CLINICAL IMAGE

17α-hydroxylase deficiency associated with adrenal myelolipoma

Lingyu Chang, Dexin Yu, Fang Wang

Department of Radiology, Qilu Hospital of Shandong University, Jinan, China

A 31-year-old woman presented with limb weakness that had started 20 days before. She was diagnosed with hypokalemia (potassium, 2.10 mmol/l; reference range [RR], 3.50–5.30 mmol/l) and treated with potassium supplements. She had hypertension for more than 3 years and suffered from primary amenorrhea, hypoplastic breasts, and vaginal infantilism. She had no pubic or axillary hair. Laboratory work-up revealed decreased levels of cortisol (0.1 ng/ml; RR, 50–250 ng/ml), a significantly increased plasma level of adrenocorticotropic hormone (ACTH) (225.80 pg/ml; RR, 7.20–63.30 pg/ml), and elevation of 11-deoxycorticosterone and corticosterone levels (2945.4 pg/ml; RR <100 pg/ml and 122.12 ng/ml; RR, 0.53–15.60 ng/ml, respectively). Plasma renin activity (PRA) was decreased (0.91 pg/ml; RR, 4–38 pg/ml) and aldosterone levels were within the normal range (76.78 pg/ml; RR, 40–310 pg/ml). Levels of estradiol, testosterone, and dehydroepiandrosterone sulphate were markedly reduced (1.4 pg/ml; RR, 15–350 pg/ml; 10.4 pg/ml; RR, 80–600 pg/ml; and 0.9 ng/ml; RR, 830–3770 ng/ml, respectively).

Computed tomography (CT) and magnetic resonance imaging showed a fat-containing mass in the left adrenal gland and bilateral soft-tissue lesions at the orifice of the inner ring of the inguinal canal, as well as the absence of the uterus, ovaries, and vagina (FIGURE 1A–1D). Chromosome analysis revealed a 46,XY karyotype (genetic male), indicating a diagnosis of male pseudohermaphroditism. All of these findings led to the suspicion of 17α-hydroxylase deficiency (17OHD) caused by a mutation in the *CYP17A1* gene. The patient underwent genetic testing, and mutation analysis revealed 2 heterozygous genetic variants in exons 1 and 6 (FIGURE 1E and 1F).

A surgery was performed. Results of the histological examination indicated left adrenal medullary lipoma (AML) and bilateral atrophic testicular tissue. The diagnosis of 17OHD associated with AML was made.

17OHD due to mutations in the *CYP17A1* gene (10q24.3), inherited in an autosomal recessive pattern, has been previously described as a rare cause of congenital adrenal hyperplasia (CAH). It is characterized by hypertension, hypokalemia,

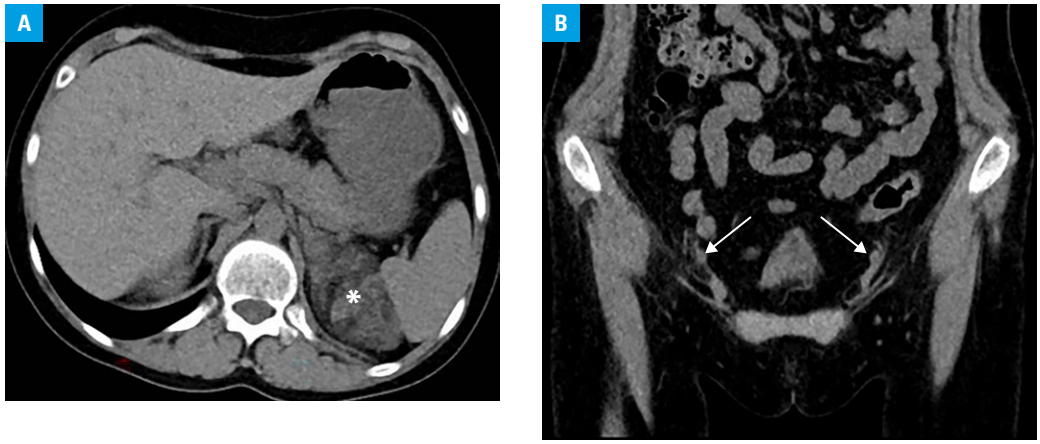
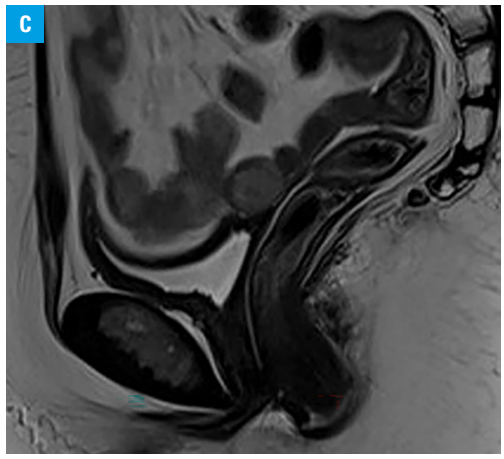
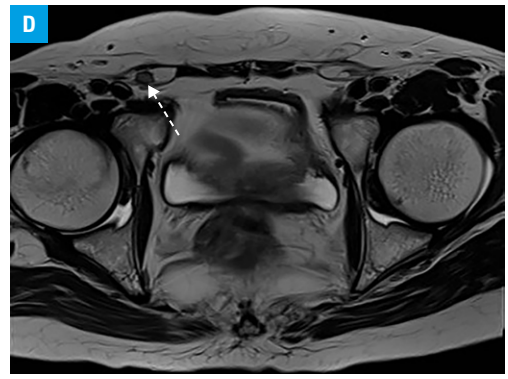
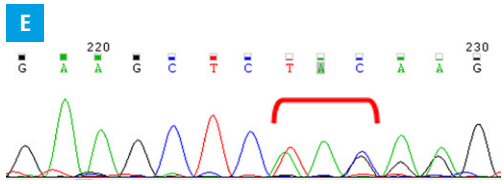


