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*Case Report*

# One case of congenital adrenal cortical hyperplasia with 17-hydroxylase deficiency

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## Case Presentation

Congenitaladrenalhyperplasia (CAH) [1] is an autosomal recessive disorder causing associated enzyme deficiency or defects in the adrenal cortical hormone synthesis pathway due to genetic mutations. Resistance of cortisol biosynthesis causes excessive secretion of corticotropin-releasinghormone and CRH) and adrenocorticotropichormone (ACTH), leading to adrenal and pituitary hyperplasia.17-hydroxylase deficiency [2] is a rare type of CAH with an incidence of about 1 / 5000 to 1 / 100000. The patients have 17-hydroxylase deficiency in vivo due to CYP17A1 gene mutation, glucocorticosteroid and sex hormone generation disorder with excess halocorticoid synthesis.The diagnosis and treatment of one patient with 17-hydroxylase deficiency in our department is now reported.

Patient with basic medical history, 24 years old and a female social sex, was referred to our hospital for "limb numbness for 7 days and sudden weakness of limbs".Five days before the patient was admitted to another hospital due to weak limbs. After blood biochemistry and abdominal CT, he was diagnosed as "1. hypokalemia; 2. abdominal occupation", and the effect was not good after potassium supplementation treatment.Two days prior to admission, we was transferred to the emergency department of our hospital, and blood gas showed: blood potassium 2.18mmol/L,pH7.548,HCO332.2mmol/L; abdominal enhanced CT showed: abnormal bilateral adrenal strengthening nodules and mass shadow.The patient has not had menarche, and had no secondary sexual development, denied the chronic history of hypertension and diabetes, healthy parents, non-close relatives married, and had no history of similar diseases in the family.

On physical examination, the patient was 170cm in height, weighed 70kg, upper 76cm, lower 94cm, and lower / upper 1.236. The admission blood pressure was 133 / 93mmHg, the heart rate was 95 times / min, the physical examination had no axillary hair, pubic hair, thoracic deformity, breast stage TannerI, and the vulva was female naive type.No beard, Cui hair growth increased, limb muscle force grade V, muscle tension normal 1.3 laboratory inspection ion full items: potassium 3.49mmol/L(3.5-5.5), sodium 144 mmol/L (135-145), calcium 2.10mmol/L(2.1-2.8), inorganic phosphorus 1.28mmol/L(0.97-1.6), magnesium 0.86mmol/L(0.5-1.6).Sex hormone 6 + androgen 2: FSH (FSH)52.1mIU/mL (0-21.5), Luteloginogen (LH)17.8mIU/mL (0-95.6), Estrostradiol (E2)<5.00pg/ml(12.4-398), Prolactin (PRL)32.50ng/ml(4.8-23.3), Testosterone (TTE)<2.50ng/dl (0-80), Progesterone (PGN)8.32ng/ml(0.057-23.9), Androenedione <0.3ng/ml(0.3-3.5), Serum dehydroepiandrosterone <15.0ug/dL (35 – 430). The 24-hour urinary free cortisol (24h-UFC): <10ug / 24h (49-270). Primary aldehyde screening: renin (RENIN)0.24pg/ml(1.80-24.5), aldosterone (ALD)43.73pg/ml (29-240).Horizontal position test: lying position RENIN0.19pg/ml(1.80-24.5),ALD46.48pg/ml (29-240); standing position RENIN0.29pg/ml(2.80-28.5),ALD45.71pg/ml (31-351).Autoantibodies for all items: all are negative.Cortisol (Cor) rhythm: Cor8A m<1.00ug/dL<5-25<<Cor4Pm<1.00ug/dL<Cor<1.00ug/dL<ACTH rhythms: ACTH8Am71.8pg/ml (10-46); ACTH4Pm85 pg/ml; ACTH059 pg/ml.1.4 Imaging examination of abdominal enhancement CT: bilateral abnormal adrenal enhancement of nodules and mass shadow, internal fat density shadow and uneven enhancement scan, with the right size of about 17x12mm and about 98x83mm as shown in (Figure 1A) .X-line of chest: the thoracic vertebra bent slightly to the right is shown in Figure 1B.Pituitary MRI horizontal sweep shows: the pituitary form is slightly full, the height of about 0.9cm, see Figure 1C.X-ray of hand: the epiphyseal of the distal ulna appears, the epiphyseal is not closed; the distal radius is not closed; 8 wrist bone; bone age is less than the actual age, see Figure 1D.Gynecology B ultrasound: uterine body size is about 22x8x4mm, considered; bilateral ovaries were not detected.B ultrasound: diffuse lesions of left thyroid lobe; hypoecho nodules of bilateral thyroid lobe (TI-RADSIII).

