

Case Report

Leydig Cell Testicular Tumour Presenting as Isosexual Precocious Pseudopuberty in a 5 Year-old Boy with No Palpable Testicular Mass

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Abstract. Leydig cell testicular tumors are very rare in children and cause isosexual precocious puberty. Palpable testicular mass or asymmetric testes are common findings on routine examination. We report on a 5-yr-old boy with a Leydig cell tumor of the testis presented with isosexual precocious puberty but no scrotal palpable mass. To our knowledge, this is the first reported Leydig cell tumor in a boy without palpable scrotal mass.

Key words: Leydig-cell tumor, testicular, precocious puberty, neoplasm, testis

Introduction

Stromal testis tumors are infrequent in children. There are no large series reported in the literature (1, 2). Leydig cell tumors are universally benign during childhood. The majority of patients present between 5 and 10 yr of age, most commonly with precocious puberty (3). Androgenization signs include prominent external genitalia, frequent erections, pubic and axillary hair, early growth spurt and deepening of the voice (4). An elevated testosterone level

with low or normal serum gonadotropin, FSH (follicle-stimulating hormone) and LH (luteinizing hormone), levels is consistent with Leydig cell tumor. Ultrasonography is necessary for diagnosis because it is sometimes difficult to detect on physical examination (5). Leydig cell tumors should be treated by simple orchidectomy. Testis-sparing excision is a reasonable consideration when the volume of normal testicular tissue surrounding the mass is acceptable or the lesion is bilateral (6). To our knowledge, this is the first reported case of Leydig cell testicular tumor presenting with isosexual precocious puberty in a 5-yr-old boy with no palpable testicular mass on routine physical examination.

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Case Report

A 5-yr-old boy was presented for pediatric evaluation of painful and frequent erections that had been present for over six months. The parents noticed a penis enlargement and recent growth spurt with deepening of the voice (Fig. 1). An exhaustive clinical examination revealed prominent external genitalia with no pubic hair but continuous painful erections. No palpable testicular anomaly was diagnosed during physical examination. The testes volume on palpation was approximately 4 ml for the right testicle and 3.5 ml for the left testicle. Blood samples were subjected to laboratory tests, including measurement of the levels of FSH, LH and testosterone hormones. At presentation, the levels of testosterone and D-4 Androstenedione were 6.79 ngr/ml and 10 ngr/ml, respectively. The levels of FSH and LH were normal (0.8 U/ml and 0.2 U/ml respectively). Scrotal ultrasound examination showed a well-delimited intraparenchymal right testicular mass. The lesion was hyperechogenic, homogeneous and poorly vascularized (Fig. 2).

Following referral to the Paediatric Surgical Team, the patient underwent right radical inguinal orchidectomy. The postoperative levels of testosterone and D-4 androstenedione were 0.13 ngr/ml and 0.3 ngr/ml respectively (both in normal range in prepuberal boys).

Pathologic examination of the right testis revealed a well-circumscribed encapsulated solid nodule of 2.5 × 1.7 × 0.8 cm in size embedded within the testicle (Fig. 3). The epididymis and albuginea were not involved. The cut surface was homogeneously mahogany brown. Microscopically, the tumor had a diffuse and solid pattern of growth. The tumor's mass consisted of medium and large well-defined cells with abundant and deeply eosinophilic cytoplasm, which was vacuolated at the peripheral zones. The scant stroma of the tumor contained a rich vascular net. In this particular case, Reinke's crystalloids were not found. Immunohistochemically, vimentin,



Fig. 1 The 5-yr-old patient showing a prominent external genitalia and no palpable testicular mass.

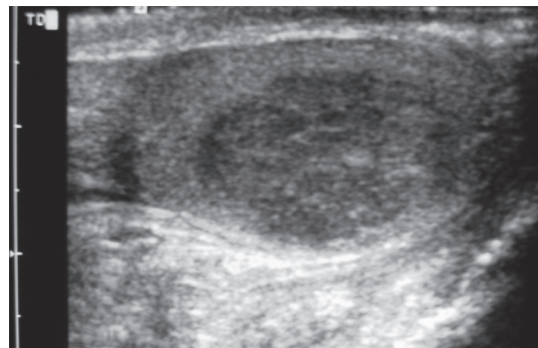


Fig. 2 Sonographic findings of the affected testicle: solid nodule 2.5 × 1.7 cm embedded within the testicle and no involvement of the tunica albuginea and epididymis.

Melan A (Mart-1) and inhibin were expressed in the cytoplasm of the tumor's cells (Fig. 4). The index of proliferation (MIB 1) was moderate.

