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Central Precocious Puberty as a Complication of Congenital Adrenal Hyperplasia in a Boy: Case Report

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Abstract:

Precocious puberty has intense influence on physical and psychosocial well-being of affected children and raises a lot of concerns as well as uncertainties in family.Here,we report a case of Central precocious puberty (CPP)superimposed on peripheral precocious puberty (PPP) due to congenital adrenal hyperplasia(CAH).

Introduction :

Precocious puberty is defined by the development of secondary sexual characteristics before 8 years of age in girls and 9 years in boys.[1] A Danish epidemiologic study estimated that incidence of precocious puberty was less than 5 per 10000 boys[2] and a study of Korean population estimated the prevalence of CPP to be 1.7 per 100000 boys.[3] The prevalence of PPP in boys is not well documented. Data from two studies of Indian subcontinent reported that precocity is less observed in boys compared to girls and PPP was more common than CPP in boys (55% vs 35%).[4]

Precocious puberty classifies into two major categories based on the etiology - Central precocious puberty (GnRH dependent) and Peripheral precocious puberty (GnRH independent).

Central precocious puberty also called true precocious puberty, is caused by early activation of hypothalamic-pituitary-gonadal (HPG) axis, resulting in early but normal development, symmetric progression of secondary sexual characteristics, and increasing growth velocity. It is idiopathic in more than 80% cases and is more common in girls. Secondary causes of CPP include Central Nervous System (CNS) tumour (commonest tuber cinereum hamartoma), infection, congenital defect, radiation or injury.[5-7] Peripheral precocious puberty, also called pseudo-precocious puberty does not involve the HPG axis and is caused by release of sex steroid from adrenal, gonad or exogenous source or ectopic gonadotropin production from germ cell tumour. Peripheral precocious produce incomplete, atypically sequenced or rapid pubertal progression.[8,9]

Considerable limitations persist in optimally managing this condition as cultural and social issues, such as stigma and shame associated with early pubertal development responsible for not seeking early medical advice as well as less adherence to treatment.

Case presentation:

An 8year old boy, was brought by his parents due to their anxiety about the boy's continuing growth in phallic length along with erection since the age of one and half (1.5) year. There was also appearance of pubic hair at 2-3year of age and axillary hair after that. Parents also gave history of sudden height gain from 3rd year of age. For last 6-7 months, he had developed adult body odour and acne. He had no history of headache, visual problems, behavioral changes or neurological deficits, any head trauma or surgery. Family history and perinatal history was unremarkable. He was treated with oral medroxyprogesterone and hydrocortisone since his 3rd year of age by a registered physician and drug compliance was poor and was on irregular follow up.

Physical examinations revealed, weight was on 97th centile, height was 143cm above 97th centile,height SD score (SDS) + 2.7, mid parental height 164.6 cm, target height 156 cm to 173 cm and his predicted height lies above target height, BMI 18.8 Kg/m2 (on 90th centile). His stretched penile length was 8 cm, and testicular volume of 5 mL on the right and 6 mL on the left, pubic hair distribution matched with Tanner stage 4 and had sparse axillary hair (Tanner stage 2). There were no skin or bone lesions suggestive of McCune Albright syndrome. Systemic examinations were unremarkable.

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Fig.-1: *Masculine appearance of this 8yr old boy.*