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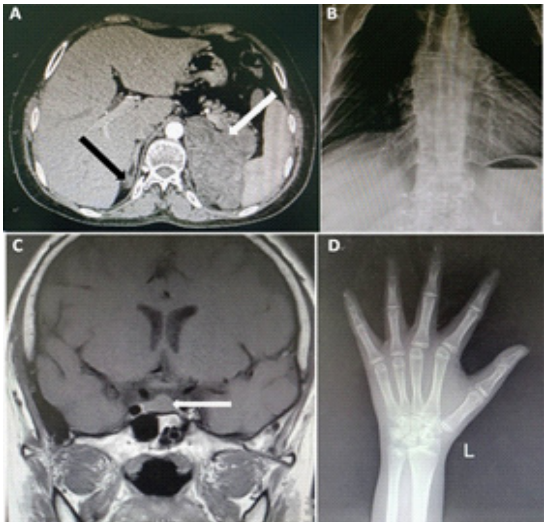


Figure 1: Shows the enhanced CT of the patient's abdomen, right adrenal hyperplasia by the black arrow, left adrenal hyperplasia by the white arrow; Figure C shows the patient's head MRI and hyperplastic pituitary by the white arrow.1.5 Chromosome analysis and genetic testing The analysis of chromosome karyotype: 46, XX.Genetic test: patient samples had a homozygous mutation of c.987delC in the 17-hydroxylase / 17,20 clease-related gene CYP17A1, and pedigree verification showed that the mutation was a heterozygous mutation of c.987delC from both the parents, in line with the genetic rules of the disease, as shown in (Figure 2).

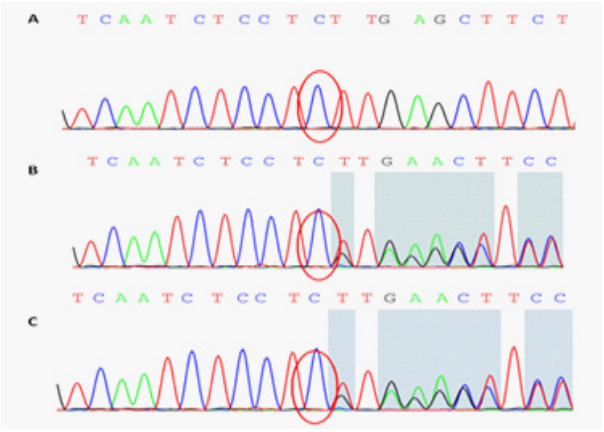


Figure 2: Results of genetic testing for patients and both parents.

Figure A shows the patient genetic test results showing the homozygous mutation of c.987delC for chr10:104592419; Figure B shows the result of chr10:10459 d e l 9; **Figure C** shows the result of c.987delC for chr10:104592419.1.6 Diagnosis and treatment In terms of diagnosis, the patient had a history of hypokalemia, hypertension, primary amenorrhea, and no secondary sign development on physical examination. Laboratory tests indicated hypokalemia and alkalosis; ACTH levels were increased, and the levels of renin, urinary free cortisol, estradiol, androdione, and dehydroepiandrosterone were low. The results of the medium-dose dexamethasone inhibition test showed that the urinary 17-hydroxycorticosteroid (17-OHCS), urinary 17-ketone steroid (17-KS) and ACTH levels were all reduced compared with before drug administration, as shown in (**Table 1**). Imaging examination shows: the basement uterus and the ovary is not explored, the ulnar radius epiphyseal has not been closed, the bone age is less than the actual age; pituitary and adrenal hyperplasia. Chromosomal was 46, XX, and genetic testing revealed the presence of a homozygous mutation in the CYP17A1 gene. Combined with the above clinical data, the patient was diagnosed as: congenital adrenal cortical hyperplasia; 17-hydroxylase / 17,20 lyase deficiency. In terms of treatment, prednisone acetate was administered at 12 PM daily from February 26, and blood pressure, ion whole term, 24-h urine ion quantification, 17-hydroxyprogesterone (17-OHP), sex hormone 6 and androgen II were continuously monitored, as shown in (**Table 2**). After discharge, prednisone acetate was given 5 mg/d, instructed to take orally at 12 am every day to inhibit ACTH to improve the symptoms of hypokalemia and hypertension, and 0.5 mg/d estradiol valerate orally early daily to promote secondary sexual development in women.

