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Precocious puberty and hypertension secondary to testicular tumor in a Nigerian boy: Case report.

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Abstract

Precocious puberty is an uncommon cosmopolitan disease, characterized by attainment of secondary sexual characteristics before the age norm for sex. Reports of precocious puberty with attendant hypertension are rare. Detection of the cause of hypertension and precocious puberty which can be central or peripheral is a prerequisite for institution of appropriate management.
The outcome of the time, resources and efforts expended in obtaining care for this condition is dependent on the knowledge and expertise of the health care provider. Other determinants of outcome include the understanding of the minor concerned, the parental skills and parental resources.
We present an 8 year old Nigerian boy with features of precocious puberty and hypertension. We highlight the not so desirable outcome and challenges associated with previous and current management of this patient. Hopefully, this report will increase awareness on this condition and improve management practices amongst health practitioners in similar settings.

Keywords: Precocious puberty, Hypertension, Testicular tumour, Diagnostic challenges.

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Introduction

Precocious puberty is an uncommon disease characterized with the attainment of features of puberty before the set age. A male child is said to have precocious puberty when there is physical and hormonal sign of puberty at an age more than 2.5 or 3 standard deviations earlier than the average or earlier than 9 years. The first clinical sign of puberty in boys is testicular enlargement (testicular volume greater than or equals to 4 mls, using orchidometer). Precocious puberty is estimated to occur in 1/5000 to 1/10,000 children and it is ten times less common in boys than in girls. Reports on precocious puberty amongst Nigerians are scanty [1-6].

About 25%-75% of boys with precocious puberty may have structural central nervous system abnormality [6]. The causes of precocious puberty are broadly categorized into two: central and peripheral causes. Example of causes of central precocious puberty include tumors (hypothalamic harmatoma, optic glioma, chiasma tumor), increased intracranial pressure (from previous damage/infection of the central nervous system) and idiopathic (>90% of cases). Peripheral precocious puberty can result from disorders of the gonads (tumors), or the adrenals (tumors or congenital adrenal hyperplasia).

The main pathophysiology for central precocious puberty (gonadotrophin-dependent precocious puberty) is early activation of the pulsatile gonadotrophin-releasing hormone secretion from the hypothalamus leading to activation of the hypothalamo-pituitary-gonadal axis and consequent development of secondary sexual characteristics in the affected children [2,6]. The effect of excessive sex hormones, secreted from abnormal gonads or adrenal gland, on target organs are responsible for the physical changes seen in peripheral precocious puberty, also known as gonadotrophin-independent precocious puberty.

The scarcity of publications on precocious puberty in the West African Sub-region and the need to sensitize general practitioners and paediatricians working in similar environment about the occurrence of this condition informed our desire to report this case. We also highlight the importance of proper investigations and its place in proper management.

Case Report

An 8 year old boy presented with 3 year history of left testicular pain and swelling, rapid body growth and growth of body hair. The complaint of pain and swelling of his left testicle was noted three years before presentation when patient was aged 5 years. There was associated rapid general body growth and growth of hair on the face, armpit and pubic area, in addition to the development of deepening of the voice and other body changes reminiscent of puberty. There was no associated history of recurrent headache, effortless vomiting, double vision, previous head injury or meningitis. There was no history of use of exogenous steroid. There was no family history of tumor or precocious puberty. The patient is the 3rd of three children in a monogamous family. His eldest sister who

was 16 years old attained menarche at 15 years of age while his immediate elder brother, aged 13 years, is yet to show any sign of secondary sexual development. He was delivered at full-term gestation by spontaneous vaginal delivery. There was no history of recurrent vomiting in the neonatal period. At the onset of the testicular pain and swelling when child was 5 years old, he was taken to a private hospital where an unnamed intramuscular injection was given without any respite and growth continued unabated with the two testes, penile shaft, and pubic/facial hair growing to adult size. This necessitated another visit to another hospital from where he was referred to our facility.

