LETTER TO EDITOR (VIEWER'S CHOICE)

PSEUDOPRECOCIOUS PUBERTY IN A CHILD WITH A TESTICULAR TUMOR

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A nine year old boy presented with the appearance of secondary sexual characteristics since two years. He was 149 cms tall (SDS=2.3) and weighed 40 kg (SDS=1.4). On examination, he had a stocky and muscular built. On genital examination he had an adult Sexual Maturity Rating (SMR) and a right testicular firm, oval, well circumscribed, non tender mass measuring 4 cm x 5 cm. The left testis measured 3 ml. Family history of precocious puberty was negative. Endocrine evaluation revealed suppressed gonadotropins and elevated testosterone [Follicle stimulating hormone - 1.2 mIU /ml (1-7 mIU/m), Luteinizing hormone (LH)-1.6 mIU /mL (1.6-5.7 mIU/mL), testosterone - 10.3ng/mL (2.3-8.65 ng/mL)]. A Gonadotropin Releasing Hormone (GnRH) stimulation test confirmed gonadotropin independent precocious puberty. Clinical examination, hormonal analysis (17-hydroxyprogesterone and cortisol), and ultrasound examination of the adrenals showed no evidence of congenital adrenal hyperplasia. Tumour markers in form of lactate dehydrogenase, β-Human Chorionic Gonadotropin (HCG) and alpha-fetoprotein were normal. X-ray of the wrist and hand showed complete fusion of the epiphysis i.e. adult bone age. Bone scan was normal. Ultrasonography (US) of the scrotum showed the right testes enlarged with a heterogeneous solid mass (3cmx4.8cm) with multiple bright foci suggestive of a leydig cell tumour. Abdominal Computed Tomography (CT) was normal. Surgery was advised. A frozen section analysis (FSA) done intraoperatively was suggestive of a benign leydig cell tumour, hence a right sided radical inguinal orchidectomy was performed. Diagnosis was confirmed on histopathology. It composed of large, closely packed cells with eosinophilic cytoplasm, bland nuclei, and small nucleoli. Microscopic features of a malignant variant were absent. Patient has been asked to follow-up biannually.

Gonadotropin-independent sexual precocity in males represents a group of heterogeneous disorders including HCG- or androgen-producing tumors, McCune-Albright syndrome (MAS), congenital adrenal hyperplasia (CAH), and true familial male precocious puberty. (1-5) McCune-Albright syndrome was excluded due to the absence of cafe-au-lait lesions and a negative bone scan. CAH was ruled out as 17-hydroxyprogesterone (17-OHP) and cortisol were normal. In boys with familial male-limited gonadotropin-independent precocious puberty, family history is usually positive and signs of sexual development usually appear before the age of 4 years. As our patient had asymmetric enlargement of the testes with gonadotropin-independent sexual precocity, a leydig cell tumor was considered and confirmed on histopathology. Leydig cell tumour (LCT) is the most frequent interstitial neoplasms of the testis, accounting for 0.8-3% of all testicular tumors and 4-9% of tumors of the testis in prepubertal males.(6-8) Though they may be seen at any age, there are two major peaks; pre-pubertal boys and adult in their 30s-40s. The aetiology of this tumour is not comprehensively understood. However, the disruption of the hypothalamic-pituitary-testicular axis seems to lead to excessive stimulation of Leydig cells by increased LH production.(6) Thus, LCTs are often associated with an excess of sex steroid production, although clinical symptoms of endocrine disturbances are not always reported.(6) Classically, LCT clinically presents with testicular mass (90%), precocious puberty (10%) (sudden external genital growth, pubic hair growth, accelerated skeletal and muscle development, and mature masculine voice), pain and feminizing symptoms (gynecomastia, breast tenderness). Exceptionally, diagnosis is made by an incidental finding. (9) Endocrine evaluation and imaging methods are required to reach a diagnosis. Histopathology confirms the diagnosis. Histologically LCT is characterized by Reinke crystals or nuclear inclusions classically seen in adults and infrequently seen in the pediatric population. This finding is not necessary for diagnosis. (10) LCTs have a mild behavior, however in 10% of cases may presents with metastasis, particularly to the lymph node, lung and liver. Malignant tumors occur exclusively in adults and are unaccompanied by endocrine changes. The therapy of LCTs is surgical, and the standard therapy is orchidectomy. (11) There are data suggesting the possibility of treating these lesions through organ-sparing procedures (12-15), but more evidence is needed to support this approach as the standard therapy even for small lesions. The combination of symptoms at presentation, laboratory values and FSA can adequately inform the surgeon and determine the surgical management of patients with LCT. Observation is sufficient in patients in whom a benign Leydig cell tumor is treated with radical inguinal orchidectomy. Patients with malignant tumors require regular follow-up with imaging. The prognosis for benign Leydig cell tumors is excellent.

