A Case Report

Leydig Cell Tumour In Children; A Case Report And Literature Review

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ABSTRACT

Leydig cell tumours (LCTs) comprising of 1 to 3 per cent of testicular cancers in children, one of the single most common symptom in prepubertal patients is painless testicular swelling with or without a sign of precocious puberty. Other symptoms depend on age and the type of tumour. The tumour is usually asymptomatic if secretes androgens can cause precocious puberty in young children. If the tumour secretes estrogens, it can cause rarely gynecomastia in young boys. In adults, also this causes several problems including gynecomastia, sexual dysfunction, infertility, feminine hair distribution, gonadal atrophy, and reduced sex drive. Other causes of precocious puberty include central precocious puberty, hormone exposure from the environment; problems with adrenal gland such as adrenocortical carcinoma, and congenital adrenal hyperplasia (CAH) should be excluded in all cases. In the presence of a testicular mass, a Leydig cell tumour is the most likely diagnosis. Pathological studies, especially Immunohistochemistry (IHC), plays a great role in differentiating this tumour from other malignancies. Here we are reporting pure LCTs in a ten-year-old boy presented with gynecomastia.

Keywords: Gynecomastia, precocious puberty, testicular tumour

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1. Introduction

Leydig cell tumours (LCTs) are a member of the sex cord-stromal tumour group. It arises from Leydig cells and categorizes as one of the most common nongerm cell tumours (NGCTs) (1, 2). They presented at any age especially in children between 5 and 9 years with precocious pseudopuberty or gynecomastia, and men between 20 and 60 years (1, 2).

The main clinical presentation includes unilateral testicular mass in 90 %, Isosexual precocious pseudopuberty, a gynecomastia in 20 % and elevated levels of 17-ketosteroid (3).

Radical inguinal orchiectomy is considered as a classical treatment (4), but in young children with tumours tend to follow a benign course due to maintenance of fertility testis-sparing surgery by tumour enucleation suggested as the treatment of choice (5, 6).

2. Case presentation

The patient is a 10- year old boy who admitted to the out-patient clinic with the history of left painful scrotum since last month. Physical examination revealed a testicular asymmetry and trans-illumination test showed a dark shadow in the left testis and gynecomastia but no sign of precocious puberty (Fig 1).

Penis size was 2.5 cm, and with severe meatusstenosis, pubic and both axillary sites were hairless.

Figure 1.

First testicular Doppler ultrasound of the bilateral testis identified; left testis with 22*12 mm size containing a hypoechoic space-occupying lesion with the size of 8.7*8 mm with multiple calcifications, and right side of 19*11 mm. The volume of the left and right testicles were of 22 ml and 19 ml respectively. His height and weight were in the normal range of 50th percentage for sex and age. Laboratory evaluation for Teratomas tumour markers revealed alpha-fetoprotein (AFP) < 2.0 IU/mL with the references of < 7.25, and human chorionic gonadotropin (HCG) titration < 0.1 IU/mL with the references of up to 2.6 (ECL, Roche).

The patient was under observation for two weeks, then the second testicular colour Doppler ultrasonography (CDUS) of both testes showed right testis with 20*9 mm size with normal echogenicity and left testis with the size of 21*10 mm which is contained with a well-defined and hypoechoic mass with the size of 8.5*7 mm and has internal coarse areas of calcification. Which suggested a differential diagnosis of large cell calcifying Sertoli cell or Leydig cell tumour, Teratomas and revealed the normal size and echogenicity of both epididymis. No hydroceles in both scrotum and with the normal parenchymal vascularity. Hormonal assessment is shown in (Table 1) and all of them were in the normal range before the operation. After 2 weeks workup, a left-testis-sparing surgery was performed.

Initial histologic reports revealed a 1-centimetre mass compatible with Leydig cell tumour with foci...
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of calcification, neoplastic cells with eosinophilic cytoplasm and large cell calcifying Sertoli cell tumour in its deferential diagnosis but according to immunohistochemistry (IHC) stain, tumoural cells express inhibin, vimentin, calretinin and melan-A and negative for s100 and AFP and the final diagnosis of Leydig cell tumour was confirmed (Fig 2).