Essential finding at presentation showed a big for age boy with well-built muscles, facial and pubic hair, deep baritone voice, not pale, anicteric, not febrile, no significant peripheral lymph node enlargement and sexual maturity rating of Tanner stage 4.

Weight=45 kg (>95th percentile for age and gender)

Height=147 cm (>95th percentile for age and gender)

BMI=20.8 Kg/m^2 (between 75th and 85th percentile for age and gender)

Stretched penile length=16 cm (>3 Standard deviation for age; expected for age=6.3 ± 1.0 cm)

Testicular volume = >25 mls (longest diameter 6 cm on the R and 5.5 cm on the L)

The testes were hard in consistency, rough surface, and nodular with very little discomfort to pressure. There were no palpable intra-abdominal masses. He had a very high blood pressure of 160/130 mmHg (>99th percentile for age, gender, and height percentile) at presentation and was commenced on tablet Amlodipine 10 mg daily and the BP reduced to 130/100 4 days after and subsequently became normal on daily Amlodipine. He had a normal pulse rate of 84 beats per minute. The heart sounds were normal.

An initial assessment of precocious puberty secondary to testicular tumor was made and the following investigations were done.Hormonal profile showed greatly elevated testosterone, other hormones were within normal limit. Serum Electrolytes, Urea, Creatinine, B-hCG and Alpha fetoprotein were with normal limit (Table 1).

S/N	Investigation	Value	Reference range	Remark
1	Hormonal assay			
	LH	0.3	0.7-7.4 m/U/ml	Low
	FSH	0.4	1.0-14.0 m/U/ml	Low
	Prolactin	4.2	1.8-17 ng/ml	Normal
	Estradiol	39.4	4.0-94 ng/ml	Normal
	Testosterone	11.6	2.0-10 ng/ml	High
	Progesterone	0.01	0.13-1.22 ng/ml	Low
2	Tumour makers			
	hCG	1.1	0.1-5.7 mIU/ml	Normal
	AFP	7.3	<8.5 ng/ml	Normal
3	Electrolyte, Urea, Creatinine			
	Bicarbonate	23	20-30 mmol/L	Normal
	Chloride	98	90-110 mmol/L	Normal
	Sodium	133	120-140 mmol/L	Normal
	Potassium	3.3	3-5 mmol/L	Normal
	Urea	1.9	1.7-9.1 mmol/L	Normal
	Creatinine	63	60-120 umol/L	Normal

Table 1. Investigation results.

FNAC of the testes showed few unremarkable epithelial cells. Most smeared slides were acellular and had background of red blood cell. A diagnosis of acellular testicular mass was made. A unilateral testicular biopsy for definitive diagnosis was advised but parent refused to give consent to allow the patient undergo unilateral orchidectomy for histology despite extensive counseling. Patient was thereafter lost to follow up (Figure 1).

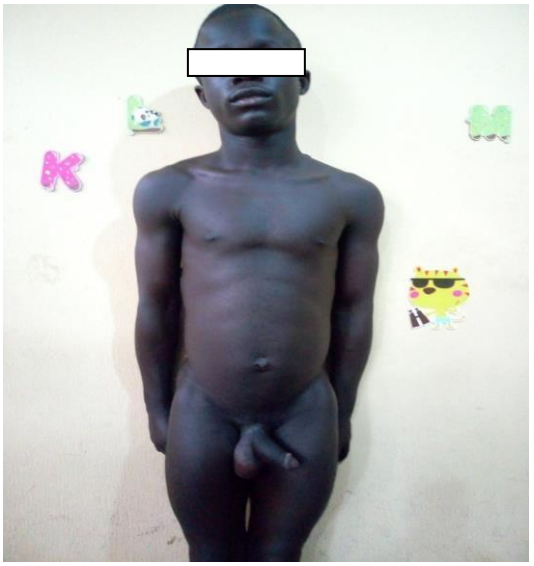

Figure 1. Bilateral testicular tumor in an 8 year old boy with tanner stage 4 sexual maturity rating.

