

When the history of the disease is the key to diagnosis: About a challenging case of congenital adrenal hyperplasia

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Abstract

Background: A 17 alpha-hydroxylase deficiency (17OHD) is a rare form of congenital adrenal hyperplasia (CAH). Congenital adrenal hyperplasia (CAH) is a group of disorders resulting from defect of one of enzymes necessary for biosynthesis of cortisol.

Case: A 33-year-old female suffered from 17OHD. She presented with primary amenorrhea, lack of secondary sexual characteristics, and hypertension complicated by ruptured cerebral aneurysm. Laboratory tests showed hypokalemia, low levels of androgens (testosterone and dehydroepiandrosterone), corticosteroid, and high levels of adrenocorticotrophic hormone and progesterone. The clinical manifestations, imaging and laboratory results appeared to be consistent with a diagnosis of CAH in the patient, due to the observed 17 α -hydroxylase deficiency.

Conclusion: 17OHD is a rare disease associated with primary amenorrhea and hypertension. This case shows the importance of vital signs measurement, medical history and commitment to a systematic approach.

Keywords: Congenital Hyperplasia; Hypertension; Primary amenorrhea; 17 alpha hydroxylase-deficiency

1. Introduction

Deficiency in sex steroids and excessive mineralocorticoid production cause characteristic symptoms and signs such as delayed puberty with primary amenorrhea and hypertension. Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder due to a defection any of several enzymes involved in steroidogenesis; different genotypes induce different phenotypes. 17 α -hydroxylase/17,20-lyase deficiency (17OHD) is a rare type of CAH that causes cortisol and sex hormone deficiency and aldosterone excess [1-3].

Recognition of this entity is important, because the hypertension, hypokalemia, and symptoms respond to steroid replacement. We report on a patient with 17 alpha-hydroxylase deficiency who is initially presented with an atypical manifestation.

2. Case report

A 33-year-old woman was transferred from neurosurgical department to the endocrinology department after surgery of ruptured cerebral aneurysm in the aim of exploring secondary severe hypertension.

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She had a history of hypertension, found incidentally 4 years previously, which did not be explored. The patient's parents were non-consanguineous and there was no family history of chronic illness, including hypertension and had normal pubertal and reproductive histories.

A part from hypertension, she had also primary amenorrhea but the decision was to investigate this amenorrhea later given the vital prognosis engaged.

Upon physical examination, the patient was tall with a height of 173cm, a weight of 61.7 kg and a body mass index of 20.6 kg/m². Blood pressure was 15/07 Cmgh . The patient's breast development had only progressed to Tanner stage B1P1 and external genitalia were phenotypically female, but were infantile.

Laboratory investigations revealed hypokalemia (2.6 mmol/L). Abdominal ultrasound revealed a left adrenal mass with imaging characteristics of malignancy (size greater than 4cm, area of necrosis, absolute washout less than 60% and relative washout less than 40%). The right adrenal gland was described as normal.

Urinary catecholamines were negative and the Renin aldosterone ratio was not elevated.

Other positive investigations were low serum cortisol(3.09 ug/dl) and high ACTH (198.3 pg/ml) (Table 1)

Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were elevated, but estradiol and testosterone were low , suggesting a diagnosis of primary gonadal failure

(hypergonadotrophic hypogonadism).

Due to the severe initial presentation with signs of malignancy in adrenal imagery , the decision was to realize left adrenalectomy . The histological result revealed hyperplasia without signs of malignancy. And the patient was put on spironolactone (25mg)

3 months after, she presented with normal kaliemia ,and blood pressure not elevated above 140mmgh systolic .The adrenal tomography revealed hyperplasia of the right adrenal gland with nodular lesion on the arm 12x13mm, spontaneous density of 31HU and Wash out at 73% evoking an adenoma.

