Pediatric Leydig Cell Tumor: Biochemical Mimicry of Adrenal Disease and a Cause of Central Precocious Puberty

Tumor Pediátrico de Células de Leydig: Mimetismo Bioquímico de Doença Adrenal e Causa de Puberdade Precoce Central

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Palavras-chave: Criança; Neoplasias Testiculares; Puberdade Precoce; Tumor de Células de Leydig

To the Editor,

Leydig cell tumors (LCTs) are the most frequent hormonal testicular neoplasms in childhood, typically manifesting as peripheral precocious puberty (PPP) due to autonomous testosterone secretion.[1] Recent data indicate that pediatric testicular tumors are benign in 60% to 75% of cases, with teratomas and LCTs representing the most common benign histological types.[2]

A five-year-old boy presented with virilization (Tanner stage G3, P2) and advanced bone age of nine years. Total testosterone was 1.96 ng/mL [reference range (RR): 0.03 - 0.32 ng/mL], with suppressed LH and FSH at 0.30 mIU/mL (RR for LH: 1.7 - 8.6 mIU/mL; FSH: 1.5 - 12.4 mIU/mL). Unusually, 17-hydroxyprogesterone (17-OHP) was elevated at 10.2 ng/mL (RR: 0.59 - 3.44 ng/mL), raising suspicion for congenital adrenal hyperplasia (CAH). To rule out CAH and testicular adrenal rest tumors (TART), further investigation showed basal cortisol, electrolytes, and adrenocorticotropic hormone (ACTH) were normal. Adrenal ultrasonography showed no abnormalities. Furthermore, tumor markers, including serum lactate dehydrogenase (LDH: 224 U/L; RR: 120 - 3700 U/L), alpha-fetoprotein (AFP: 2.9 IU/mL; RR: 1 - 8 IU/mL), and beta-human chorionic gonadotropin (beta-hCG: < 0.2 mIU/mL; RR: < 1 mIU/mL), were negative. Although no palpable masses were detected, scrotal ultrasonography revealed a well-demarcated, solid, hypoechoic nodule confined to the right testis (16 × 13 mm). The left testis appeared normal, making TART highly unlikely. The patient underwent right radical orchiectomy, with histopathological confirmation of benign LCT.

Three months postoperatively, total testosterone (< 0.03 ng/mL) and 17-OHP (0.4 ng/mL) normalized. However, 10 months after surgery, the patient exhibited height velocity acceleration and new pubertal signs. Hormonal re-evaluation confirmed hypothalamic-pituitary-gonadal axis activation, with elevated LH of 2.18 mIU/mL, FSH of 2.70 mIU/mL, and rising total testosterone of 0.36 ng/mL. At this point, ACTH (13.6 ng/L), LDH (238 U/L), AFP (2.1 IU/mL), and beta-hCG (< 0.2 mIU/mL) remained stable, and thyroid function was normal (TSH: 0.92 mIU/L; Free T4: 13.4 pmol/L). Secondary central precocious puberty was diagnosed. Treatment with gonadotropin-releasing hormone analog (triptorelin) was initiated with a favorable clinical response.

This case illustrates two critical challenges. First, 17-OHP secretion by LCTs, although rare, can mimic an adrenal condition due to intratumoral enzymatic defects.[3] Therefore, performing a testicular ultrasound is mandatory in the investigation of PPP.[4] Second, prolonged exposure to sex steroids can “prime” the gonadotropin-releasing hormone pulse generator, subsequently leading to activation of the hypothalamic–pituitary–gonadal axis.[5] In conclusion, Leydig cell tumors are rare entities that pose significant diagnostic challenges and require strict long-term monitoring after surgical treatment due to a high risk of subsequent central precocious puberty.

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Table 1 – Hormonal parameters at diagnosis and follow-up.

Parameter	Value at diagnosis	Post-op 3 months	Post-op 10 months	Reference range
FSH (mIU/mL)	0.30	1.3	2.70	1.5 – 12.4
LH (mIU/mL)	0.30	1.4	2.18	1.7 – 8.6
Total testosterone (ng/mL)	1.96	< 0.03	0.36	0.03 – 0.32
DHEA-S (µg/dL)	50.9	29.4	70.9	2.8 – 85.2
17-OHP (ng/mL)	10.2	0.4	0.4	0.59 – 3.44
ACTH (ng/L)	22	20	13.6	< 63.3
Serum LDH (U/L)	224	-	238	120 – 3700
Serum AFP (IU/mL)	2.9	-	2.1	1 – 8
Serum Beta-hCG (mIU/mL)	< 0.2	-	< 0.2	< 1
TSH (mIU/L)	0.84	-	0.92	0.27 – 4.2
Free T4 (pmol/L)	17.8	-	13.4	7.4 – 28.2

FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; DHEA-S: Dehydroepiandrosterone sulfate; 17-OHP: 17-hydroxyprogesterone; ACTH: Adrenocorticotropic hormone; LDH: Lactate dehydrogenase; AFP: Alpha-fetoprotein; Beta-hCG: Beta subunit of human chorionic gonadotropin; TSH: Thyroid-stimulating hormone; T4: Thyroxine. Post-op: Post-operative. The symbol “-” indicates that the parameter was not assessed during this evaluation.

AUTHOR CONTRIBUTIONS

MID: Study conception and design, data acquisition, analysis and interpretation, writing and critical review of the manuscript.

RSP, AMS: Data acquisition and interpretation, critical review of the manuscript.

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All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PARENTAL CONSENT

Obtained.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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