X-ray of Left hand and wrist for bone age showed feature of advanced bone age compatible with 18 years. Chest X-ray shows normal cardiac size, cardio-thoraxic ratio is 14.5/16. Aortic arch is prominent? rotation. Despite normal cardiac size, there is suggestion of left atrial enlargement. Left upper lobe vessels engorgement, lung fields are clear. No pleural effusion. Bony thorax and overlying soft tissue are within normal limit.

Ultrasound of the testes showed both testes were enlarged, and heterogeneous with lobulated outline They show background nodularity and certain multiple isoechoicnodules (Right>Left) Right testis measures 4.74 cm × 2.56 cm × 2.75cm (Volume 20.68 mls) and the left testis measures 4.67 cm × 2.35 cm × 3.83cm (20.03 mls).

Doppler insonation reveals slightly increased vascularity of the mediastinum testis. However, there is no significant vascularity of the nodules. The epididymis of both testes is also thickened. The Pampiniform plexus are significantly dilated giving the classical 'bag of worm' appearance. Average vein diameter ranges from 2.7 mm–3.4 mm. No other intra-scrotal lesion. An impression of an enlarged nodular testis with varicocele was made. Although the cause of the varicocele was unknown. Abdominal Ultrasound scan was reported normal with no abnormality detected. Ethical clearance for the case report was obtained from the Research Ethics Committee of LAUTECH Teaching Hospital, Osogbo, Osun State with protocol number LTH/EC/2021/01/500.

Discussion

Testicular tumors occur in 0.5/100,000 to 2/100,000 children and adolescents [7]. Leydig cells tumors are the most common hormonal secreting testicular tumors; they are rare tumors, accounting for 1%-3% of all testicular tumors and they occur in 3%-5% of prepubertal boys, presenting mainly with clinical features of precocious puberty from 5 years of age [8-10]. Leydig cell tumors mostly affect one testis but bilateral testicular involvement occurs in 3%-10% of cases [11]. Malignancy is reported in 10% of cases, though Leydig cell tumor is usually considered a benign paediatric tumor. Surgical removal of the tumor is the main stay of management with resultant regression of pubertal signs in affected children [12]. This is the first case of testicular tumor in paediatric age group from our centre and it affected both testes with clinical evidence of testosterone secretion. There was no evidence of malignancy or metastasis though definitive histologic diagnosis was not available because parents refused to give consent. Fine needle aspiration cytology report was inconclusive. This case report is an example of some of the challenges encountered in many developing countries with the diagnosis and management of paediatric endocrine disorders which has also been previously discussed by some authors [3,13]. The level of awareness of the presentation and management of different types of paediatric endocrine disorder is still very low in our environment causing late presentation and rejection of medically recommended therapy.

Hypertension in precocious puberty secondary to testicular tumor could be from increased body mass of the affected children. Children with precocious puberty have been reported to have high blood pressure for age compared to normal children of same age because of greater body size for chronological age [14]. Physicians managing children with precocious puberty should carefully evaluate the blood pressure of such children for early diagnosis and management. Testosterone and its active metabolite, 5α-dihydrotestosterone, has also been shown to cause increased blood pressure through inflammatory activation, increased oxidative stress, increased vasoconstriction as well as changes in cardiovascular physiology like sympathetic activation, and insulin resistance [15,16]. Therefore, the very high testosterone in the index patient may also be contributory to the high blood pressure recorded in him. It is however worthy of note that hypertension has severally been reported as late effect of chemotherapy for testicular cancer [17].

The constraints in exhaustively investigating this child makes proper management a herculean task or almost impossible as only hypertension has been fairly managed. The precocious puberty is yet to be properly managed. Furthermore, fertility issues, quality of life from a poorly characterized and treated testicular tumour and therapy for the precocious puberty are yet to be fully addressed. This leaves so much to be desired for both the patient and the physicians in a resource constrained environment.

Conclusion

Testicular tumors, though rare in the paediatric age group, is an important cause of precocious puberty and it may be complicated with hypertension before or during treatment. Early diagnosis and treatment will go a long way in reducing the negative psychosocial impact on affected children. Adequate attention should also be paid to the management of hypertension where found.

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