Estrogen Production by Sertoli cell tumor in unusual case of Testicular feminization syndrome

Shahab Noorian , MD*,Fatemeh Agamahdi MD*,Sorour Aligani MD,**

1.Department of Pediatrics Endocrinology and Metabolisms Emam Ali Hospital ,karaj, Iran.

2.APCP Founder of Dr,Alijani pathology laboratory

Case presentation

A 5-year-old patient was brought by her parents to our pediatric endocrinology Outpatient clinic with history of progressive bilateral breast budding and enlargement since 3 months ago. . Her previous medical history were uneventful; there was no family history of precocious puberty. Parents were married, nonconsanguineous, she has 1 other sibling who is well . At presentation, our patient was a well looking girl, She had a full female phenotype : On initial physical examination the breasts were abnormally developed compatible with Tanner stage III . The gynecological exam reveals normal external female genitalia, the vagina and hymen were seen, but Pubic hair was not. Clinically her weight was 24 kg (90 percentiles on CDC growth charts), her height was 124 cm (95th percentile on CDC growth charts), there was no advanced bone age in X Ray.

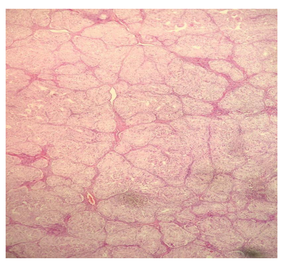
Excepting elevated estrogen levels other hematological and biochemical profiles including thyroid function test were normal. The levels of gonadotropins were measured and found (FSH 3.18 mIU/mL, LH 0.8 mIU/mL), estradiol was 64 pg/ml.but initial ultrasonographic study of abdomen and pelvic ultrasonography showed no abnormality ,brain MRI was also normal .After getting all this investigation , we came to conclusion the patient may be suffered from constitutional precautious puberty.

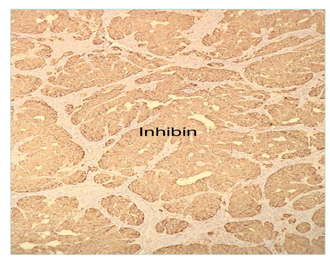
Despite this She was regularly monitored, after 3 months her breasts began to grow rapidly became as large as tanner stage of IV and she had 4 cm increasing in her height. Repeat of hormonal assay showed high levels of estradiol, 145pg/ml but tumor markers levels were normal, with a total BHCG of 0.1mlU/ml and an alpha-fetoprotein of 0.9IU /ml. At this time second thorough abdominal and pelvic ultrasonography workup revealed a round solid hypo echo and vascular structure mass measuring about 26.23mm in her left pelvic cavity . Surprisingly The pelvic MRI also detected , the lack of uterus and ovaries and short blind- end vagina, with oval shape structure measuring about 10 .6mm in right side of pelvic cavity. For this reason The blood sample was sent to the molecular karyotyping laboratory for detection of chromosomal abnormality. This test confirmed the suspected diagnosis of - testicular feminization syndrome 46XY. Our patient underwent an explorative laparotomy 3 months after her initial presentation to our clinic and a solid tumor localized to her left side of pelvic cavity was identified. After resection of tumor, Gross examination showed the well-circumscribed yellow- pale mass measured about 2 × 2.5 cm in diameter. The mass was capsulated and congested blood vessels were seen at the outer surface of tumor. Following surgery Sample sent for pathologist, histopathological report confirmed the diagnosis of a Sertoli cell tumor composed of proliferated variable sized tubules lined by polygonal cells with small uniform nuclei and abundant cytoplasm with a mild atypical mitosis less than 5 per 10hpf , no necrosis microscopic criteria in favor of benign pattern .

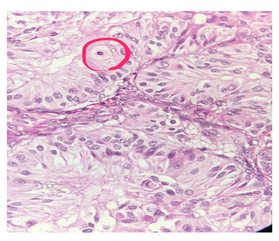
Immunohistochemical study of the tumor cells showed negative staining for EMA alpha-fetoprotein and positive staining for inhibin

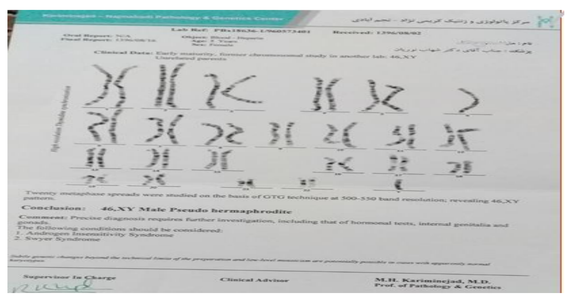
Our patient is well now without evidence of tumor recurrence or metastasis during six months of post-surgery follow-up. Levels of plasma estrogen rapidly returned to the normal prepubertal range and breast enlargement also. Since testicular estrogen and peripheral conversion of androgen to estrogen help to patient feminization, Our plan is follow her every three months and removal of other testes after puberty when feminization will be complete

