Central autonomisation of peripheral precocious puberty

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Introduction

Precocious puberty defines itself by the appearance of secondary sexual characters before the age of 9 years old for boys.
Congenital adrenal hyperplasia (CAH) is an autosomal recessive disease resulting from mutation of genes encoding enzymes for hormone production (cortisol, aldosterone, and androgenes), it is the most frequent cause of peripheral precocious puberty (PPP)
We bring back the case of a precocious pseudo puberty (PPP) iso sexual having evolved towards a central precocious puberty (CPP) revealed by an advance of secondary bone age because of a delay of diagnosis of CAH by 21 hydroxylase block enzyme.

Observation

It's about a 7 years old boy, eldest in a family of 04 children, from a full-term pregnancy of a non-consanguineous marriage, accepted for reappraisal of a PPP linked to a bilateral testicular increase of measuring volume between 6-8ml a Tanner stage G2P3.
Birth weight 3900g / Size, Apgar unspecified, vaccination well done without notion of loss of salts.
His brother aged 4 is followed for CAH revealed by PPP tightly controlled under hormonal treatment, the remaining siblings are healthy.
The diagnosis of PPP was made at the age of 4 years and 8 months with Clinical signs of hyper androgenism appeared since the age of 3 such as acne located on face and bust, a husky voice, a wingspan android: broad shoulders, good muscle development
Appearance of external genitalia: P3G1 testicular volume of 2.5ml right 3ml left, no axillary hair, no erection neither ejaculation.
Stature advance (+ 3DS corresponding to age of 11 years) and weight with BMI about 24kg /m ² as well as bone age of thirteen-year-old in spite of a suppressive treatment by Dexamethasone 0,25mg / j, Acetate of cyproterone 25mg / j, hydrocortisone 10mg / j
During a revaluation at the age of 6 years and 9 months, an increase in testicular volume was found (4ml to Prader orchidometer) which motivate gonadal check up and scrotal ultrasound to eliminate differential diagnosis such as tumors and adrenal inclusion of testis.

Results

Hormonal check up at the diagnosis of CAH: ACTH: 269 pg/ml (N 7.2 – 63.3)
Cortisol 8h: 103,5nmol/l (171- 536) **17OHP: 21.09 ng/ml (0.31- 2.111) composit S: 1,3nmol/l (1,4-5)**
Testo: 14.67 nmol/l (0.1- 1.12) LH: 0.1µ UI/l (0.2 -1.4) FSH: 0.11µUI/l (0.2-3.8)
motivated by the increase of testicules size:1/scrotal ultrasound :,each measuring 30mm homogeneous appearance e (anterior size: right 17X7mm, left18.6X7 mm)
2/gonadal check up: FSH: 2,34mUI/ml (nl<1) LH: 1,94mUI/ml (nl<1) Testo: 1,72nmol/l (0,1-1,12)
Pituitary-hypothalamic MRI was not requested.Gonadotrophines analogues (GnRHa) treatment was initiated six months after the time of diagnosis of PPC. 3,75mg 1 injection/month
Test of GnRHa 100ug after 3months of TRT **: LH: 0,51mui/ml FSH: 0,33mui/ml Testo : 20 ng/dl**

Bone age	Bone age, years	Percentage of mature height	Percentage of mature height B&P
Accelerated (n=14)	10	89.5	82.8
	11	89.9	88.3
	12	91.7	90.1
	13	96.1	94.5
Normal (n=38)	8	84.2	79.0
	9	89.0	82.7
	10	91.1	86.2
	11	91.5	90.6
	12	94.1	92.2
	13	96.6	95.8

Bone age	Bone age, years	Percentage of mature height	Percentage of mature height B&P
Accelerated (n=15)	10	84.2	74.7
	12	88.4	80.9
	13	89.2	85.0
	14	92.8	90.5
	15	96.0	95.8
Normal (n=18)	9	85.3	75.2
	10	88.0	78.4
	11	89.0	80.4
	12	92.0	83.4
	13	93.8	87.6

