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A case report of male pseudohermaphroditism caused by 17 α-hydroxyenzyme deficiency

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ABSTRACT. *Bckground. 17α-hydroxylase deficiency is a very rare congenital adrenal hyperplasia, which is caused by the mutation of CYP17A1 gene encoding 17α-hydroxylase. The main clinical features include hypertension and hypokalemia, and false hermaphroditism can also be found in men. Case. A 37-year-old phenotypic female with 17 α-hydroxyenzyme deficiency showed hypertension and hypokalemia. Laboratory tests showed that high levels of progesterone, follicular stimulating hormone, luteinizing hormone, karyotype: 46,XY,CYP17A1 gene exons 8 Asp487-Ser488-Phe489 deletion homozygous mutation, and finally diagnosed as 17 α-hydroxyenzyme deficiency. Conclusion. 17 OHD is a rare disease, which is easy to be missed or misdiagnosed, karyotype analysis and gene sequence analysis are helpful to differential diagnosis and diagnosis.*

KEYWORDS: *17α-hydroxyenzyme deficiency; Congenital adrenal cortical hyperplasia; Male pseudohermaphroditism*

1. Introduction

17 α-hydroxylase deficiency (17 α-OHD) is a very rare type of congenital adrenal cortical hyperplasia (CAH) [1]. Since 1966, when Biglieri et al reported [2] the first case of 17a -hydroxylase deficiency has been reported, only about 200 cases have been reported in the world [3]. This paper reports a case of male pseudohermaphroditism caused by 17 α-hydroxylase deficiency in order to improve clinicians' understanding and attention to the disease and to give timely and accurate diagnosis and treatment.

2. Case report

*General situatio*n: the patient, a 37-year-old phenotypic female. Admitted to

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hospital on October 30, 2018, due to fatigue aggravation for 1 month. Congenital uterine absence, hypertension history of 10 months. There are no similar patients in the family.

Physical examination: she is 1.73 m in height, 78 kg in weight. The arterial blood pressure was 177/120 mmHg. Normal intelligence. No axillary hair, pubic hair, beard, throat is not obvious, female voice, breasts at Tanner I stage, external genitalia female appearance, clitoris hypertrophy, blind end of vaginal.

Laboratory examination: Karyotype was 46, XY. Blood potassium 3.12 mmol/L (normal range 3.5-5.5 mmol/L); captopril test negative. The details of the hormone test are shown in Table 1.

Imaging examination: 8 carpal bones could be seen in the wrist of both hands, and the distal epiphysis of ulna and radius were partially closed (Fig. 1). Adrenal CT showed fat-containing low-density shadow in the left adrenal body and enlargement of the left adrenal gland (Fig. 2). Gynecological color Doppler ultrasound showed congenital absence of uterine sonography; testicular and epididymal color Doppler ultrasound: no epididymis and testicular tissue were found.

Gene sequencing: it was found that the deletion of 9 base (GACTCTTTC) in Exon 8 of CYP17A1 gene, that is, a lack of 3 amino acids (Asp487-Ser488-Phe489) homozygous mutation (Fig. 3).

The patients had hypertension, hypokalemia, negative captopril test (not supporting primary aldosteronism), low levels of cortisol, and increased ACTH and gonadotropin. Adrenal CT showed that the left adrenal gland was enlarged. X-ray evaluation showed that the bone age was less than the actual age, there was no gonadal deficiency, and the karyotype was 46XY. The homozygous mutation of Asp487-Ser488-Phe489 deletion occurred in Exon 8 of 17A1 gene, so it was diagnosed as 17 α-OHD, congenital adrenal cortical hyperplasia and male pseudohermaphroditism.

The social and psychological sex of the patient was female, the chromosome karyotype was male, and the patient finally chose the female sex. Therefore, glucocorticoid replacement therapy (prednisone 2.5 mg, Q8H); estrogen replacement therapy to promote the development of secondary sexual characteristics (estrogen valerate 0.5 mg, QD); potassium supplementation (10 ml potassium chloride solution, TID); potassium retention (spironolactone 40 mg, bid). Cryptorchiectomy or orchiectomy was not performed because no cryptorchidism and testicular tissue were found. One month later, blood pressure: 159/ 100 mmHg, the blood potassium was 3.69 mmol / L, the treatment regimen was changed to prednisone 2.5 mg, BID, and Estradiol valerate 0.5 mg, bid. Three months later, blood pressure: 135 /95 mmHg, blood potassium: 4.20mmol / L, and continued close follow-up.

