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Clinical and genotypic characterization of simple virilizing forms of congenital adrenal hyperplasia

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INTRODUCTION AND OBJECTIVES

Congenital adrenal hyperplasia (CAH) is a recessive disease in 90% caused by 21-hidroxilase deficiency. The clinical manifestations are related with the severity of enzyme deficiency and are classified in classical and non classical forms. The classical form is the most severe with genital ambiguity in female newborns and universal virilization. In 75% there is also aldosterone deficiency with salt wasting. The objectives of our study were to describe the phenotypical manifestations and genotype of a cohort with simple virilizing form (SV) of CAH.

METHODS

Retrospective analysis of 13 children with clinical simple virilizing form of CAH with genetic confirmation followed in a pediatric endocrinology unit. The parameters analyzed were age and clinic of presentation, stature, target and final height, bone age, hormone levels, molecular diagnosis and treatment.

RESULTS AND CONCLUSIONS

n=13 , 7♂

Age of diagnosis

- 4.0±1.05 years (mean±SD), earlier in females
- There was a prenatal diagnosis (because of family history) and a neonatal screening diagnosis

Phenotype

Virilization	11
Accelerated growth	8
Precocious pubarche	7
Genital ambiguity	4
Scrotal hyperpigmentation	1

Stature

Stature at Diagnosis (cm)	Stature at Diagnosis SDS	Target Height (cm)	Target Height SDS
121,3	3,3±2,3	167,2±6,2	-0,58±0,72

- Stature at diagnosis SDS was significantly higher than the target height SDS (p<0,001)
- In the 5 patients with final height the final height SDS was not significantly different from target height SDS (p=0,51)

Hormone levels

17OHP ng/mL	Androstenedione ng/mL	DHEA µg/dL	Testosterone ng/dL	Renin pg/ml
121,5 ± 107	7,5±2,8*	186,4±156	169±71	197±99

Molecular diagnosis

Proband	CYP21A2 mutation	Genotype	% enzimatic activity
I	1688G>T	Homozigoty	<20%
II	1688G>T, 1767_1768insT	Compound Heterozigoty	20-50%; none
III	1004 A; 1767_1768ins	Compound Heterozigoty	1%,
IV	1004A	Homozigoty	1%
V	1004A , 2113T	Compound Heterozigoty	1-2%; none
VI	1004T>A; 1688G>T	Compound Heterozigoty	1% , 20-50%
VII	92C>T,	Homozigoty	30-60%
VIII	1004T>A; 2497G> A	Compound Heterozigoty	<1%
IX	999T>A 1762_173insT	Compound Heterozigoty	<5%, 1-2%;
X	1004T>A e g.1999C>T	Compound Heterozigoty	1-2%; <5%
XI	655A/C>G 999T>A	Compound Heterozigoty	1-2%; <5%
XII	999T>A 1762_173insT	Compound Heterozigoty	<5%, 1-2%;
XIII	999T>A; g.655A/C	Compound Heterozigoty	<5%, 1-2%

Bone age

- Was significantly advanced at diagnosis (5,3 ±1,2 years; p <0,001)

Treatment

- 66% of females needed surgical treatment at mean age of 4,5 years (clitoroplasty and vaginoplasty)
- Hidrocortisone 100% (15 mg/m2/day)
- Fludrocortisone 38% (60 microg/m2/day)
- LHRH analogue 30% (6,3 years)

Concordance between final height and target height was related with relatively early diagnosis and treatment. Precocious virilization in all and genital ambiguity with surgical correction need in 66% of females reinforce the attempted management.

Our study supports inclusion of CAH in the newborn screening particularly for the classical form patients.

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