Tableau 1: Bofnig & Schwarz table predicted height

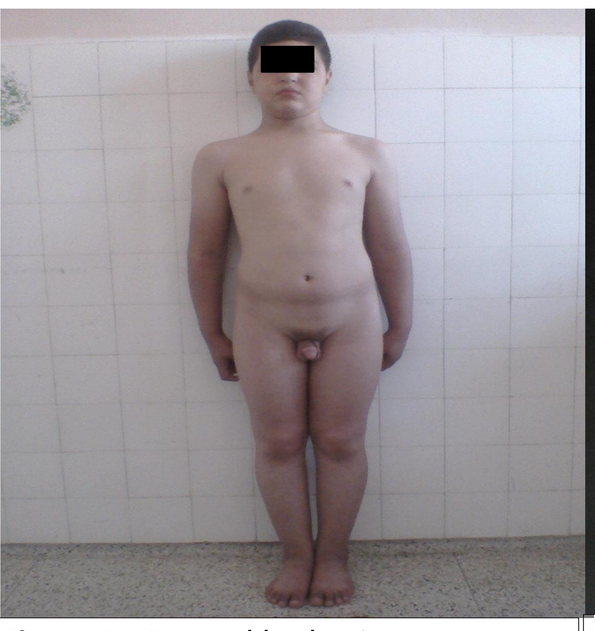

Figure 1: General look wingspan android, broad shoulders

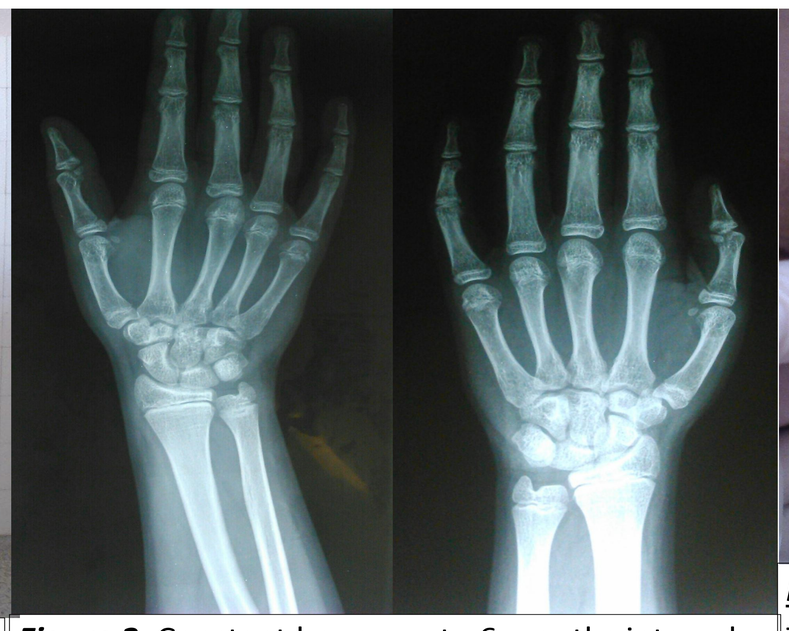

Figure 2: Constant bone age to 6 months interval corresponding to 14 years and a half

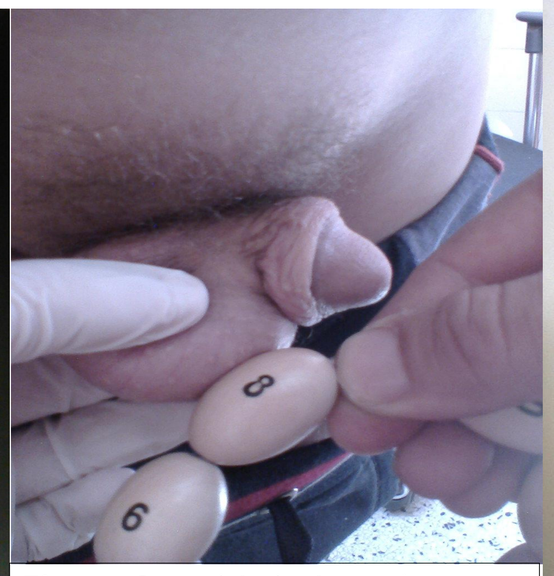

Figure 3: pubic hair and testicular volume of 8ml sized by **Prader** orchidometer

