

High-dose Hook Effect in 17-Hydroxyprogesterone Assay in 21-hydroxylase deficiency



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AIMS and OBJECTIVE

False-negative results can occur an extremely high level of substrate at the assay system. This is called the “high-dose hook effect”.

PATIENT AND RESULT

14 year-old female patient was referred with short stature, amenorea and hirsutism. Height, weight and blood pressure were 140.5cm (SDS:-3.5), 43.4kg (SDS:-1.6) and 120/80mmHg. She had stage 1 Tanner breast, stage 5 pubic hair and hirsutism (mFG scale: 28) with android distribution. The clitoris was enlarged 4cm in longitudinal axis and 1.5cm in transverse diameter of the glands (Picture 1).

Laboratory: Sodium 138 mmol/L, potassium 4.3 mmol/L, 17-OHP <0.05 ng/ml (0.2-1.3), DHEA 720.6 ug/dL (35-430), androstenedione 13 ng/mL (0.3-3.3), testosterone 4,4 ng/ml (0.1-0.7), ACTH 319 pg/mL (4.7-48.8), cortisol 7.8 ug/dL (6.7-22.6), renin 69.7 mIU/mL (2.8-39), aldosterone 664.1 pg/mL (25-315), LH 3.1 mIU/ml, FSH 6.3 mIU/ml, estradiol <20 pg/mL, progesterone 31.9 ng/ml (25-315), prolactin 12.6 ng/ml (Table 1).

Pelvic ultrasonography was normal (uterus 8 ml and ovaries 2/ 2.3 ml). The karyotype was 46, XX.

Unexpected result of low serum 17-OHP level led to the suspicion of a “high-dose hook effect”. The measurement was repeated after 1/10 dilution of serum, and high level of 17-OHP was detected (115.4 ng/ml) with ELISA test (DiaMetra, Segrate, Italy).

Homozygous p.I173N (c.518T>A) mutation was detected in the CYP21A2 gene.

These values confirmed the diagnosis of 21-hydroxylase deficiency. Firstly hydrocortisone then dexamethasone therapy were initiated (Picture 2).

Picture 1: Patient's hirsutism and eksternal genitalia



Table 1: Clinical and laboratory findings

	Before Treatment	Hydrocortisone (0-3 months)	Dexamethasone (3-6 months)
Breast/ Tanner stage	T1	T1	T4
LH (mIU/ml) (N: 2.1-10.8)	3.1	1.1	1.1
FSH (mIU/ml) (N: 4.5-22)	6.3	5.1	1.8
Estradiol (pg/ml) (N: 24-114)	<20	68	146
Progesteron (ng/ml) (N: 0.1-1.5)	31.9	39.5	-
Sodium (mmol/L) (N: 136-146)	138	138	137
Potassium (mmol/L) (N: 3.5-5.1)	4.3	4.2	4.0
Renine (mIU/mL) (N: 2.8-39)	69.7	95.5	35.9
Aldosterone (pg/ml) (N: 25-315)	664.1	585.1	34.5
ACTH (pg/mL) (N: 4.7-48.8)	319	103	8.9
Cortisol (ug/dl) (N: 6.7-22.6)	7.8	-	-
DHEA (ug/dl) (N: 35-430)	720.6	728.9	8.1
Total testosterone (ng/ml) (N: 0.1-0.7)	4.4	3.8	0.1
Androstenedion (ng/mL) (N: 0.3-3.3)	13	-	-
17-OHP (ng/ml) (N: 0.2-1.3)	<0.05 / 115.4*	182.1*	1.2

DISCUSSION

Excessive accumulation of steroid precursors are occur due to the shunt throught the adrenal androgen biosentetic pathway. Large quantities of antigen impair antigen-antibody binding, resulting in low antigen levels (false negative result) in laboratory assays which can be satisfied by dilution of the sample or a change of sample antigen to antibody ratio either by assay reformulation.

This is the first case of the hook effect for 17-OHP immunoassay in 21-hydroxylase deficiency. Hook effect needs to be suspected in patients with CAH when steroid precursors are incompatible.

Picture 2: Patient's breast development after HC and Dxm