**Table 1:** Dexamethasone test before and after control urine 17-OHCS.

| Control | Before Dexa | 3days after Dexa | 5days after Dexa | reference value |
|---|---|---|---|---|
| Urine 17-OHCS（mg/L） | 8.26 | 3.57 | 3.62 | — |
| 24hUrine17-OHCS（mg/d） | 12.39 | 8.93 | 6.52 | 2.0-10.0 |
| Urine 17-KS（mg/L） | 5.71 | 4.02 | 7.34 | — |
| 24h Urin17-KS（mg/d） | 8.56 | 10.05 | 13.21 | 6.0-25.0 |
| Urine volume（L） | 1.50 | 2.50 | 1.80 | — |
| 17-αOHP（ng/mL） | 0.56 | 0.15 | 0.08 | 0.05-2.34 |
| Cor8Am（ug/dL） | ＜1.00 | ＜1.00 | — | 5-25 |
| ACTH 8 Am（pg/ml） | 71.80 | ＜5.00 | —— | 10-46 |

The follow-up patient was discharged on the March 5,2021 and followed up 3 months after discharge, reviewed for blood potassium 4.48 mmol/L, estradiol (E2)5.2pg/ml, 24 h urinary free cortisol (24h-UFC), 399ug / 24h, and levels were increased compared with those at diagnosis. Review cortisol and ACTH rhythm: Cor 8Am 1.26ug/dL; Cor4Pm<1.00ug/dL ; ACTH 8Am 29.10pg/ml(10-46); ACTH 4Pm26.90pg/ml, ACTH levels decreased, but the rhythm has not appeared. The abdominal CT showed: bilateral abnormal strengthening nodules and mass shadow of the adrenal glands, including solid, lipid and confounding density, and the right scan was about 16x12mm, and the left was about 113x83mm, which showed little change from the previous. After this follow-up, the adjusted prednisone tablet was 7.5 mg/d acetate, and the patient continued to follow-up thereafter 2 Discussion of 17-hydroxylase deficiency representing about 1% of CAH was first reported by Biglieri et al [3] in 1966.CYP17A1[4] is the pathogenic gene of the disease, located at 10q24-25, the gene spans 6569bp, composed of seven introns and 8 exons, expressed in both human adrenal and gonad [5].More than 100 mutations in the CYP17A1 gene are associated with 17-hydroxylase deficiency, including point mutations, insertion, deletion, and frameshift mutations, and the mutations are mostly located at the C terminus. Genetic mutation studies in 26 Chinese OHP patients showed [6].The c.985_987delinsAA and c.1460_1469del are the most common types of mutations, accounting for 60.8% and 21.7% of the mutant alleles, respectively.CYP17A1 encodes a cytochrome P450c17 protein with two enzymatically active [7]: 17-hydroxylase acting on 17-hydroxylation of progesterone and pregnenolone; 17,20-lyase catalyzes the conversion of 17-hydroxyenolone and 17-hydroxyprogesterone to deHEA and androdione, respectively.17-hydroxylase deficiency contains two types, a deficiency of 17-hydroxylase / 17,20-lyase deficiency (17-hydroxy-

**Table 2:** Pre-hospital treatment.

| Control | Dexa | | | | reference value |
|---|---|---|---|---|---|
| | | 1day after | 3days after | 5days after | |
| blood pressure（mmHg） | 139/93 | 122/84 | 106/74 | 115/79 | Sp90-139 Dp60-89 |
| potassium（mmol/L） | 2.92 | 5.19 | 5.35 | 5.34 | 3.5-5.5 |
| sodium（mmol/L） | 142 | 133 | 133 | 136 | 135-145 |
| calcium（mmol/L） | 1.98 | 2.25 | 2.21 | 2.29 | 2.1-2.8 |
| magnesium（mmol/L） | 0.72 | 1.02 | 1.02 | 0.9 | 0.5-1.6 |
| P（mmol/L） | 1.41 | 1.65 | 1.54 | 1.60 | 0.97-1.6 |
| 24hurinary potassium（mmol/d） | 68 | — | 54 | — | 25-100 |
| 24hurinary sodium（mmol/d） | 168 | — | 139 | — | 130-260 |
| 24hurinary chloride（mmol/d） | 172 | — | 112 | — | 170-250 |