3. Discussion

Congenital adrenal cortical hyperplasia (CAH) is a group of autosomal recessives (AR) disease. It is caused by the congenital lack of steroid hormone

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synthase in adrenal cortex caused by gene defect. Due to the enzyme deficiency related to adrenocortical hormone synthesis, cortisol synthesis is partially or completely blocked, which increases the CRH-ACTH compensation secretion of hypothalamus-pituitary and leads to adrenocortical hyperplasia. Among all CHA, 17α hydroxylase deficiency is very rare, only 1% [4].

According to previous reports, there are two common causes of loss of 17-hydroxyenzyme activity in Chinese population: Y329K, 418X and Asp487 -Ser488-Phe489 deletion. In this case, the 9 base (GACTCTTTC) deletion of codon 487-489 in Exon 8 was consistent with the most common gene mutation in Chinese. Although the mutation did not lead to the shift of reading frame, three amino acids (Asp487-Ser488-Phe489) were missing in the peptide chain of the synthesized protein, which shortened the peptide chain and changed the primary junction of the protein. Structure and conformational [5] affected the activity of enzyme protein. Fardella et al. [5] after expression in vitro confirmed that this mutation completely lost the activity of P450c17 enzyme encoded by Fardella et al.

The main clinical manifestations of 17 α-hydroxyenzyme deficiency are as follows: (1) sexual dyslexia: female patients can show primary atresia or delayed adolescence. Most of the male patients showed pseudohermaphroditism, the external genitalia was childish female type, with blind vagina, while the internal genitalia was male, the testicles were small and stunted, which could be located in the abdominal cavity, inguinal area or scrotum plica [6]. (2) low renin hypertension, hypokalemia: the patients often had different degrees of hypertension, often accompanied by hypokalemia, fatigue and weakness. Even muscle paralysis. (3) Bone metabolic disorders: due to lack of estrogen and androgen, there can be bone mineralization disorders and delayed healing of epiphysis. The patients were characterized by osteoporosis and backward bone age, and the height of the patients could continue to grow slowly after adulthood. (4) fatigue and weakness: the level of blood cortisol was low, fatigue and resistance decreased [7].

To reduce blood pressure and correct hypokalemia in the choice of glucocorticoid drugs, adult patients should choose long-acting preparations such as dexamethasone, the appropriate time to take before bed, in order to maximize the inhibition of ACTH [8]. Although dexamethasone has a strong inhibitory effect on ACTH, it has a great effect on growth and development, so it has a strong effect on preadolescence [9-10]. Hydrocortisone, which has a short half-life and has little effect on growth and development, is recommended. Attention should be paid to long-term follow-up, especially the dose of glucocorticoid should be adjusted flexibly according to the changes of blood pressure, blood potassium.

17 α-hydroxyenzyme deficiency patients often take “hypokalemia, hypertension” as the first symptom, and doctors with insufficient clinical experience are easy to be misdiagnosed as “primary aldosteronism”, so the diagnosis is usually delayed and is not conducive to timely treatment. Especially for the patients with male pseudohermaphroditism, if the lack of karyotype and other related tests, it is easy to mistake the patient as a female[7].

In general, the main clinical features of 17 α-hydroxyenzyme deficiency include

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hypertension and hypokalemia, and adolescent dysplasia [11]. Therefore, for the "female" patients who come to see a doctor with "no menarche", if they find that hypertension and hypokalemia exist at the same time, they should be highly alert to the possibility of the disease, and should pay special attention to the abnormal characteristics of the external genitalia when examining their bodies. In order to confirm whether there is male pseudohermaphroditism, chromosome karyotype analysis can be carried out, which is generally not difficult to identify.

Declaration of Interest: The authors declare no conflict of interest.

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