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CASE REPORT

17α-hydroxylase/17,20 carbon chain lyase deficiency caused by p.Tyr329fs homozygous mutation: Three case reports

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Abstract

BACKGROUND

p.Tyr329fs is a cytochrome P450c17 mutation among Chinese individuals. However, data on 17-α-hydroxylase deficiency caused by cytochrome P450c17 p.Tyr329fs homozygous mutation are lacking. This paper is a case report of three patients homozygous for p.Tyr329fs who were diagnosed with 17-α-hydroxylase deficiency between 2005 and 2019.

CASE SUMMARY

Case 1 presented with hypertension, hypokalemia, sexual infantilism and delayed bone age. The patient had a 46, XY karyotype, was homozygous for p.Tyr329fs and was recently treated with dexamethasone 0.375 mg qn. Case 2 presented with hypokalemia, sexual infantilism, osteoporosis and delayed bone age. The patient had a 46, XY karyotype, was homozygous for p.Tyr329fs and was treated with dexamethasone 0.75 mg qn at the last follow-up. Serum potassium and blood pressure could be maintained within normal range for cases 1 and 2. Case 3 presented with amenorrhea, sexual infantilism, osteopenia and delayed bone age. The patient had a 46, XX karyotype, was homozygous for p.Tyr329fs and was treated with dexamethasone 0.75 mg qn and progynova 1 mg qd. Outpatient follow-up revealed an adrenocorticotropic hormone (8 AM) of < 5.00 pg/mL.

CONCLUSION

The homozygous p.Tyr329fs mutation usually manifests as a combined deficiency, and definitive diagnosis depends primarily on genetic testing.

Key Words: Cytochrome P450c17; 17-α-hydroxylase-17,20-lyase deficiency; Phenotype;

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Core Tip: 17-α-hydroxylase deficiency is a rare type of congenital adrenal hyperplasia. The clinical manifestations of 17-α-hydroxylase deficiency are hypo-reninemic hypertension, hypokalemia, male pseudohermaphroditism, female sexual infantilism and primary amenorrhea. The disease is caused by mutations in the gene encoding cytochrome P450c17 that lead to 17-α-hydroxylase/17,20 carbon chain lyase deficiency. The present study presents the data of three patients who were diagnosed with 17-α-hydroxylase deficiency that was caused by p.Tyr329fs homozygous mutation. These three cases suggest that the homozygous p.Tyr329fs mutation usually manifests as a combined deficiency and that the definite diagnosis depends on genetic testing.

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INTRODUCTION

Seventeen α-hydroxylase deficiency (17OHD) is a rare type of congenital adrenal hyperplasia described in 1966 by Biglieri *et al*[1]. The incidence of 17OHD is estimated to be 1 per 50000 individuals[2]. The clinical manifestations of 17OHD are hypo-reninemic hypertension, hypokalemia, male pseudohermaphroditism, female sexual infantilism and primary amenorrhea[1,3] due to the involvement of adrenal and gonadal glands[4]. The disease is caused by mutations in the gene encoding cytochrome P450c17 (CYP17), causing 17-α-hydroxylase/17, 20 carbon chain lyase deficiency[5,6]. The involvement of adrenal glands leads to cortisol synthesis defects in patients harboring CYP17 mutations that are overcompensated by adrenocorticotropic hormone (ACTH) secretion. This stimulates the synthesis of large amounts of 11-deoxycorticosterone (DOC) and corticosterone[7]. High levels of DOC induce hypertension, hypokalemia and suppression of the renin–angiotensin system[7]. In the gonads, 17-α-hydroxylase/17, 20 carbon chain lyase deficiency results in lack of androgen synthesis, leading to the lack of characteristic features in males and sexual development in females[8].

To date, more than 200 cases have been reported worldwide with over 100 gene mutations[9], including 80 inactivating mutations in Chinese patients[10]. These mutations vary across ethnic groups and geographical regions. The two most common mutations in the Chinese population are p.Tyr329fs and del D487-F489[10]. In 2004, the Ruijin Hospital reported the first p.Tyr329fs homozygous mutation in China[11]. The frequency of p.Tyr329fs mutation in patients with 17OHD in China[10] necessitates an in-depth analysis of the phenotype of patients with this mutation to facilitate improved clinical diagnosis and treatment. Therefore, the present study reports the data of three patients who were diagnosed with 17OHD due to p.Tyr329fs homozygous mutations at the Department of Endocrinology of the First Hospital affiliated to the University of Science and Technology of China (Anhui Provincial Hospital) from 2005 to 2019. A literature review was conducted to compare the three cases with other reported cases.