The decision was to explore the primary amenorrhea which was reported previously. Laboratory investigations were completed by dosage of DHEA-S and 17-OHP which were low

Abdominal and pelvic MRI revealed hypoplasia of the uterus without visualization of ovaries

The clinical manifestations, imaging and laboratory results appeared to be consistent with a diagnosis of CAH in the patient, due to the observed 17 α hydroxylase deficiency

In order to confirm this diagnosis, genetic analysis of the CYP17A1 sequence was indicated but not performed yet

The patient was initiated with Hydrocortisone 30 mg daily for the treatment of CAH. She was not yet putted on estrogen substitution until exploring the vascular risk because she had presented the cerebral ruptured aneurysm

3 months later , the patient gained weight (8 kilos) , the ACTH is decreased but still elevated . The DOC is elevated and the DHEA-S is low . Hydrocortisone was replaced by 1mg of Dexamethasone daily , and the discussion is about the possibility that the adrenal adenoma is becoming independent ?

After 6 months (the patient missed her 3-month check-up) , the ACTH and Deoxycorticosterone DOC were normal and the decision was to reduce Dexamethasone 0.5 m g \square 0.25 mg

The cushing syndrome still developing and because of hypertension risk the adrenalectomy still a therapeutic possible option to discuss after the coming control.

Table 1 Laboratory results before and after medication

Laboratory test	Before medication	After medication	Reference range
ACTH	319 ng/l	124 ng/l	7,20-63,30
		13ng/l	
11 Désoxycorticostérone DOC	6,87 pmol /ml	7,95 pmol /ml	N : 0,12-0,60
	2271 pg/ml	0,19 pmol/ml 2627 pg/ml	N : 40-200
Aldostérone	56 pmol/l	*	32.5-655pmol/l
	20.2pg/ml		11.7-236 pg/ml
Rénine	<0.5 mUI/L	*	2.8-39.9 mUI/l
Rapport Aldostérone/Rénine	11	*	<64
DHEA-S	<0,38 µg/dl	<0,1µmol/l	60,90- 337 µg/dl
17 OHP	0.6 nmol/l	*	0.6-2.4 nmol/l
	0.2 ng/ml		0.2-0.8 ng/ml
Cortisol	1,49µg/dl	*	
FSH	135,2 mU/ml	*	5-20 mU/ml
LH	47,3 mU/ml	*	5-22 mU/ml
Œstradiol	25,8 pg/ml	*	27-161 pg/mL
Testostérone	0,03 ng/ml	*	0,2 à 0,8 ng/ml

ACTH, adrenocorticotrophic hormone; PRA, plasma renin activity; LH, luteinizing hormone; FSH, follicle stimulating hormone Hormone levels were measured in blood samples taken at 0800–0900 h. Normal age-adjusted reference values are show * = Not done

3. Discussion

17 α -hydroxylase deficiency is a rare form of CAH, with an estimated incidence of 1 in 50,000 to 100,000, and accounts for about 1% of all CAH cases [1,2].

The classical presentation of 17OHD is hypertension, hypokalemia, and delayed puberty with lack of secondary sexual characteristics in a female of pubertal age group [3].

Our patient had all the classical features.

The most common enzyme defect causing CAH is 21-hydroxylase deficiency (21-OHD), followed by 11 β -hydroxylase deficiency (11 β -OHD). Clinically, these enzyme deficiencies are characterized by hyperandrogenism or heterosexual precocious puberty in females; however, clinical features of 17 α -hydroxylase deficiency differ from those of 21-OHD or 11 β -OHD in that there is no hyperandrogenism, but rather, sexual infantilism [4,5].

The diagnosis of 17OHD is based on clinical, biochemical, and molecular features. In our case, biochemically, there were decreased concentrations of DHEA, androstenedione, testosterone, estradiol, and cortisol, and increased concentrations of 11-DOC and ACTH. Since clinical and biochemical features are diverse, depending on the type of mutations in the CYP17A1 gene, genetic analysis is critical for confirmative diagnosis [4,5,6,7].

Once diagnosis is made, immediate adequate intervention should be initiated in order to prevent complications such as hypertension or hypokalemia and to induce sexual development at the appropriate time [7,8].

Treatments for 17 α -hydroxylase/17,20-lyase deficiency include appropriate glucocorticoid replacement and sex steroid hormone supplementation. The aim of glucocorticoid treatment is to reduce ACTH and 11-deoxycorticosterone to normal levels, using a physiological dose of 0.25-1.0 mg/day dexamethasone and 2-5 mg/day prednisone.

