13]. Staging should include peritoneal cytology, exploratory laparotomy, and unilateral salpingo-oophorectomy [12]. For more extensive disease, staging operation should include unilateral oophorectomy or salpingo-oophorectomy, total omentectomy, resection of any metastatic lesions from the peritoneal surfaces, pelvic and periaortic lymphadenectomy, and peritoneal cytology [12, 13, 16]. Bilateral ovarian involvement is uncommon in stage 1A tumors and wedge biopsy is not recommended if the contralateral ovary appears grossly normal [16]. Prognostic factors include the stage of the tumour, the size of the tumour, the degree of nuclear atypia, and mitotic activity [10]. Chemotherapy is not required in patients with stage 1A tumors [16], nor does it appear to be indicated for tumours that have been complicated by rupture [16]. Expert pathologic review is recommended to ensure the correct diagnosis of this rarely encountered neoplasm [11]. Treatment for more disseminated, metastatic, or recurrence of tumours that are Stage 1C or higher is more difficult. Optimal adjuvant treatment is not known [7, 10, 14]. Serum estradiol, CA-125, and inhibin may be used for follow-up postoperatively [10, 17].

Fortunately, prognosis and outcome for juvenile GCT and GTCT are good in most cases. It is a hormonally active tumour, thus diagnosis can be made quickly in early stage disease. In Cronje's tumor registry review, precocious puberty subsided and physiologic puberty occurred at the normal expected age in all cases after tumour removal [10]. The most favorable prognostic factor for juvenile GCT is early stage disease [15]. Most juvenile GCT recurrences occur in the first year after initial diagnosis, but may be as late as 4 years [18]. Recurrence is usually rapid, leading to death within 13 to 16 months. Close surveillance may be warranted for a longer duration [18].

There does not appear to be a consensus on appropriate postoperative assessments and follow-up in the literature. The follow-up of our patient consisted of clinical assessments (history/physical) and pelvic-abdominal imaging. She has been followed every 3 months for 1 year; she remains tumour free clinically or radiographically.

Juvenile granulosa cell tumour of the ovary is a very rare ovarian tumour and a rare cause of peripheral precocious puberty. The treatment of choice is surgery which is necessary for histological diagnosis, staging, and remission of clinical signs of precocious puberty. An excellent prognosis is possible in an early stage disease and our case presentation confirms the good prognosis and complete remission of clinical symptoms following surgery.

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REFERENCES

1. Wang Yi, Wang W, Xu C, Huang X, Zhong L, Kang X et al. Childhood ovarian juvenile granulose cell tumour: A retrospective study with three cases including clinical features, pathologic results and therapeutics. *J Paediatr Hematol Oncol. 2011; 3: 24 1- 5.*
2. *Mahin Hashemipour, Mohammad Hassan Moaddab, Masoud Nazem, Parvin Mahzouni, Mehdi Salek.* Granulosa cell tumor in a six-year-old girl presented as precocious puberty. JRMS 2010 Jul-Aug; 15(4): 240-242.

3. Scully RE. Sex cord-stromal tumours. In Pathology of the Female Genital Tract. A. Blaustin, Ed. 1977 New York, Springer-Verlag, 581-601.
4. Mava Y, Chinda JY, Alhaji MA, Nggada HA. Childhood ovarian juvenile granulosa cell tumour: a case report and review of literature. Niger J Paed 2012; 39 (4):199 –201.
5. Lack EE, Perez-Atayde AR, Murthy AS, et al. Granulosa theca cell tumors in premenarchal girls: a clinical and pathologic study of ten cases. Cancer. 1981; 48:1846-54.
6. Schumer ST, Cannistra SA. Granulosa cell tumor of the ovary. *J Clin Oncol.* 2003; 21:1180-1189.
7. Frausto SD, Geisler JP, Fletcher MS, Sood AK. Late recurrence of juvenile granulosa cell tumour of the ovary. *Am J Obstet Gynecol. 2004; 191 (1): 366 – 7.*
8. Merras-Salmio L, Vettenranta K, Mottonen M, Heikinheimo M. Ovarian granulosa cell tumors in childhood. Pediatr Hematol Oncol 2002; 19(3):145-56.
9. Kristin RR, William M. An unusual case of juvenile granulose cell tumour of the ovary. Radiol Case Reports 2009; 4: 178.
10. Cronjé HS, Niemand I, Bam RH, Woodruff JD. Granulosa and theca cell tumors in children: a report of 17 cases and literature review. Obstet Gynecol Surv. 1998; 53(4): 240-7.
11. Mohammed A, Malami SA, Calvin B, Abdullahi K. A histopathological study of ovarian neoplasms in children in a tertiary hospital of northern Nigeria. *Afr J Paediatr Surg 2010; 7 (2): 75-7. doi: 10.4103/0189-6725.62848.*
12. Pectasides D, Pectasides E, Psyrri A. Granulosa cell tumor of the ovary. Cancer Treat Rev. 2008; 34(1): 1-12.
13. Plantaz D, Flamant F, Vassal G, Chappuis JP, Baranzelli MC, Bouffet E, et al. Granulosa cell tumors of the ovary in children and adolescents. Multicenter retrospective study in 40 patients aged 7 months to 22 years. Arch Fr Pediatr. 1992; 49: 793-798.
14. Young RH, Dickersin GR, Scully RE. Juvenile granulosa cell tumor of the ovary. A clinicopathological analysis of 125 cases. Am J Surg Pathol. 1984; 8 (8): 575-596.
15. Kdous M, Hachicha R, Gamoudi A. Early isosexual precocious pseudopuberty revealing a juvenile granulosa cell tumor in a six-year-old girl. Gynecol Obstet Fertil. 2004; 32: 311-314.
16. Powell JL, Otis CN. Management of advanced juvenile granulosa cell tumor of the ovary. Gynecol Oncol. 1997; 64: 282-284.
17. Boggess JF, Soules MR, Goff BA, Greer BE, Cain JM, Tamin HK. Serum inhibin and disease status in women with ovarian granulosa cell tumors. Gynecol Oncol. 1997; 64: 64-9.
18. Frausto SD, Geisler JP, Fletcher MS, Sood AK. Late recurrence of juvenile granulosa cell tumor of the ovary. Am J Obstet Gynecol. 2004; 191(1):366-7.