A Rare Cause of Congenital Adrenal Hyperplasia due to P450 Oxidoreductase Deficiency: a Case Report

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The authors declare that there are no conflicts of interest

BACKGROUND

Cytochrome P450 oxidoreductase (POR) deficiency is the newest form of congenital adrenal hyperplasia first described in 2004. Cytochrome P450 oxidoreductase is a protein that transfers electrons from NADPH to all 50 microsomal forms of cytochrome P450. Mutations that cause POR deficiency result in partial deficiency of the enzymes 21-hydroxylase and 17α-hydroxylase. Remarkable clinical features of the POR deficiency are genital ambiguity in both sexes, glucocorticoid deficiency and Antley-Bixler skeletal malformations. Mild mutations may give rise to polycystic ovary syndrome in women and gonadal insufficiency in men.

CASE

The patient was brought to hospital at the age of 5 years due to micropenis. There was no parental consanguinity. The karyotype analysis of the patient revealed 46,XY. He had a bifid scrotum and a micropenis. The left gonad was palpated in the scrotum and the right one in the inguinal canal. Ultrasonographic evaluation revealed that both gonads were testis and there was no mullerian structures. His baseline 17-OH progesterone and ACTH levels (9.16 ng/ml, 110 pg/ml, respectively) were high and cortisol level (10 µg/dl) was normal. A standard dose ACTH stimulation test was performed and test results revealed a peak cortisol level of 10.2 µg/dl and peak 17-OH progesterone level of 14.12 ng/ml (Table 1). The patient was started on hydrocortisone treatment. He underwent surgery for hypospadias and chordee repair (Figure 1). Molecular genetic analysis of the patient demonstrated a **c.1329_1330insC (p.I444Hfs*6)** heterozygous mutation which was a previously described and well-known mutation for POR deficiency (Figure 2).

	Basal	30 minute	60 minute
ACTH (pg/ml)	110		
Cortisol (µg/dl)	10	10.2	10.1
17 OH-progesteron (ng/ml)	9.16	14.20	12.38
DHEA-S (µg/dl)	15	15	15
Testosteron (ng/dl)	0.73	0.79	0.84
Androstenedion (ng/ml)	0.02	0.02	0.02

ACTH: adrenocorticotrophic hormone, DHEA-S: Dehydroepiandrosterone sulphate

Table 1- Standard dose ACTH stimulation test

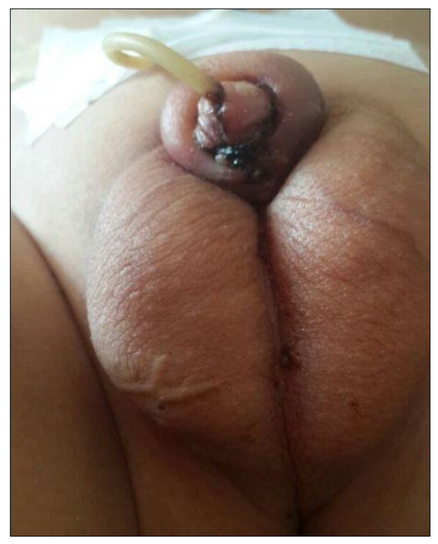

Figure 1- External genitalia of the patient after surgical repair of hypospadias and chordee

CONCLUSIONS

As in our case, 12% of the reported patients have only one identified mutation for POR deficiency. This rare disorder should be born in mind in 46,XY cases with ambiguous genitalia and hormonal profiles compatible with partial deficiencies of 21-hydroxylase and 17α-hydroxylase/17,20-lyase enzymes.

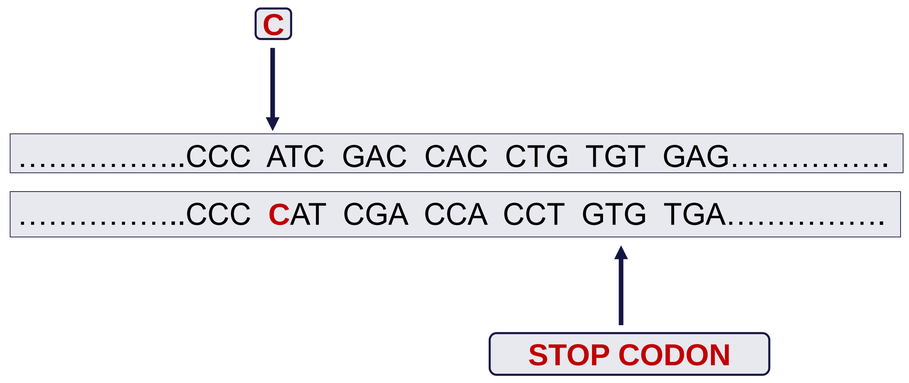

Figure 2- c.1329_1330insC (p.I444Hfs*6) mutation described in POR deficiency

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