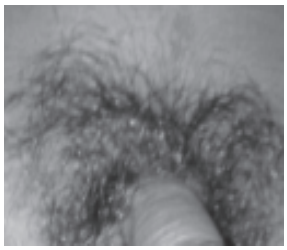

Fig.-2: *External genitalia of this 8yr old boy.*

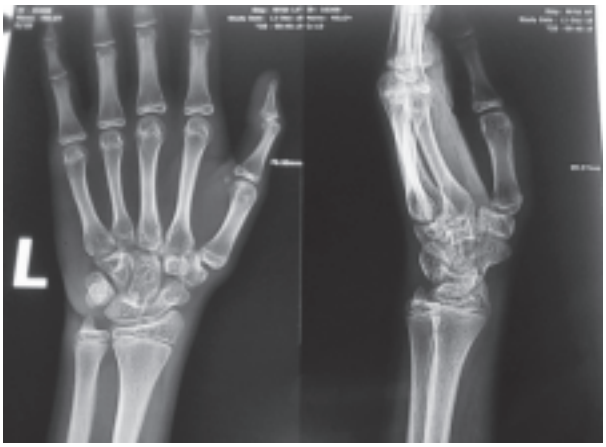

Fig.-4: *X-ray of bone age of this 8yr old boy.*

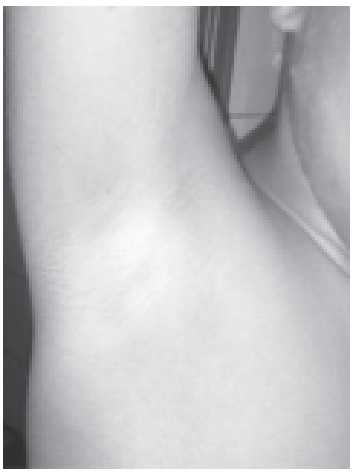

Fig.-3: *Sparse axillary hair.*

This 8 year old boy, had signs of puberty as evidenced by appearance of pubic hair and axillary hair, increased penile length and enlarged testicular volume, his laboratory evaluations were low cortisol, high ACTH and raised 17-hydoxy-progesterone and DHEA-S which suggested peripheral precocious puberty (PPP) due to congenital adrenal hyperplasia (CAH). Rapid ACTH stimulation test confirmed diagnosis of CAH. FSH, LH and free testosterone levels were in pubertal range and his bone age was also advanced. GnRH stimulation test was not done as his basal LH level was high which favoured CPP. Finally, his diagnosis was Central precocious puberty on peripheral precocious puberty due to congenital adrenal hyperplasia as his testicular volume was more than 4 mL and had high LH value. We advised oral hydrocortisone and GnRH-analouge. The patient was on regular follow up and responded to treatment.

Discussion:

Puberty is a complex transitional phase in children generally comprising of growth acceleration and development of secondary sexual characteristics. Several genetic, environmental and nutritional factors play an important role in the onset and progression of puberty.[10] Any boys with signs of puberty before nine years of age should be evaluated for precocious puberty. PPP in boys results from increased androgen production by the testes or adrenal glands. CAH is the most common cause of PPP in boys and CAH can present with GnRH-dependent precocious pubertyrarely. Clinical observations suggest several hypotheses about the mechanism of CPP in CAH - 1) the chronic elevated level of androgen precursors causing premature reactivation of the GnRH pulse generator of the hypothalamus 2) there is a direct correlation with advanced bone age 3) the decline in androgen levels after hydrocortisone treatment may cause the increase in gonadotropin secretion through a negative feedback.[1,11,13,14] Inspite of clinical and hormonal evidence of central precocious puberty ultimately an adrenal pathology was established in 2 different case reports. Their age of initial presentation was (2 year and 10 month respectively), our case presented at 1.5 year, but they presented to reporting authors at age of (6 year and 6½year respectively) and 8 year in our case with features of CPP. Their initial presentation was like PPP and had increased penile length, pubic hair development but testicular volume was < 4 mL.[11,12] A case series containing three male children having CAH with Gonadotrophin-releasing hormone (GnRH) dependent CPP was comparable to our case which was more florid in

Table-I

Showing laboratory evaluations

Tests	Result	Normal values
Serum Electrolytes		
Serum Sodium	141mmol/L	135-145 mmol/L
Serum Potassium	4.1 mmol/L	3.5-5.1 mmol/L
Serum Chloride	102 mmol/L	95-107 mmol/L
Serum TCO2	24 mmol/L	22-30mmol/L
Basal Cortisol	63.3nmol/L	138-690nmol/L
Basal ACTH	743 pg/mL	Not detectable to 46 pg/mL
17-OH-Progesterone	176 ng/dL	3-90 ng/dL
Serum Testosterone	300 ng/dL	3-10 ng/dL
FSH	1.25 IU/L	0.26-3 IU/L
LH	2.55 IU/L	0.02-0.18 IU/L
	Rapid ACTH stimulation test	
Name of Test	0 hr	After 60 min
Basal ACTH	727 pg/ml (Normal range- Not detectable to 46 pg/ml)	
Basal Cortisol	96 nmol/L (Normal range:138-690nmol/L)	88.5 nmol/L
DHEA-S	329.5 µg/dL (Normal range:13-83 µg/dL)	378 µg/dL
17-OH- Progesterone	120 ng/dL (Normal range:3-90 ng/dl)	190 ng/dL
X-ray for bone age	Corresponds to 13-14 yrs, advanced bone age	
USG of abdomen	Normal	
TSH	4.59 mIU/L	0.47- 5.01mIU/L
FT4	14.53 pmol/L	9-19.05 pmol/L
MRI of pituitary gland	Normal pituitary gland	

presentation.[15] Our patient was a simple virilizing (SV) variety of CAH as he presented with precocity without feature of salt wasting. Usually, patients with SV CAH, present with PPP, but may develop CPP due to premature activation of the hypothalamic-pituitary-gonadal axis. Y Gani et al, observed that among 34 children of CAH, 10 children with PPP due to CAH, developed CPP during their follow up in a endocrine clinic of South Africa.[16] Their CPP development was triggered by the chronic mild to moderate intermittent elevation of androgens in patients who are non-compliant with medication like our case. SV boys with advanced bone age of >12 years may have spontaneous CPP when treatment with hydrocortisone is initiated lately. Our patient's bone age was about 13-14 year and developed CPP due to advanced bone age. Here, the hydrocortisone suppresses the production of adrenal androgens and stimulates the release of gonadotrophins as inhibitory effects of adrenal androgens disappeared.[16] It appears that proper glucocorticoid replacement to achieve adequate control of hyperandrogenemia during early life might prevent development of CPP in these patients.[14] All the patients were on replacement therapy with hydrocortisone and GnRH analogue after evaluation and in our case, we followed the same footsteps.[13,16]

Conclusion:

CAH causing PPP, may turn into CPP in boys. Early identification and treatment with hydrocortisone and GnRH analogue should be started as soon as possible, because delay in management can lead to permanent short stature, sexual anxiety and sexual abuse.

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