CASE PRESENTATION

Chief complaints

Case 1: The social gender of the patient was female, and her height was 1.63 m at presentation. She had slightly dark skin and was of Han ethnicity. She was diagnosed

with 17OHD at 16 years of age.

Case 2: The social gender of the patient was female. She was of Han ethnicity. The patient was diagnosed with 17OHD at the age of 27 years.

Case 3: The social gender of the patient was female. At the time of diagnosis, the patient was 16 years of age with a height of 1.55 m.

History of present illness

Case 1: The patient was admitted to the Neurosurgery Department of our hospital due to spontaneous subarachnoid hemorrhage in November 2011. Cerebral angiography on November 16, 2011 exhibited a middle basilar artery aneurysm that was treated with aneurysm embolization.

Case 2: None.

Case 3: In March 2019, the patient was admitted due to amenorrhea.

History of past illness

Case 1: In May 2005, the patient was admitted to the Department of Endocrinology of the Anhui Provincial Hospital with a chief complaint of paroxysmal limb weakness for 15 years and headache and dizziness for 6 mo. The patient had a history of repeated hypokalemia since the age of 1 yr and was diagnosed with elevated blood pressure 6 mo before admission.

Case 2: The patient had undergone orchiectomy and mammoplasty at another hospital 5 yrs earlier.

Case 3: None.

Physical examination

Case 1: Physical examination showed a blood pressure of 154/133 mmHg. The patient had slightly dark skin with no obvious pigmentation, breasts at Tanner stage I and external genitalia exhibiting female sexual infantilism.

Case 2: Physical examinations after admission indicated a blood pressure of 124/90 mmHg and height of 1.68 m; the external genitalia exhibited female sexual infantilism.

Case 3: Physical examination exhibited no hypertension and hypokalemia. Breasts were Tanner stage I, and the external genitalia exhibited female sexual infantilism.

Laboratory examinations

Case 1: Laboratory tests and B-mode ultrasound tests were performed. Serum potassium was 3.06 mmoL/L, estrogen (E_2) was 149.63 pmoL/L, progesterone was 1.87 nmoL/L, testosterone (T) was 0.60 nmoL/L, luteinizing hormone (LH) was 24.01 IU/L, follicle stimulating hormone (FSH) was 42.40 IU/L, cortisol (COR) (8 AM) was 61.82 nmoL/L, COR (4 PM) was 52.31 nmoL/L, COR (12 PM) was 7.81 nmoL/L, and blood aldosterone (Ald) (lying position) was 702.27 pmoL/L.

Case 2: The lowest blood potassium levels after admission were 2.36 mmoL/L, E_2 was 151.00 pmoL/L, progesterone was 20.40 nmoL/L, T was 0.69 nmoL/L, LH was 46.60 IU/L, FSH was 119.00 IU/L, dehydroepiandrosterone sulfate was < 35.0 μg/dL, ACTH (8 AM) was 67.60 pg/mL, COR (8 AM) was 64.80 pg/mL, COR (4 PM) was 32.60 nmoL/L, COR (12 PM) was < 27.60 nmoL/L, Ald (lying position) was 353.85 pmoL/L, and plasma renin activity was 22.30 pg/mL/h.

Case 3: Auxiliary examinations after admission exhibited an FSH of 83.75 IU/L, LH of 10.38 IU/L, progesterone of 8.94 nmoL/L, T of 0.01 nmoL/L, E_2 of 19.00 pmoL/L, dehydroepiandrosterone sulfate < 35.00 μg/dL, ACTH (8 AM) of 46.2 pg/mL, COR (8 AM) of 7.43 nmoL/L, COR (4 PM) of 0.01 nmoL/L, COR (12 PM) of 0.01 nmoL/L, Ald (lying position) of 196.50 pmoL/L, and a plasma renin activity of 12.50 pg/mL/h.

Imaging examinations

Case 1: Pelvic ultrasound exhibited an absence of uterus, and the ovaries were not detected.

Case 2: B-mode ultrasound of the pelvic cavity did not exhibit uterus and ovaries. Bone mineral density suggested osteoporosis. Bone age films exhibited delayed bone

age.

Case 3: A color doppler ultrasound of the pelvic cavity suggested a primordial uterus. The bone mineral density was lower than normal. The bone age films exhibited delayed bone age. Adrenal computed tomography exhibited a slight thickening of the left adrenal gland.