FIGURE 1 Radiological and mutation analysis findings; **A** – abdominal computed tomography (CT) showing a fat-containing mass in the left adrenal gland (asterisk), measuring 5 × 9 cm; **B** – CT with coronal reconstruction showing bilateral cord-shaped, nodular soft-tissue structures in the inguinal regions (arrows)

Correspondence to:
Fang Wang, MD, Qilu Hospital of Shandong University, Wenhua West Road 107, Lixia District, Jinan City, Shandong Province, 250012 Jinan, China, phone: +86 18560 081 580, email: 329571483@qq.com
Received: October 26, 2022.
Revision accepted: November 2, 2022.
Published online: November 15, 2022.
Pol Arch Intern Med. 2023; 133 (1): 16369
doi:10.20452/pamw.16369







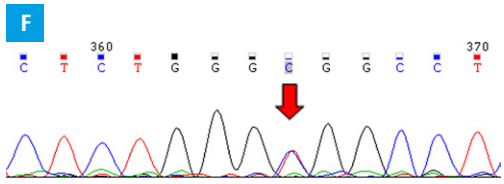


FIGURE 1 Radiological and mutation analysis findings; **C** – magnetic resonance imaging (MRI), sagittal plane, showing the absence of the uterus, vagina, and ovaries; **D** – T2-weighted MRI showing the right inguinal soft--tissue nodule with intermediate signal intensity (arrow); **E** – analysis of the heterozygous variant of c.985_987delinsAA (p.Y329Kfs*90) in exon 6 shows the replacement of nucleotide TAC by AA at codon 329, resulting in a frame-shift change with amino acid tyrosine-329 and leading to premature termination of protein translation; **F** – the p.R96W mutation causes a C-to-T transition in exon 1 that changes a CGG codon (arginase) to TGG (tryptophan), almost completely suppressing the activity of the mutant protein

and impaired sexual development. Deficiency in this enzyme can block the synthesis pathways of cortisol and lead to compensatory ACTH hypersecretion, which stimulates the synthesis of large amounts of deoxycorticosterone (DOC) and corticosterone by zona fasciculata.[1] High levels of DOC and corticosterone may induce mineralocorticoid excess, with different degrees of plasma volume expansion, hypertension, hypokalemia, and suppression of the PRA system, resulting in a very low serum aldosterone level in most patients with 17OHD.[2] In addition, impaired production of sex hormones causes sexual development abnormalities.

AMLs consist of bone marrow hematopoietic cells and adipose tissue. Most studies have shown that persistently high concentrations of ACTH are associated with the development of AMLs.[3,4] As glucocorticoid synthesis in patients with 17OHD is impaired, feedback secretion of ACTH is increased, which is a potential trigger for the development of AML.

This report presents a very rare case of CAH due to 17OHD associated with AML. Adrenal CT should be regularly performed in patients with CAH to monitor for the development of AML. In our patient, an exploratory laparotomy was required to remove the remaining gonads due to the high risk of future gonadoblastoma.

ARTICLE INFORMATION

ACKNOWLEDGMENTS We thank Fujun Genetics Technology, Inc. for whole-exome sequencing presented in this study, as well as Professors Ling Jiang and Fei Yan from the Endocrine Department of Qilu Hospital for their useful suggestions.

FUNDING None.

CONFLICT OF INTEREST None declared.

HOW TO CITE Chang L, Yu D, Wang F. 17α-hydroxylase deficiency associated with adrenal myelolipoma. Pol Arch Intern Med. 2023; 133: 16369. doi:10.20452/pamw.16369

REFERENCES

1 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.

2 Biglieri EG, Shambelan M, Slaton PE, Jr. Effect of adrenocorticotropin on desoxycorticosterone, corticosterone and aldosterone excretion. J Clin Endocrinol Metab. 1969; 29: 1090-1101.

3 Nermoen I, Falhammar H. Prevalence and characteristics of adrenal tumors and myelolipomas in congenital adrenal hyperplasia: a systematic review and meta-analysis. Endocr Pract. 2020; 26: 1351-1365.

4 Hamidi O, Raman R, Lazik N, et al. Clinical course of adrenal myelolipoma: a long-term longitudinal follow-up study. Clin Endocrinol. 2020; 93: 11-18.