The clinical course and follow up after surgery were uneventful, and he was discharged

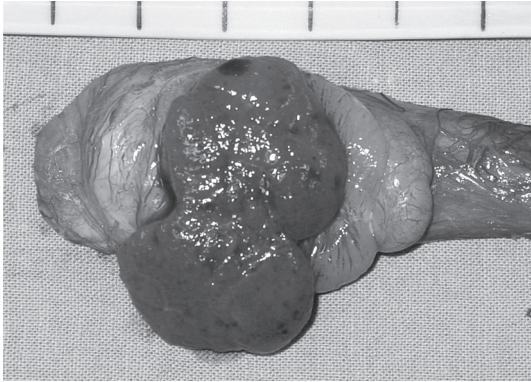


Fig. 3 Macroscopic appearance of the tumour (dark brown in color, $2.5 \times 1.7 \times 0.8$ cm in size) showing minimal testicular tissue surrounding the well-circumscribed mass.

home 48 h later. At two years after operation, his growth is satisfactory, with normal values of testosterone and normal results of left scrotal ultrasound.

Discussion

Testicular tumors account for only 1% of all pediatric solid tumours with an incidence of 0.5 to 2/100,000 individuals (2). Leydig cell tumors in children are far more uncommon, comprising only 5% of all primary testis tumors in prepubertal males (4, 5). Testosterone-secreting Leydig cell testicular adenomas represent 1–3% of all testicular tumors. The majority of these tumors have been observed in men aged 30–60 yr, and less than 25% have been reported in prepubertal boys (6, 7). Bilateral Leydig cell tumor has been

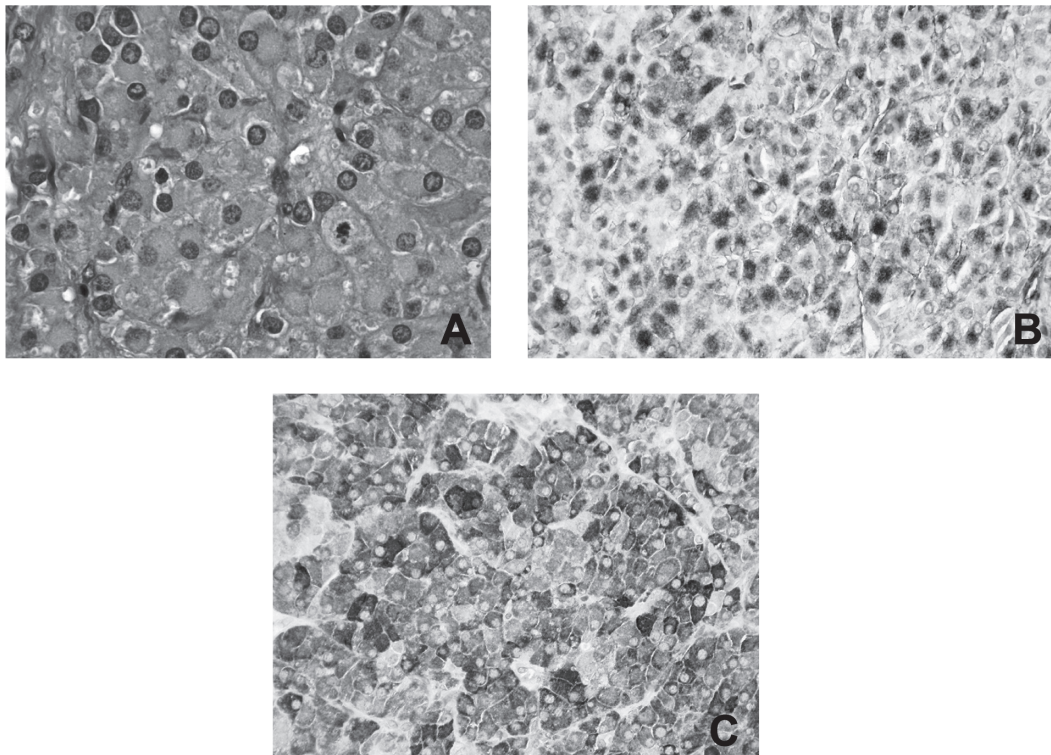


Fig. 4 (A) Microscopic characteristics of Leydig cell tumor of the testis showing a granular acidophilic cytoplasm, prominent nucleolus and rare mitosis (HE $\times 40$). (B) Positive immunohistochemical findings with vimentin. (C) The cytoplasm of the tumor cells is strongly reactive to inhibin.

reported in only 3–10% of cases (1). Almost all of these boys present with isosexual precocious pseudopuberty associated with increased testosterone, low gonadotropin levels and testicular palpable mass (2).

Precocious pseudopuberty refers to development of secondary sex characteristics in the absence of hypothalamic-pituitary modulation due to abnormal production of sex hormones. Diverse sex steroid-producing entities could cause isosexual precocity. The clinical characteristics include rapidly somatic growth spurt, pubic and axillar hair, facial acne, painful erections, penis enlargement and deep voice (7–9). With the exception of our case, all pediatric patients reported in the available literature presented with a palpable testicular mass on clinical examination.