FINAL DIAGNOSIS

Case 1

Genetic tests were completed (Supplementary Figure 1), and a diagnosis of p.Tyr329fs homozygous mutation was confirmed. The karyotype analysis indicated a 46, XY karyotype. Dexamethasone was reduced to 0.375 mg qn at discharge. Recently, the patient was treated with dexamethasone 0.375 mg qn. Serum potassium and blood pressure could be maintained within normal range.

Case 2

The karyotype analysis revealed a 46, XY karyotype. Genetic testing was performed (Supplementary Figure 2), and the patient was diagnosed with p.Tyr329fs homozygous mutation.

Case 3

Genetic testing was completed (Supplementary Figure 3), and the patient was diagnosed with p.Tyr329fs homozygous mutation. The karyotype analysis exhibited a 46, XX karyotype.

TREATMENT

Case 1

During hospitalization, the patient was administered 1.0 M of oral potassium chloride sustained-release tablets tid and nitrendipine 10 mg for replacement therapy. Blood potassium recovered to 3.60 mmoL/L during hospitalization, and blood pressure was 145/97 mmHg before discharge. Oral prednisone 10 mg bid was prescribed at discharge. The patient did not attend the follow-ups as instructed and took prednisone irregularly from 2005 to 2011. The blood pressure during this period is unknown.

Case 2

Intravenous potassium supplementation and oral potassium chloride sustained release tablets 1.0 M tid were administrated during hospitalization.

Case 3

Progynova 1 mg qd and dexamethasone 0.75 mg qn were administered at discharge.

OUTCOME AND FOLLOW-UP

Case 1

In February 2013, the patient was admitted again due to repeated edema of both lower limbs for more than 1 yr. At admission, blood potassium was 4.39 mmoL/L, blood pressure was 148/96 mmHg, height was 1.80 m, and ACTH (8 AM) was 7.88 pg/mL. Bone age films exhibited delayed bone age.

Case 2

At discharge, dexamethasone 0.75 mg qn was administered, blood potassium returned to 3.82 mmoL/L, and blood pressure was 120/88 mmHg. Dexamethasone 0.75 mg qn was prescribed at the last follow-up to maintain blood pressure and serum potassium in the normal range.

Case 3

Outpatient follow-up in August 2019 exhibited that ACTH (8 AM) was < 5.00 pg/mL. A B-mode ultrasound of the pelvic cavity exhibited a uterine body of 26 mm × 18 mm × 12 mm, cervix of 30 mm × 13 mm and endometrial thickness of 3 mm. The ovaries were not detected. The patient was treated with progynova 1 mg qd and dexamethasone 0.75 mg qn at the last follow-up.

DISCUSSION

Among cytochrome P450c17 mutations, p.Tyr329fs is the most common mutation among the Chinese population. However, data on 17OHD caused by CYP17 p.Tyr329fs homozygous mutation are lacking. This report presents cases of three patients with 17OHD and homozygous for p.Tyr329fs (Tables 1 and 2). The results of gene sequencing, family pedigree and details of the primers used for CYP17A1 gene testing are provided in the Supplementary Materials. The three case presentations in the present study suggest that the homozygous p.Tyr329fs mutation usually manifests as a combined deficiency. The definite diagnosis depends mainly on genetic testing.

17OHD is an autosomal recessive genetic disease and is caused by defective expression of the *CYP17A1* gene. This gene encodes the P450C17 protein, which is a microsomal cytochrome P450 enzyme with the activities of 17-α-hydroxylase/17, 20 carbon chain lyase[7,9]. *CYP17A1* gene mutations can cause defects and dysfunction of these two enzymes. The synthesis of COR and sex hormones such as T, E_2 and dehydroepiandrosterone sulfate is blocked, which leads to secondary sex characteristic dysplasia, primary amenorrhea, delayed bone age and osteoporosis[7,9]. The height of patients can often continue to increase during adulthood, and they can eventually be taller than the average female[7,9]. The reduction in COR and sex hormones decreases the negative feedback, which stimulates the increase in ACTH, LH and FSH along with adrenal hyperplasia[7,9]. ACTH and melatonin are homologous, and patients may have skin pigmentation. The accumulation of the precursor progesterone leads to an increase in the conversion to corticosterone and DOC. These two hormones have glucocorticoid-like effects, and the patients generally do not have clinical manifestations of adrenal insufficiency. Corticosterone and DOC are precursors of Ald and can also retain sodium and remove potassium, leading to hypertension with hypokalemia. Liquid retention inhibits renin activity and Ald production. Therefore, Ald in these patients can appear to decrease, be normal or increase. As an intermediate product in the process of COR synthesis, 17-hydroxyprogesterone can be elevated, decreased or normal in these patients. Therefore, it is not used as a screening indicator. In the present report, despite some variability in the clinical presentation among the three cases, these biochemical changes were observed.

