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Case of Early Pubertal Development in A 3-Year-Old Girl: Considering Rare Peripheral Causes

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Abstract:
Ovarian sex cord-stromal tumors, particularly Sertoli-Leydig cell tumor (SLCT), are uncommon, especially in pediatric populations. A typical presentation of these tumors includes precocious pseudopuberty, characterized by hormonal changes.
This type of tumor poses a significant challenge for clinicians in terms of diagnosis and treatment.We describe the case of a 03-year-old girl who was admitted to our clinic for investigation and management of premature breast development and pubic hair growth over a two-month period, with the presence of an abdominal mass on clinical examination. Biological, radiological and histological examinations were in favour of SLCT.
Although idiopathic causes account for the majority of precocious puberty cases in girls, significant etiologies such as ovarian tumors, including SLCT, should be considered. Early recognition and accurate diagnosis are crucial for appropriate management and improved outcomes. The prognosis of Sertoli-Leydig cell tumors is excellent for well-differentiated forms diagnosed early but more guarded for advanced or poorly differentiated cases, which may require additional therapies.

Keywords: Precocious puberty, Pediatric ovarian tumor, Hormone-secreting tumor, Abdominal mass, Early diagnosis

Introduction:

Precocious puberty, defined as the onset of pubertal development at an abnormally early age, represents a significant deviation from typical developmental timelines. This condition is characterized by the premature activation of the hypothalamic-pituitary-gonadal (HPG) axis, leading to the early appearance of secondary sexual characteristics. In girls, precocious puberty is typically diagnosed when these changes occur before the age of 8, and in boys before the age of 9.
The etiologies are variable and may be central or peripheral. Ovarian tumors, though relatively rare (accounting for only 0.2% of all ovarian tumors in child), can be a significant cause. Particularly notable are stromal tumors of the sex cords, such as granulosa and Sertoli cell tumors. These tumors secrete estrogen and steroids, which can induce early signs of puberty in girls. Early diagnosis and management of these tumors are crucial for improving prognosis, especially regarding potential long-term effects on adult size and the child's psychological well-being.

Case report

A 3-year-old girl with no significant medical history was referred to our clinic for evaluation and management of a breast enlargement and pubic hair development, which had been progressively evolving over the past 2 months. Clinical examination revealed no signs of pituitary tumor syndrome with no headaches, visual disturbances, growth abnormalities, cranial nerve deficits, or symptoms of increased intracranial pressure. Her height was 104 cm (+2.5 SD) and weight 16 kg (+1 SD). Her BMI was calculated at 14.8 kg/m², which, based on the IOTF curves for her age, places her in the normal weight category.

On genital examination, she exhibited Tanner stage 3 breast development and pubic hair growth. Abdominal palpation revealed generalized tenderness, along with a large, firm, painless mass fixed to both the deep and superficial planes of the pelvis, measuring approximately 13 × 12 cm. The remainder of the physical examination was unremarkable.

Her serum laboratory findings were consistent with peripheral precocious puberty: estradiol: 81,99 pmol/L; testosterone: 3,1 ng/ ml FSH: less than 0.51 mIU/L; LH: less than 0.08 mIU/L; alpha-fetoprotein:1,12 ng/ml.

The abdominal ultrasound showed a well-defined, hypoechoic, vascular mass measuring 11cm, supra uterine and supra vesical more developed on the right side presumably ovarian.

An MRI of the abdomen and pelvis was performed to further characterize the mass, revealing a large right ovarian supra vesical mass, initially suggestive of a dysgerminoma, measuring 11,8*57*107 cm. The staging workup showed no evidence of metastatic spread to other sites.

