CLINICAL, BIOLOGICAL AND GENETIC ASPECTS OF CONGENITAL ADRENAL HYPERPLASIA IN CHILDREN AT THE CENTRAL HOSPITAL OF ARMY IN ALGIERS

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INTRODUCTION

Congenital adrenal hyperplasia (CAH) is a rare genetic defect. Its prevalence is not available in Algeria, it is estimated at one case per 15,000 births worldwide. The most common form is due to 21-hydroxylase deficiency associated with mutations in the 21-hydroxylase gene, which is located at chromosome 6p21. Molecular defects of CYP21A2 systematically decrease the activity of this enzyme and result in expression of varying severity and phenotypes.

AIM

The aim of our study is to describe the clinical, biological and genetic characteristics of a population of children followed for CAH in the Endocrinology department at the Central Hospital of Army in Algiers between 2007 and 2021.

METHOD

The study included 26 patients (13 boys and 13 girls) aged 2 to 31 years, followed for CAH.
Clinical data from the neonatal period and at the first consultation have been described.
The results of the initial biological assessment have been specified (17OHP, Cortisol, ACTH).
The genetic study was done in 18 patients with a complete characterization of CYP21A2 mutations and the rare other forms (11 B Hydroxylase, 3 B SHD).

RESULTS

The diagnosis of CAH was made at birth in 11 of our patients, and during the first 2 months in 8 patients. Four children at the age of 4. The other 3 patients between 11 and 14 years old.
Parental consanguinity is found in 10 of our patients.
None of the children had high blood pressure.
Four out of 13 girls have Prader 4 male virilization. One girl exhibited Prader 5 full male virilization.
Seventeen of the 26 patients presented the classic salt wasting form.
Biologically, 17 OHP was found greater than 20 ng/ml in 62% of our patients (16/26).
ACTH > 60 pg/ml is found in half of the cases.
The mean plasma cortisol is 142,46 nmol/l [3,36 – 180,76].
The most frequent genetic defect was the IVS2-13A / C> G mutation which is found in 9/18 children (50%), 7/9 of the patients presented with a classic wasting salt form.
The p.I172N mutation was found in 4 children (22%) in the heterozygous state, and all presented a simple virilizing form.
A rare mutation p.Q41Afs * 39 was found in one case: a girl who presented a biological profile of an 11 beta hydroxylase.

Patient	Age	Sexe	Age of diagnosis	consanguinity	Clinical form	phenotype	17 OHP ng/ml	Cortisol 1 nmol/l	ACTH 1 pg/ml	Genotype
1	2	M	50 days	-	SW		9,24	146	5,4	NA
2	5	F	Birth	+	SW	Prader 3	198	267	25	large lesion of CYP21A2 homozygote
3	9	F	Birth	+	SW	Prader 4	10,67	NA	50	large lesion of CYP21A2 homozygote
4	6	F	Birth	NA	SW	Prader 3	>20	NA	NA	IVS2-13A/C>G + p.L307Ffs *5
5	16	F	Birth	NA	SW	Prader 4	19	NA	NA	IVS2-13A/C>G + p.L307Ffs *5
6	3	F	20 days	+	SW	Prader 3	7,22	58	106	p.Q41Afs*39 hétérozygote
7	19	F	Birth	-	SV	Prader 3	3,36	NA	NA	p.I172N/p.R356W
8	12	F	4 years	-	NCCAH	Premature pubarche	13	238	65	p.I172N/p.V281L
9	12	M	4 years	-	NCCAH	PPP	>20	151	118	p.I172N/p.V281L
10	25	M	12 years	NA	SV	PPP	9,35	NA	145,5	NA
11	8	F	Birth	+	SW	Prader 4	26,6	NA	NA	IVS2-13A/C>G
12	6	F	15 days	+	SW	Prader 3	108	NA	NA	p.R483P homozygote
13	6	M	44 days	NA	SW		>20	19	181	p.Q318* homozygote
14	8	F	Birth	-	SW	Prader 3	>20	35,4	698	IVS2-13A/C>G homozygote
15	4	M	15 days	-	SW		54,23	100,8	294	IVS2-13A/C>G homozygote
16	7	F	Birth	-	SW	Prader 3	180,76	8,9	19,6	p.Q318* homozygote
17	5	M	Birth	-	SW		> 20	NA	NA	NA
18	20	F	Birth	-	SV	Prader 5	>20	253	125,42	IVS2-13A/p.R316X
19	3	M	20 days	-	SW		> 20	NA	921	NA
20	3	M	11 days	+	SW		15,49	NA	8,54	NA
21	16	M	4 years	+	SV	PPP	18,00	171	1803	NA
22	10	F	Birth	+	SW	Prader 4	25,04	56,4	951	IVS2-13A/C>G homozygote
23	13	M	10 years	-	SV	PPP	>20	NA	NA	IVS2-13A / p.I172N
24	7	M	4 years	+	SV	PPP	7,15	130	1451	NA
25	31	M	14 years	NA	SV		124,6	NA	961,5	NA
26	3	M	25 days	+	SW		218,77	360	NA	IVS2-13A/C>G / p.V281L homozygote

Table 1:Clinical, biological and genetic patients data. SW : salt wasting, SV: simple virilizing, PPP: Pseudo Precocious Puberty, NA: Not Available..

CONCLUSIONS

The frequency of the underlying mutations in our patients, with the classical form of CAH, varied but were quite similar to those reported in the Mediterranean region. Therefore, identifying CYP21A2 abnormalities in Algerian patients and comparing them with incidence and severity in different populations will create a valuable diagnostic tool for genetic counseling.

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