According to the degree of enzyme deficiency, 17OHD can be divided into complete combined deficiency, partial combined deficiency and isolated 17, 20-lyase deficiency. Combined deficiency refers to the combined absence of 17-α-hydroxylase and 17,20 carbon chain lyase activities, whereas isolated 17, 20-lyase deficiency only affects the gonads[9]. The sex hormone synthesis is impaired, and glucocorticoid synthesis is not affected. Patients with complete combined deficiency have typical clinical manifestations such as hypertension and hypokalemia. Genetic females (46, XX) and males (46, XY) display female genitalia, the lack of adolescent gonadal development and delayed bone age caused by the lack of sex hormones. Patients with a partial combined deficiency may have spontaneous regular or irregular menstruation without associated hypertension and hypokalemia, and the pudendum may be hermaphroditism[12].

Low-dose glucocorticoids are the first choice for the management of 17OHD. The goal of the treatment is to reduce DOC production rather than reduce it to the normal range because long-term glucocorticoid replacement can inhibit the adrenal axis and increase osteoporosis. If glucocorticoids alone cannot manage the blood pressure and potassium levels, a mineralocorticoid receptor antagonist such as spironolactone or eplerenone can be used in combination. Patients who have reached puberty and display adult female phenotype should receive estrogen replacement therapy as soon as possible to promote the development of secondary sex characteristics. Additionally, it should be started with small doses and gradually increased to the adult dose. For patients with an intact uterus, progesterone and medroxyprogesterone acetate can be used to induce withdrawal bleeding. For patients with 46, XY karyotype with partial combined deficiencies and those raised as males from an early age, androgen replacement therapy is needed after the patient reaches puberty[9]. Reports from

Table 1 Clinical characteristics of the patients

Patients	Consanguineous	Hypertension and hypokalemia	Female (46, XX) primary amenorrhea and undeveloped secondary sex characteristics	Male (46, XY) feminization of the genitalia	Skin pigmentation	Bone age delay	Bone mineral density was below that of normal peers	CT indicated adrenal hyperplasia
Case 1	No	Both	--	Yes	No	Yes	Yes	Yes
Case 2	Yes	Hypokalemia only	--	Yes	No	Yes	Yes	Unknown
Case 3	Unknown	No	Yes	--	Yes	Yes	Yes	Yes
Yang *et al*[17], 2006	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Liang *et al*[18], 2008	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Wei *et al*[19], 2018	Unknown	Hypertension only	--	Yes	Yes	Yes	Unknown	Unknown
Papi *et al*[20], 2018	Unknown	Both	--	Yes	Unknown	Yes	Yes	Yes
Sun *et al*[21], 2017	Unknown	Both	Yes	--	Unknown	Unknown	Unknown	Unknown

CT: Computed tomography.

Table 2 Clinical and biochemical characteristics of the patients

Patients	Age in yr	Height in cm	Blood pressure in mmHg	Blood potassium in mmoL/L	FSH in IU/L	P in nmoL/L	T in nmoL/L	E_2 in pmoL/L	LH in IU/L	PRA in pg/mL/h	DHEAS in mg/dL	ACTH (8 AM) in pg/mL	COR (8 AM) in nmoL/L
Case 1	16	163	154/133	3.06	42.40	1.87	0.60	149.63	24.01	NA	NA	47.1	61.82
Case 2	27	168	124/90	2.36	119.00	20.40	0.69	151.00	46.60	NA	< 35	67.6	64.80
Case 3	16	155	110/70	3.55	83.75	8.94	0.01	19.00	10.38	12.50	< 35	46.2	7.43

Reference range: Blood potassium: 3.50-5.50 mmoL/L; FSH: 1.27-19.26 IU/L (Male), 1.00-11.30 IU/L (Female); P: 0.44-6.55 nmoL/L (Male), 1.00-3.80 nmoL/L (Female); T: 6.07-27.10 nmoL/L (Male), 0.00-2.65 nmoL/L (Female); E_2: 0.00-206.00 pmoL/L (Male), 124.00-1468.00 pmoL/L (Female); LH: 1.24-8.62 IU/L (Male), 1.10-11.60 IU/L (Female); PRA: 50-790 pg/mL/h; DHEAS: 35-430 μg/dL; ACTH (8AM): 6-56.7 pg/mL; COR (8AM): 184.85-623.53 nmoL/L. ACTH: Adrenocorticotropic hormone; COR: Cortisol; DHEAS: Dehydroepiandrosterone; E_2: Estradiol; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; NA: Not available; P: Progesterone; PRA: Plasma renin activity; T: Testosterone.