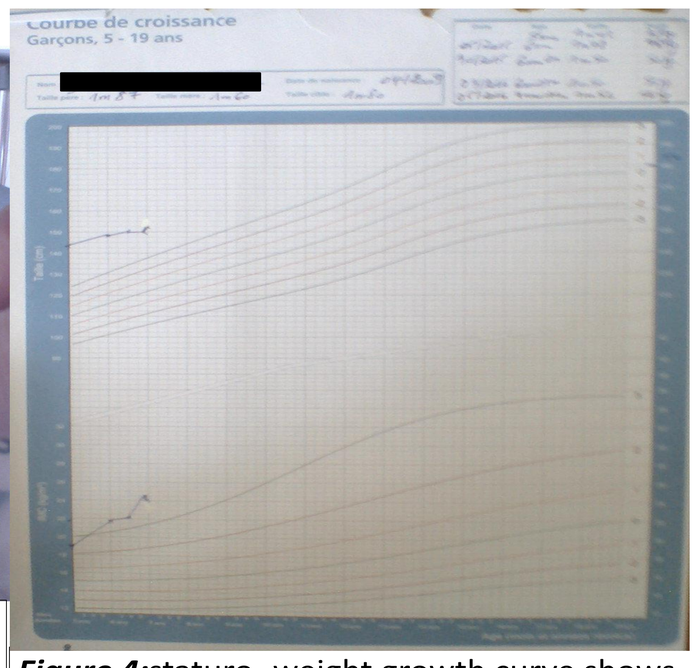

Figure 4:staturo- weight growth curve shows an advance + 3 Standard deviation

Discussion

although fetal adrenal steroidogenisis is established in early gestation, a boy with CAH rarely has signs of virilization at birth, despite plasma testosterone concentration that are often within the normal adult male range. Studies have shown that patients with CAH and CPP had significant increase in growth and accelerated bone age during the first two years of life which is explained by the effects of androgens during early infancy growth through both direct and indirect actions of testosterone :
Direct action by stimulation of sulfation of proteoglycans in chondrocytes. Testosterone acts synergistically with growth hormone (GH), the indirect effect is the result of increasing GH secretion.
Gonadotrophine anlogues (GnRHa) treatment of CAH complicated by CPP was first described in 1985 by **Pescovitz et al.(1)**
Others study reports on the effectiveness of GnRHa therapy in arresting puberty and in improving final height in late treated cases of CAH (2)
Our patient required 30 mg / day hydrocortisone lifelong treatment, while GnRHa will be stopped at a chronological age of 13 years
The predicted final height (PH) was calculated in our patient according to tables of **Bofnig &Schwarz** (table 1) because: child with CAH has a growth pubertal peak lower than the one of a normal child making moot application of curves **Bayley& Pinneau** done on healthy children.According to the latest consensus endocrine society indicates a treatment with GH when CAH **if the PH is lower than -2.25 SDS** (4).The GH combination with GnRHa was ranked among the treatments improving linear growth. We did not use GH therapy in our case because **PH: 169,5cm** corresponding to **-1SDS** and due to the patient's stature advance whereas in our country the treatment by GH is only recommended for patients with GH deficiency in our country

Conclusion

CPP can be observed at the time of diagnosis in patients belatedly diagnosed with or undertreated for CAH, particularly in countries where a routine neonatal screening programme for this condition is lacking. GnRHa treatment appears to improve linear growth and final height, bringing it closer to the one expected from genetic potentials .

Knowledgements:

1-Pescovitz OH, Cassorla F, 1985 LHRH analog treatment of central precocious puberty complicating congenital adrenal hyperplasia. Ann N Y Acad Sci 485: 174-181
2- W.Bofnig* and Schwarz Overestimation of final height prediction in patients with classical congenital adrenal hyperplasia using the Bayeley and Pinneau method. J Pediatr Endocr Met 2012 ; 25 (7-8) : 645-649
3- Soliman AT, 1997 Congenital adrenal hyperplasia complicated by central precocious puberty: linear growth during infancy and treatment GnRHa. Metabolism 46: 513-517.
4-Speiser . Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guidline. J Clin Endocrinol Metab 2010;95:4133– 60.
PS: no conflits interest

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