Ultrasound examination of Leydig cell tumors typically reveals a solid hyperechogenic mass that is well differentiated with respect to the surrounding parenchyma. Testosterone has a plasma life of less than 30 min, and postoperative levels are expected to be normal, as in our particular case.

Molecular abnormalities such as activity mutations of the LH receptor (a G protein-coupled receptor) could cause gonadotropin-independent male limited precocious puberty characterized by autonomous hyperplasia and hyperfunction of Leydig cells. These somatic mutations have recently been described in three pediatric cases of Leydig cell testicular tumors (10).

Microscopically these tumors are characterized by a diffuse and solid pattern of growth with large polygonal cells containing eosinophilic cytoplasm. One third of the cases show the typical Reinke's crystalloids of cytokeratin. Immunohistochemically, vimentin, Melan A and inhibin are expressed in the cytoplasm of the tumor cells. Proliferative index defined by MIB 1 expression is usually moderate (8, 9, 11).

Although Leydig cell tumors are usually benign, about 10% of the reported cases evolve

into a malignant neoplasm. The only certain criterion for malignancy is metastasis, and that is why follow-up must be prolonged (1, 12). The treatment for this type of lesion is radical orchidectomy by inguinal approach with clamping of the spermatic cord associated with lymphadenectomy when regional nodes are involved. Testis-preserving surgery for prepubertal cases of epidermoid cyst, teratomas and Leydig cell tumors has shown encouraging results at long-term follow-up and is becoming an attractive option. Actually, we feel, like others, that testis-sparing excision is a reasonable consideration when the volume of normal testicular tissue surrounding the mass is acceptable or the lesion is bilateral (2, 6, 12). Long-term follow-up is necessary in all cases after surgery, even after radical surgery.

Conclusion

In summary, we recommend a prompt scrotal ultrasound scan when precocious puberty is diagnosed, even in the absence of a palpable testicular mass. The recommended treatment is unilateral orchidectomy or testis-sparing surgery in selected cases.

References

1. Petkovic V, Salemi S, Vassella E, Karamitopoulou-Diamantis E, Meinhardt UJ, Fluck CE, *et al.* Variable clinical presentation, diagnostic features, follow-up and genetic analysis of four cases. *Horm Res* 2006;67:89–95.
2. Carmignani L, Salvioni R, Gadda F, Colecchia M, Gazzano G, Torelli T, *et al.* Long-term follow-up and clinical characteristics of testicular Leydig cell tumor: experience with 24 cases. *J Urol* 2006;176:2040–3.
3. Alonso FJ, Osorio VA. Leydig cell tumor presenting as precocious pseudopuberty in a 4-year-old boy. *Arch Esp Urol* 2004;57:426–8.
4. Criscuolo T, Sinisi AA, Perrone L, Graziani M, Bellastella A, Faggiano M. Isosexual precocious pseudopuberty secondary to a testosterone-

- secreting Leydig cell testicular tumour: true isosexual development early after surgery. *Andrologia* 1986;18:175–83.
5. Ilondo MM, van den Mooter F, Marchal G, Vereecken R, Wynants P, Lauweryns JM, *et al.* A boy with Leydig cell tumour and precocious puberty: ultrasonography as a diagnostic aid. *Eur J Pediatr* 1981;137:221–7.
 6. Metcalfe PD, Farivar-Mohseni H, Farhat W, McLorie G, Khoury A, Bagli DJ. Pediatric testicular tumors: contemporary incidence and efficacy of testicular preserving surgery. *J Urol* 2003;170:2412–5.
 7. Kaufman E, Akiya F, Foucar E, Grambort F, Cartwright KC. Viralization due to Leydig cell tumor diagnosis by magnetic resonance imaging. Case management report. *Clin Pediatr (Phila)* 1990;29:414–7.
 8. Kirsch AJ, Bastian W, Cohen HL, Glassberg KI. Precocious puberty in a child with unilateral Leydig cell tumor of the testis following orchiopexy. *J Urol* 1993;150:1483–5.
 9. Polepalle SK, Shabaik A, Alagiri M. Leydig cell tumor in a child with spermatocyte maturation and no pseudoprecocious puberty. *Urology* 2003;62:551–2.
 10. Liu G, Duranteau L, Carel JC, Monroe J, Doyle DA, Shenker A. Leydig-cell tumors caused by an activating mutation of the gene encoding the luteinizing hormone receptor. *N Engl J Med* 1999;341:1731–6.
 11. Canda AE, Atmaca AF, Ozdemir AT, Akbulut Z, Balbay MD. Testis sparing surgery for sequential bilateral testicular tumors. *Can J Urol* 2009;16:4677–81.
 12. Jou P, MacLennan GT. Leydig cell tumor of the testis. *J Urol* 2009;181:2299–300.