foreign countries indicate that patients with partial combined deficiencies are successfully fertilized by the freezing and thawing embryo technology and had a live birth, one of which had an unknown type of gene mutation[13], whereas another case was a homozygous 3 bp deletion mutation in exon 1 of the *CYP17A1* gene[14].

All three patients included here underwent genetic testing. All three were homozygous for the p.Tyr329fs mutation, which is the tyrosine encoded by codon 329 in the *CYP17A1* gene is changed to a threonine. A frameshift mutation is induced, which generates a truncated protein containing only 417 amino acids lacking the highly conserved heme-binding regions of codons 435 and 455. This region plays a key role in the catalytic function of the enzyme[15]. In the present report, the blood COR and sex hormones of the three patients were significantly reduced, manifesting as female sexual infantilism, primary amenorrhea, and male pseudohermaphroditism. Two patients showed typical hypertension and/or hypokalemia, whereas one patient had

no hypertension and hypokalemia and was considered to have a partial combined deficiency. Some authors in China[16] tested the enzyme function by transfecting HEK-293T cells *in vitro* and observed that the p.Tyr329fs mutation completely inactivated 17-α-hydroxylase and 17,20 carbon chain lyase. Although the disease is an autosomal recessive genetic disease, one patient had a clear history of a consanguineous marriage of parents. No reports of natural conception in patients with this mutation type have been reported.

CONCLUSION

The p.Tyr329fs mutation is one of the most common genetic mutations in patients with 17OHD in China. Its definite diagnosis depends on genetic testing. Blood pressure and serum potassium usually return to normal following glucocorticoid treatment. After the patient reaches puberty, estrogen therapy can be used to promote the development of secondary sex characteristics.

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REFERENCES

1 **Biglieri EG**, Herron MA, Brust N. 17-hydroxylation deficiency in man. *J Clin Invest* 1966; **45**: 1946-1954 [PMID: 4288776 DOI: 10.1172/JCI105499]
2 **Grumbach MM**, Hughes IA, Conte FA. Disorder of sex differentiation. In: Larsen PR, Kronenberg HM, Melmed S, editors. Williams Textbook of Endocrinology (10th edition). Philadelphia: Saunders; 2003
3 **New MI**. Male pseudohermaphroditism due to 17 alpha-hydroxylase deficiency. *J Clin Invest* 1970; **49**: 1930-1941 [PMID: 5456802 DOI: 10.1172/JCI106412]
4 **Chung BC**, Picado-Leonard J, Haniu M, Bienkowski M, Hall PF, Shively JE, Miller WL. 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. *Proc Natl Acad Sci USA* 1987; **84**: 407-411 [PMID: 3025870 DOI: 10.1073/pnas.84.2.407]
5 **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. *DNA* 1987; **6**: 439-448 [PMID: 3500022 DOI: 10.1089/dna.1987.6.439]
6 **Matteson KJ**, Picado-Leonard J, Chung BC, Mohandas TK, Miller WL. Assignment of the gene for adrenal P450c17 (steroid 17 alpha-hydroxylase/17,20 lyase) to human chromosome 10. *J Clin Endocrinol Metab* 1986; **63**: 789-791 [PMID: 3488328 DOI: 10.1210/jcem-63-3-789]
7 **Wong SL**, Shu SG, Tsai CR. Seventeen alpha-hydroxylase deficiency. *J Formos Med Assoc* 2006; **105**: 177-181 [PMID: 16477341 DOI: 10.1016/S0929-6646(09)60342-9]
8 **Yanase T**, Simpson ER, Waterman MR. 17 alpha-hydroxylase/17,20-lyase deficiency: from clinical investigation to molecular definition. *Endocr Rev* 1991; **12**: 91-108 [PMID: 2026124 DOI: 10.1210/edrv-12-1-91]
9 **Auchus RJ**. Steroid 17-hydroxylase and 17,20-lyase deficiencies, genetic and pharmacologic. *J Steroid Biochem Mol Biol* 2017; **165**: 71-78 [PMID: 26862015 DOI: 10.1016/j.jsbmb.2016.02.002]
10 **Bao X**, Ding H, Xu Y, Cui G, He Y, Yu X, Wang DW. Prevalence of common mutations in the CYP17A1 gene in Chinese Han population. *Clin Chim Acta* 2011; **412**: 1240-1243 [PMID: 21420394 DOI: 10.1016/j.cca.2011.03.019]
11 **Sun SY**, Bi YF, Liu JM, Wang WQ, Zhao YJ, Ning G, Li XY. [A novel homozygous mutation (TAC/AA) at codon 329 in CYP17A1 gene causes 17α-hydroxylase deficiency--case report and pedigree study]. *Zhonghua Neifenmi Daixie Zazhi* 2004; **20**: 568-568
12 **Tao H**, Lu ZL, Zhang B, Wang Y, Sun ML. [Clinical characteristics of 17α-hydroxylase / 17, 20 -lyase deficiency and long term follow up results]. *Zhonghua Yixue Yichuanxue Zazhi* 2005; **2005**: 442-445 [DOI: 10.3760/j.issn:1003-9406.2006.02.001]
13 **Levran D**, Ben-Shlomo I, Pariente C, Dor J, Mashiach S, Weissman A. Familial partial 17,20-desmolase and 17alpha-hydroxylase deficiency presenting as infertility. *J Assist Reprod Genet* 2003; **20**: 21-28 [PMID: 12645864 DOI: 10.1023/a:1021206704958]
14 **Kitajima M**, Miura K, Inoue T, Murakami Y, Kitajima Y, Murakami N, Taniguchi K, Yoshiura KI, Masuzaki H. Two consecutive successful live birth in woman with 17α hydroxylase deficiency by frozen-thaw embryo transfer under hormone replacement endometrium preparation. *Gynecol Endocrinol* 2018; **34**: 381-384 [PMID: 29068264 DOI: 10.1080/09513590.2017.1393512]