REFERENCES

1. Weinstein LS, Shenker A, Gefman PV, Merino MJ, Friedman E, Spiegel AM. Activating mutations of the stimulatory G protein in the McCune- Albright syndrome. N Engl J Med. 1991; 325: 1688-1695
2. Styne DM. New aspects in the diagnosis and treatment of pubertal disorders. Pediatr Clin North Am. 1997; 44: 505-529
3. Shenker A, Laue L, Kosugi S, Merendino Jr JJ, Minegishi

T, Curtler Jr GB. A constitutively activating mutation in the luteinizing hormone receptor in familial male limited precocious puberty. Nature. 1993; 365: 652-654
4. Kraaij R, Post M, Kremer H, Milgrom E, Epping W, Brunner HG, Grootegoed JA, Themmen AP. A missense mutation in the second transmembrane domain of the luteinizing hormone receptor causes familial male-limited precocious puberty. J Clin Endocrinol Metab. 1995; 80: 3168-3172
5. Laue L, Wu SM, Kudo M, Hsueh AJ, Cutler Jr GB, Jelly DH, Diamond FB, Chan WY. Heterogeneity of activating mutations of the human luteinizing hormone receptor in male-limited precocious puberty. Biochem Mol Med. 1996; 58: 192-198
6. Al-Agha OM, Axiotis CA. An in-depth look at Leydig cell tumor of the testis. Arch Pathol Lab Med. 2007; 131: 311-317
7. Kim I, Young RH, Scully RE. Leydig cell tumors of the testis. A clinicopathological analysis of 40 cases and review of the literature. Am J Surg Pathol. 1985; 9: 177-192
8. Henderson CG, Ahmed AA, Sesterhenn I, Belman AB, Rushton HG. Enucleation for prepubertal Leydig cell tumor. J Urol 2006; 176: 703-705
9. Hsi-Yang Wu, Mda, Howard M. Snyder, Md. Pedia¬tric Urologic Oncology: Bladder, Prostate, Testis. Urol Clin N Am. 2004; 31: 619-627
10. Ortiz DJ, Silva J, Garcia-Macias MC and Bulon YA. Leydig cell tumour of the testis: Cytological findings on fine needle aspiration. Cytopathol. 1999; 10: 216-218
11. Carmignani L, Salvioni R, Gadda F et al. Long-term followup and clinical characteristics of testicular Leydig cell tumor: experience with 24 cases. J Urol. 2006; 176: 2040-2043
12. Henderson CG, Ahmed AA, Sesterhenn I, Belman AB, Rushton HG. Enucleation for prepubertal Leydig cell tumor. J Urol. 2006; 176: 703-705
13. Wegner HE, Dieckmann KP, Herbst H, Andresen R, Miller K. Leydig cell tumor -comparison of results of radical and testis-sparing surgery in a single center. Urol Int. 1997; 59: 170-173
14. Carmignani L, Colombo R, Gadda F et al. Conservative surgical therapy for Leydig cell tumor. J Urol. 2007; 178: 507-511
15. Giannarini G, Mogorovich A, Menchini Fabris F et al. Long-term followup after elective testis sparing surgery for Leydig cell tumors: a single center experience. J Urol. 2007; 178: 872-876

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