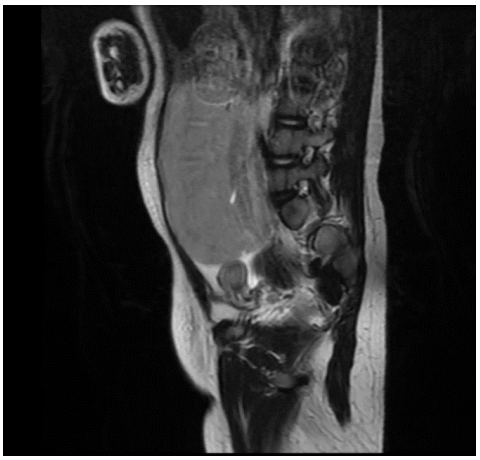

Figure 3: The coronal view of an abdominal MRI

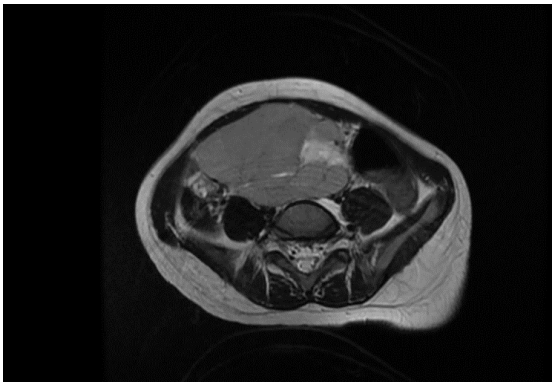

Figure 2: The axial view of an abdominal MRI

The diagnosis of precocious puberty secondary to an ovarian tumor was established based on clinico-biological and radiological findings. Following a multidisciplinary discussion involving a pediatric endocrinologist, pediatric surgeon, and pediatric oncologist, The child underwent laparotomy for tumor resection and a right ovarectomy with preservation of the ipsilateral fallopian tube was performed. Histopathological analysis identified a Sertoli-Leydig cell tumor (SLCT), exhibiting a combination of Sertoli and Leydig cells within a well-vascularized stromal background. Immunohistochemistry confirmed the diagnosis with positive staining for inhibin, calretinin, and smooth muscle actin

The patient subsequently received adjuvant chemotherapy following the TGM 95 protocol, completing two treatment cycles. One month after, follow-up evaluations showed no progression in stature, regression of secondary sexual characteristics, and normalization of the hormonal profile, with estradiol levels <5 pg/ml and total testosterone <0.05 ng/dl. Pelvic MRI confirmed the absence of any pelvic masses.

Discussion:

This case report highlights a rare and complex presentation of rapidly progressive precocious puberty attributed to a Sertoli-Leydig cell tumor (SLCT), an exceedingly rare entity in children. The incidence of SLCTs is estimated at approximately 2.6 cases per year per 100,000 girls, with malignant ovarian tumors accounting for only about 1% of all childhood cancers. **[1-2**)

The few reported cases in the literature indicate that SLCTs often initially present with secondary sexual characteristics that progress rapidly, suggestive of peripheral precocious puberty (PPP). **[3-4-5)**

Rapid progression, coupled with elevated hormone levels and the early onset of menstruation, is indicative of excessive ovarian stimulation by autonomous estrogen secretion, although this phenomenon remains uncommon in SLCTs. **[6**]

SLCTs are a rare subset of ovarian stromal tumors in children and must be considered in the differential diagnosis of PPP. These tumors are more commonly androgen-producing but may also cause hyperestrogenism due to their capacity for mixed hormonal secretion. **[7**]

In our case, histopathological analysis confirmed the diagnosis of SLCT, supported by typical morphological features and positive immunohistochemical markers such as inhibin, calretinin, and smooth muscle actin. These findings underscore the importance of such markers in differentiating hormone-producing ovarian tumors. **[8**]

Management required a multidisciplinary approach to achieve curative treatment while preserving future fertility. Unilateral oophorectomy successfully removed the tumor, with preservation of the homolateral fallopian tube, aligning with current recommendations for low-grade tumors **[9].** Adjuvant chemotherapy, following the TGM 95 protocol, was initiated due to the patient's young age and the need to address any residual risk, despite the tumor’s low-grade classification and absence of capsular invasion.

Post-treatment outcomes were favorable, demonstrating regression of secondary sexual characteristics, normalization of hormonal levels, and no evidence of residual masses on imaging. Nonetheless, this case highlights the critical importance of prolonged follow-up, given the potential for recurrence or late progression of SLCT, even in low-grade forms. Continuous hormonal monitoring, routine imaging, and targeted clinical evaluations are essential for identifying potential complications or recurrences. [**10-11**].

In conclusion, this observation underscores the importance of clinical vigilance in cases of early puberty, especially those with rapid progression and suggestive ovarian abnormalities on imaging. Optimal management relies on close collaboration between pediatric, endocrinological, surgical, and oncological teams, tailored to the unique needs of each patient.

Conclusion:

This case highlights the importance of considering peripheral precocious puberty as a potential clinical manifestation of an ovarian tumor in young children. Sertoli-Leydig cell tumors, though rare, should be included in the differential diagnosis when a girl presents with signs of virilization and early puberty. Early diagnosis and appropriate surgical intervention can lead to favorable outcomes, with excellent long-term prognosis in the absence of metastasis or malignancy.

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