<table>
<thead>
<tr>
<th>Beta-hCG</th>
<th>&lt; 0.1 mIU/mL</th>
<th>up to 2.0</th>
</tr>
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<tbody>
<tr>
<td>ESTRADIOL (CLIA)</td>
<td>&lt;10 pg/mL</td>
<td>(1-10 years); boy&lt;10-27</td>
</tr>
<tr>
<td>FSH (CLIA)</td>
<td>0.9 mIU/mL</td>
<td>(6-10 years); 0.1-1.9</td>
</tr>
<tr>
<td>LH (CLIA)</td>
<td>0.1 mIU/mL</td>
<td>(6-10 years); 0.1-0.4</td>
</tr>
<tr>
<td>Free Testosterone (CLIA)</td>
<td>1.3 pg/mL</td>
<td>(&lt;11 years); 0.2-0.9</td>
</tr>
<tr>
<td>Testosterone (ECLIA)</td>
<td>0.040 μg/mL</td>
<td>(7-12 years); 0.03-0.68</td>
</tr>
<tr>
<td>DHEA Sulfate (CLIA)</td>
<td>242.4 μg/mL</td>
<td>(5-10 years); 24.4-209.7</td>
</tr>
<tr>
<td>Cortisol, Morning (CLIA)</td>
<td>11.7 μg/dL</td>
<td>(2-16 years); 3.0-21</td>
</tr>
<tr>
<td>ACTH (CLIA)</td>
<td>22.8 mg/mL</td>
<td>up to 46.0</td>
</tr>
<tr>
<td>17 OH Progesterone (CLIA)</td>
<td>1.60 mg/mL</td>
<td>0.32—1.97</td>
</tr>
<tr>
<td>TSH (CLIA)</td>
<td>3.1 mU/L</td>
<td>0.55-5.31 μU/L</td>
</tr>
</tbody>
</table>

3. Discussion

Leydig cells as interstitial cells that are found between seminiferous tubules (7). They are responsible for secondary sexual characteristics and maintenance of spermatogenesis with producing testosterone (8).

With the surgical pathology and IHC reports, post-operative abdominal and pelvic Computed tomography (CT) was performed, which identified negative retroperitoneal adenopathy and small and large bowel and urinary bladder were unremarkable. The hormonal evaluation was performed and shown in Table 1.

These tumours are the most common sex cord-stromal tumour but rare in children, they occur especially in boys aged 5 to 10 years (peak incidence around age 5 yrs) in 20 % and adult between the age of 20 to 60 (average 47 yrs) and account for 1 to 3% of all testicular tumours (9).
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Most of these tumours have benign behaviour during this period and are mostly characterized by the secretion of androgen and sometimes estrogen. (7) If it is secreting androgens, the tumour is usually asymptomatic but can cause precocious puberty in pre-pubertal boys. If the tumour secretes estrogens it can cause feminisation in young boys. In adults, this causes several problems including gynaecomastia, erectile dysfunction, infertility, genital atrophy, and a loss of libido. (10) There are not proven reports about malignancy transformation of these tumours in children whereas in up to 10% of cases of adults these tumours appear as become malignant variant. (11, 12) Due to high testosterone levels, most children present with signs of precocious puberty such as gynaecomastia (12).

Besides, our case was referred to the clinic with a palpable mass in left testicle and gynaecomastia. However, his hormonal assessment revealed normal levels of androgen, estradiol, and no evidence of other signs of precocious puberty, such as early development of axillary and pubic hair, penile growth, and accelerated musculoskeletal development, was not seen which could be inferred different presentation of pediatric age LTCs versus adult ones. In all patients with testicular mass and gynaecomastia other causes such as teratoma, Granulosa cell and Sertoli tumours should be considered (13).