15 **Cao CX**, Wang O, Nie M, Li YX, Tong AL, Lu L, Lu ZL. [Clinical and molecular genetic analysis for a patient with 17 hydroxylase/17,20 Lyase deficiency]. *Basic Clin Med* 2009; **29**: 225-228 [DOI: 10.1007/978-1-4020-9623-5_5]

16 **Qiao J**, Han B, Liu BL, Liu W, Wu JJ, Pan CM, Jiang H, Gu T, Jiang BR, Zhu H, Lu YL, Wu WL, Chen MD, Song HD. A unique exonic splicing mutation in the CYP17A1 gene as the cause for steroid 17{alpha}-hydroxylase deficiency. *Eur J Endocrinol* 2011; **164**: 627-633 [PMID: 21282350 DOI: 10.1530/EJE-10-0933]

17 **Yang MH**, Wu XB, Li T, Wang MY. [Clinical and molecular genetic features of 17alpha-hydroxylase deficiency: study of a case]. *Zhonghua Yi Xue Za Zhi* 2006; **86**: 2900-2904 [PMID: 17288786]

18 **Liang J**, Qiao J, Chen X, Wu QQ, Heng H, Zhang T, Zhao JJ, Song HD. [A clinical and genetic analysis of a pedigree with two 46,XY patients suffering from 17alpha-hydroxylase deficiency]. *Zhonghua Nei Ke Za Zhi* 2008; **47**: 482-485 [PMID: 19040066]

19 **Wei HL**, Lu S, Wang XL, Li JW, Cui YP, Yao YS. [17α-Hydroxylase deficiency with severe hypertension as the initial symptom in a child]. *Zhongguo Dang Dai Er Ke Za Zhi* 2018; **20**: 675-679 [PMID: 30111479]

20 **Papi G**, Paragliola RM, Concolino P, Di Donato C, Pontecorvi A, Corsello SM. 46,XY Disorder of Sex Development Caused by 17*α*-Hydroxylase/17,20-Lyase Deficiency due to Homozygous Mutation of *CYP17A1* Gene: Consequences of Late Diagnosis. *Case Rep Endocrinol* 2018; **2018**: 2086861 [PMID: 29854486 DOI: 10.1155/2018/2086861]

21 **Sun M**, Yan X, Feng A, Wu X, Ye E, Wu H, Lu X, Yang H. A novel compound heterozygous mutation in the CYP17A1 gene in a patient with 17α-hydroxylase/17,20-lyase deficiency. *Discov Med* 2017; **24**: 175-182 [PMID: 29278670]

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