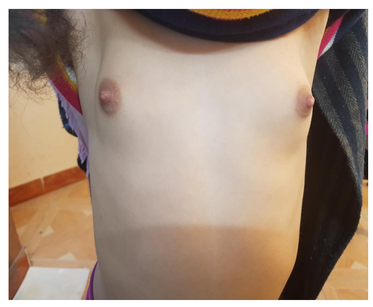
- *Immunohistochemical study of the tumor cells showed negative staining for EMA (alpha-fetoprotein)*
- *and positive staining for inhibin*

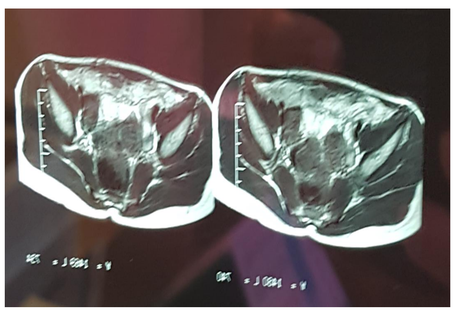


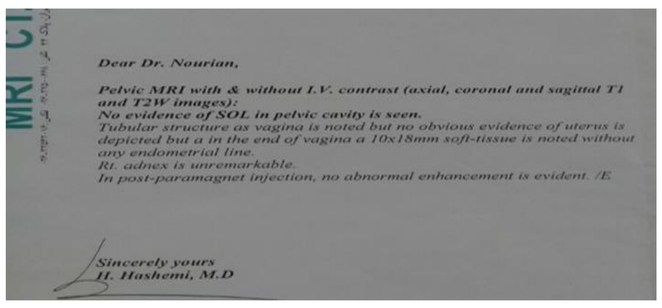












Discussion

a Children with testicular feminization have a genetic disorder that loss-of functional mutation in the androgen receptor gene, make them insensitive to androgens. This is the complete form of androgen insensitivity syndrome. Affected patient have female external genitalia, blind and short vagina, absent uterus and fallopian tubes, despite that they're born like normal girls at birth and is naturally socialized as female. These Patients have XY karyotype; the gonads are ectopic testis that usually found in abdomen, pelvis or the inguinal canal. Accurate diagnosis requires good clinical suspicious , carful hormonal profile , exact radiological investigation ,and finally karyotyping test that is the confirmative diagnostic tool for them. Many patients are diagnosed in early childhood, when the surgeon discovered testes in patients who are operated for reason of inguinal hernia , but if patient doesn't develop hernia ,syndrome is detected at puberty, when girl does not start to menstruation. But, we did not find a reported case of precautious puberty in patients with testicular feminization syndrome..

Our rare case presented with a typical picture suggestive of idiopathic CPP. But, the presence of an ovarian mass that was confirmed by computed tomography and low levels of FSH and LH pointed to an ovarian tumor as the sole cause of her precocious puberty. Her advanced bone age and accelerated height were seen because of tumor-derived estradiol. Advanced bone age, especially if it has progressed beyond the height age, serves as a nonspecific biomarker of abnormal sex steroid production

The endocrine effects of the such tumors are probably dependent upon the stromal components of these tumors . Tumors containing both Sertoli and Leydig cells have variable effects. Signs of androgen excess occur in about half of patients with Sertoli-Leydig cell tumors they have elevated blood testosterone levels [12], In addition, plasma androstenedione and, less commonly, dehydroepiandrosterone, are occasionally elevated [13. In Patients with Sertoli cell sex cord stromal tumors, estrogen production by the tumor can result in gynecomastia and may promote the female phenotype. Because The high levels of estrogen account observed in our child, we presume estrogen releasing from tumor , causing her breast development. Focal immunohistochemical positivity for inhibin confirmed the presence of the sex cord-stromal element.

Conclusions

Although in most of girls with precocious puberty, the etiology is idiopathic, Sertoli cell tumor with secretion of estrogen should be considered in the differential diagnosis for a prepubescent girl with an abdominal mass.

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Sex differentiation, gonads and gynaecology or sex endocrinology

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