Changes in tumour size (> 5 centimetres), tumour haemorrhage, and tumour necrosis may suggest malignant changes especially 5 to 10 per cent of prepubertal and adults between the ages of 30 and 60. (7) The common microscopic pathology is characterized by medium to large polygonal cells with round to oval nuclei and prominent nucleoli with rich eosinophilic cytoplasm separated by fibrovascular septa and resembling normal Leydig cells and in 30 to 40% of cases pale-staining, plump rod-shaped or rhomboid structures in the cytoplasm intranuclear structures (Reinke crystals) can be seen. (14, 15) Immunohistochemistry (IHC) stain shows positivity for Inhibin, calretinin, vimentin and Melan-A and negativity for S100, AFP and EMA and our IHC stain showed the cells of tumour positive for (inhibin, vimentin, calretinin and melan-A) but negative for S100 and AFP. (7, 16, 17) Testis-sparing as tumour enucleation seems to be a rationale for LCTs with benign behaviour (the mass is less than 2.5 cm and the tumour markers are normal before surgery) and negative intraoperative frozen section for malignancy is mandatory (5) and in children to keep the fertility can be the method of choice and observation is sufficient for this group in long term monitoring (18).

Radical inguinal orchidectomy is known as a classical treatment especially in malignant cases, and it can be accompanied by retroperitoneal lymphadenectomy (RPLND) in metastatic cases, these LCTs rarely responds to chemoradiotherapy (12, 19).

Due to the possibility of Tumor recurrence in the malignant group during the first two years after surgery, so patient monitoring at regular intervals needed. These monitoring should include precise clinical exam, check hormonal profile (luteinizing hormone [LH], follicle-stimulating hormone [FSH], testosterone, estrogen, and estradiol), tumour markers (beta-HCG, LDH, AFP) and follow up imaging (chest and abdominal computed tomography scan) at 4 months during the first year, followed by similar imaging two-yearly during the second year and yearly examinations thereafter. (20)

Metastases most frequently occur in the retroperitoneal lymph nodes, liver (45%), lung (40%) and bone (25%) (21).

4. Conclusion

Due to the extremely variable clinical presentation tumour especially children and the importance of maintaining the fertility in this group and increased incidence of malignancy, especially in Adolescence early detection and timely treatment is crucial, a testicular ultrasound should be done as an extension of the physical exam for any children with Painless swelling, sudden hydrocele or any symptoms related to the scrotum of the unknown cause even in the absence of signs of precocious puberty and referred all these patients to a pediatric urologist for further work-up.

5. Author contributions

Conception and design: KH Atqiaee
Acquisition of data: SH Salehpour
Analysis and interpretation of data: A Mohammadi
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6. Acknowledgement

Special thanks to Department of Pediatric Surgery, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.

7. Conflict of interest

The authors have indicated they have no potential conflicts of interest to disclose.

8. Funding

No external funding.

9. Ethics approval and consent to participate

Consent was obtained by Participant Parent in this study.

10. Abbreviations

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<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>ECLIA</td>
<td>Electrochemiluminescence immunoassay analyzer</td>
</tr>
<tr>
<td>CLIA</td>
<td>Chemiluminescence immunoassay</td>
</tr>
<tr>
<td>FSH</td>
<td>Follicle-stimulating Hormone</td>
</tr>
<tr>
<td>ECL</td>
<td>ElectroChemiluminescence</td>
</tr>
<tr>
<td>LH</td>
<td>Luteinizing hormone,</td>
</tr>
<tr>
<td>DHEA</td>
<td>Dehydroepiandrosterone,</td>
</tr>
<tr>
<td>ACTH</td>
<td>Adrenocorticotropic hormone</td>
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<tr>
<td>17-OH progesterone</td>
<td>17-hydroxyprogesterone,</td>
</tr>
<tr>
<td>TSH</td>
<td>Thyroid-stimulating hormone</td>
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<tr>
<td>mIU/mL</td>
<td>Milli-international units per milliliter,</td>
</tr>
<tr>
<td>pg/mL</td>
<td>Picogram/milliliter,</td>
</tr>
<tr>
<td>μg/mL</td>
<td>Microgram/mL</td>
</tr>
<tr>
<td>μg/dL</td>
<td>Microgram/deciliter,</td>
</tr>
<tr>
<td>mU/L</td>
<td>milliunits per litre</td>
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</tbody>
</table>

References


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HOW TO CITE THIS ARTICLE
url: http://transreurology.com/article_118043.html

Translational Research in Urology, 2(2): 35-40 spring 2020