HYPOSPADIAS IN A MALE PATIENT WITH 21-HYDROXYLASE DEFICIENCY AND ATYPICAL CLINICAL COURSE: PRESENTATION OF TWO BROTHERS

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Introduction:

21-hydroxylase deficiency (21OHD) is the most common form of congenital adrenal hyperplasia (CAH).Clinical and laboratory findings vary depending on the enzyme activity.

Case Reports:

Case 1: A 2-months-old male infant referred as hypospadias. He was born at term from consanguineous parents with intrauterine growth retardation. The mother had no problem during pregnancy.The external genitalia had penoscrotal hypospadias with chordee and both testes were normally sized within the scrotum. No other dysmorphic signs, skeletal malformations were observed. The karyotype analysis was 46, XY. Biochemical and baseline hormonal findings were normal except for slightly high 17-OHP (9.3 ng/ml).ACTH stimulation test revealed similar to non-classical CAH with no clinically compatible (table1). When he was 33-months-old there was signs of salt loss (hyperkalemia, hyponatremia), so performed synacthen test again. Basal ACTH was at the upper limit of the normal range, with elevated 17-OHP and progesterone levels, while androgen levels were low; basal cortisol was normal (8.56 µg/dl) but stimulated was low (8.75µg/dl). POR deficiency was considered. But any mutation of POR was not detected.

Case2: The siblings of Case1, because of this the patient brought to our clinic postnatally. His physical examination was completely normal. Biochemical and baseline hormonal findings were normal except for slightly high 17-OHP like his brother. Also adrenal insufficiency demonstrated with repeated ACTH tests (table 2).

However 24-hour urinary steroid hormone profiles of patients were compatible with 21OHD. Genetic analysis established a homozygous V281L mutation in the CYP21A2 gene in both cases.

Table 1: Case1

Age (month)	Min.	ACTH pg /ml	Kortisol µg/dl	17-OHP ng /ml	1.4 AS ng/ml	DHEAS µg/dl	Prog. ng/ml	T.test ng/ml	Renin pg/ml	Aldst. pg/ml
2	0		15,9	9,3	0,5		0,97	0,07		
	30		31,7	27,0	0,8	18,8	8,68	0,11		
5	0	82	13,9		0,51	15,5	1,64	0,03	23,6	
	30		18,4	24,0	0,58		3,74	0,03		
33	0	52	8,56	21,8	0,16	6,1	4,5	<0,1	7	623
	30		8,75	22,0	0,2	6,5	7,09	<0,1		

Table 2: Case2

Age (month)	Min.	ACTH pg /ml	Kortisol µg/dl	17-OHP ng /ml	1.4 AS ng/ml	DHEAS µg/dl	Prog. ng/ml	T.test ng/ml	Renin pg/ml	Aldst. pg/ml
2	0	22,4	5,5	4,5	0,94		1,39	1,26	6,6	219
	30		19,3	14,1	4,6	205,2	6,38	1,42		
11	0	104	18,7	36,6	0,53		9,75	0,33	82,3	
	30		20,9	40,4	0,6		10,9	0,35		
23	0	117	10,0	10,1	0,4	2,2	1,09	<0,1	35,7	192
	30		12,0	42,0	0,51	2,4	8,07	<0,1		

Tables: Showing the results of baseline hormonal and stimulation tests analysis of two cases (**Abbreviations:** Min: minute, ACTH: Adrenocorticotropic hormone, 17-OHP: 17-hydroxyprogesterone, 1,4 AS: 1,4-androstenedione, DHEAS: Dehydroepiandrosterone sulfate, Prog: Progesterone, T.test: Total Testosterone, Aldst: Aldosterone)

Conclusion:

These patients don’t exhibit the typical clinical and laboratory findings of 21OHD. Case1 is a rare male patient with 21OHD accompanied by hypospadias. In the literature, there is only one male patient that presented with insufficient virilization in 21OHD.