The administration of glucocorticoids normalizes blood pressure, serum renin and electrolyte levels with natriuresis. In addition, sex hormone replacement therapy is recommended to be administered in adolescence for secondary sexual development, maintenance of female sexual characteristics and stimulation of epiphyseal closure [8,9,10].

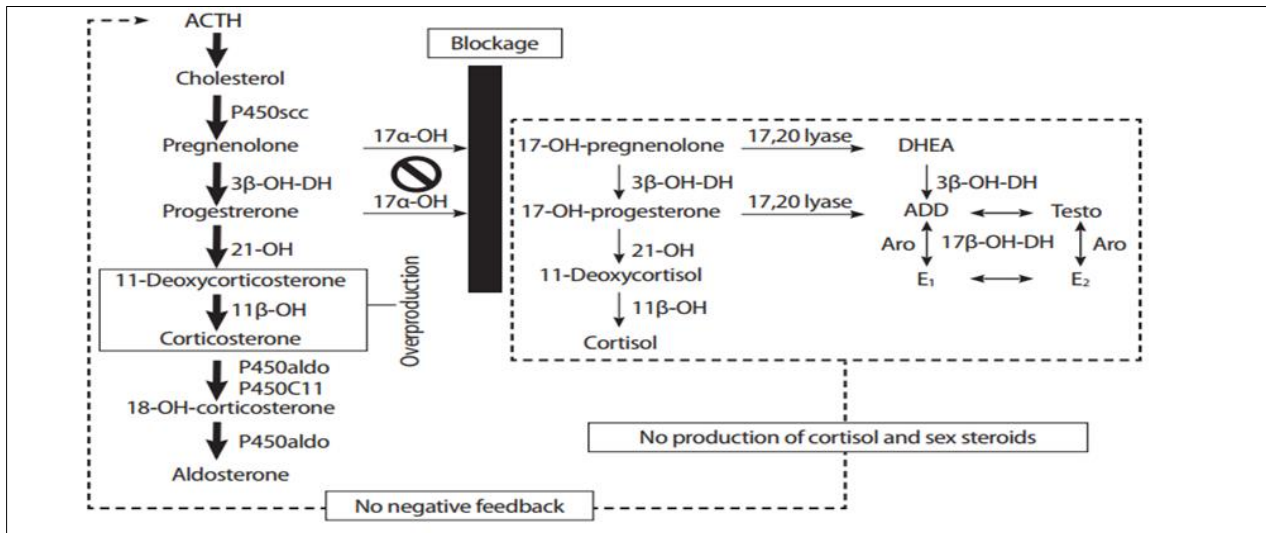


Figure 1 Pathogenesis in 17 alpha-hydroxylase deficiency (17OHD). The blockage at the 17α-OH impairs cortisol and sex steroid synthesis. The low cortisol increases ACTH production. Accumulated deoxycorticosterone and corticosterone cause plasma volume expansion and hypertension, and hypokalemia, which suppress renin and aldosterone. [5]

4. Conclusion

In summary, patients with hypokalemia, hypertension, and absence of secondary sexual development should be evaluated for 17 alpha-hydroxylase deficiency so that appropriate therapy can be pursued.

Abbreviations

- ACTH = Adrenocorticotrophic Hormone
- CAH = Congenital Adrenal Hyperplasia
- CYP17A1 = 17α-Hydroxylase Enzyme
- DOC = Deoxycorticosterone
- HH = Hypergonadotropic Hypogonadism
- TS = Tanner Stage
- 17α-OH= 17α-Hydroxylase
- 3β-OH-DH=3β- Hydroxysteroid Dehydrogenase
- 21-OH= 21-Hydroxylase
- 11β-OH= 11β- Hydroxylase
- 17β-OH-DH =17β-Hydroxysteroid Dehydrogenase
- ADD= Androstenedione
- Testo= Testosterone
- Aro= Aromatase
- E1= Estrone
- E2= Estradiol

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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