lase / 17,20-lyasedeficiency, 17OHD) and only 17,20-lyase deficiency (isolated17,20-lyasedeficiency, ILD).This patient belongs to 17OHD, and the deficiency of both enzymes resulted in limited synthesis of cortisol, androgen, and estrogen, while corticosterone, 11-deoxycorticosterone (11-deoxycorticosterone, DOC) produced increased [8]. Disorder of cortisol synthesis can weaken the negative feedback inhibition on the pituitary, leading to increased ACTH generation and adrenal hyperplasia; decreased estrogen can be menstruation, breast and female genital development; low androgens can hinder the growth of pubic and axillary hair and reduce estrogen generation as a precursor substance. Because corticosterone acts as glucocorticoid, patients generally have no manifestations of primary adrenal dysfunction; increased DOC can cause water and sodium retention and low renin hypertensive [9], accompanied by hypokalemia, alkalism and weak limbs. The vast majority of patients are similar to the patient, with low potassium and hypertension [10], different from other patients: one is the diagnosis age, at 24, but for the secondary signs at puberty, leading to late diagnosis, and most 17OHD patients mainly primary amenorrhea and puberty, diagnosis age is under 20, the patient bilateral adrenal hyperplasia, the left adrenal mass size is about 98x83mm.A similar case was reported by Lee [11] et al, mainly for abdominal pain and hypertension, with a massive adrenal cortical adenoma with a left mass size of about 100x63x86mm, which was rare in the reported cases. Imaging characteristics of nine patients with 17-hydroxylase deficiency by Wang [12] et al showed that the average maximum area of 640.1mm2 on the transverse axis of the adrenal gland was only about 3 times greater than the normal value (150mm2), while the size of the adrenal mass increased more than 10 times the normal value. In terms of treatment, exogenous supplementation of glucocorticoids can feed back to inhibit ACTH and adrenal hyperplasia, reduce the secretion of halocorticoids, help relieve hypertension and hypoblood potassium, and iatrogenic Cushing syndrome should be avoided as far as possible. For female patients with 17OHD, estrogen replacement therapy should be performed if diagnosed at the appropriate time of puberty or in adults.In recent years, when estradiol is recommended instead of oral or percutaneous estrogen, the treatment should start at a lower initial dose and gradually increase to an adult dose. Oral estradiol was started at a dose of 0.5 mg/d, then raised to 1 – 2 mg/d within 1 – 3 years or transdermal absorption at 25 g / d and then gradually increased to 75 – 100 g / d [7].In conclusion, the diagnosis of 17-hydroxylase deficiency should be identified and differentiated as soon as possible, improve the medical history and physical examination, focus on sexual development problems; improve the relevant laboratory and imaging examination, and finally make the final diagnosis through the genetic test results. Patients with 17OHD should be clearly diagnosed and treated as soon as possible, in order to obtain normal growth, development and reproductive capacity.

## References

1. Hannah-Shmouni F, Chen W, Merke DP. Genetics of Congenital Adrenal Hyperplasia[J]. Endocrinol Metab Clin North Am. 2017; 46(2):435-458.

2. Oh YK, Ryoo U, Kim D, et al. 17α-hydroxlyase/17, 20-lyase deficiency in three siblings with primary amenorrhea and absence of secondary sexual development[J]. J Pediatr Adolesc Gynecol. 2012; 25(5):103-105.

3. Biglieri EG, Herron MA, Brust N. 17-hydroxylation deficiency in man[J]. J Clin Invest. 1966; 45(12):1946-1954.

4. Picado-Leonard J, Miller WL. Cloning and sequence of the human gene for P450c17 (steroid 17 alpha-hydroxylase/17,20 lyase): similarity with the gene for P450c21[J]. DNA. 1987; 6(5):439-448.

5. Chung BC, Picado-Leonard J, Haniu M, et al. Cytochrome P450c17 (steroid 17 alpha-hydroxylase/17,20 lyase): cloning of human adrenal and testis cDNAs indicates the same gene is expressed in both tissues[J]. Proc Natl Acad Sci USA. 1987; 84(2):407-411.

6. Hang M, Sun S, Liu Y, et al. New, recurrent, and prevalent mutations: Clinical and molecular characterization of 26 Chinese patients with 17alpha-hydroxylase/17,20-lyase deficiency[J]. J Steroid Biochem Mol Biol. 2015; 150:11-16.

7. Auchus RJ. Steroid 17-hydroxylase and 17,20-lyase deficiencies, genetic and pharmacologic[J]. J Steroid Biochem Mol Biol. 2017; 165(Pt A):71-78.

8. Kota SK, Modi K, Jha R, et al. 17-α-Hydroxylase deficiency: An unusual case with primary amenorrhea and hypertension. Indian J En-

docrinol Metab[J]. 2011; 15(2):127-129.

9. Auchus ML, Auchus RJ. Human steroid biosynthesis for the oncologist[J]. J Investig Med. 2012; 60(2):495-503.

10. Kim YM, Kang M, Choi JH, et al. A review of the literature on common CYP17A1 mutations in adults with 17-hydroxylase/17,20-lyase deficiency, a case series of such mutations among Koreans and functional characteristics of a novel mutation[J]. Metabolism. 2014; 63(1):42-49.

11. Lee SJ, Song JE, Hwang S, et al. Untreated Congenital Adrenal Hyperplasia with 17-α Hydroxylase/17,20-Lyase Deficiency Presenting as Massive Adrenocortical Tumor[J]. Endocrinol Metab (Seoul). 2015; 30(3):408-413.

12. Wang Y, Tian XL, Sun HR, et al. Imaging characteristics of feminization induced by 17α-hydroxylase deficiency syndrome. Radiologic Practice[J]. Radiologic Practice. 2018; 33(09):923-926.