A Rare Case of Hypertension in a Young (Fe)male

Sir,

Congenital adrenal hyperplasia (CAH) is a syndromic disease resulting from defects in various enzymes in the pathway of steroidogenesis. The most common form of CAH is 21 alpha hydroxylase deficiency. 17 alpha Hydroxylase deficiency is a rare form of CAH, with an estimated incidence of 1 in 50,000–100,000 individuals, and represents ~1% of all CAH cases.[1-3] The first case of 17 alpha hydroxylase deficiency was reported in 1966 by Biglieri et al.[3]

We report a case of a 32-year-old female patient who presented with the chief complaints of weakness of all the four limbs for the last 5 days, which were not associated with sensory and cranial disturbances. She was a nondiabetic and a known hypertensive since 2 years; she had no significant past history except for not attaining menarche and was diagnosed with atrophic uterus by a gynecologist during her childhood.

On examination, the patient was moderately built and well-nourished with a height of 178 cm, weight of 74 kg (BMI: 23.4 kg/m²), and an arm span of 172 cm. She had poorly developed secondary sexual characters with a lack of normal breast development (B1) and

[1] O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 2011;52:e162–93.
[2] Hemmelgarn BR, Gill JS, Heard SO, et al. A cohort study. BMC Nephrol 2019;20:68.
[3] Mohamed H, Ali A, Browne LD, O'Connell NH, Casserly L, Stack AG, et al. Catheter-related blood stream infections among Irish haemodialysis patients; A prospective cohort study. BMC Nephrol 2017;18:357.

Acknowledgements

There are no conflicts of interest.

Conflicts of interest

Nil.

Financial support and sponsorship

Mumbai.

Dhirubhai Ambani Hospital and Medical Research Institute, Nephrology department and dialysis unit at Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai - 400 053, Maharashtra, India.

Address for correspondence:

Dr. Tanu Singhal, Consultant Pediatrics and Infectious Diseases, Department of Pediatrics, Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Four Bungalows, Andheri West, Mumbai.

E-mail: tanusinghal@yahoo.com
absent axillary and sparse pubic hair (Stage III). Bilateral palpable inguinal swellings were noticed. Her BP was 140/90 mmHg on presentation. Investigations showed serum creatinine of 2.6 mg/dl, LH of 74 mIU/ml (normal range 0.5–16.9 mIU/mL), Follicle-stimulating hormone (FSH) of 91.50 mIU/ml (1.5–9.1 mIU/mL), progesterone of 12.95 ng/ml (normal level: follicular phase: 0.3–0.8 ng/ml, luteal phase: 4–20 ng/ml), adrenocorticotropic hormone (ACTH) of 77.8 pg/ml (0–46 pg/ml), and prolactin of 29.4 ng/ml (4.7–23.3 ng/ml) were elevated. However, her aldosterone of 9.2 ng/dl (7–340 ng/ml), cortisol of 1.50 µg/dl (5–25 µg/dl), testosterone of 0.03 ng/ml (0.08–0.6 ng/ml), and potassium levels of 2.5 mmol/l were decreased [Table 1]. Twenty-four-hours urinary potassium was 10 meq/day. Low urine K level could be due to the very low serum potassium at the time of testing. Arterial blood gas (ABG) analysis showed metabolic alkalosis (pH: 7.42; 30 mmol/l; PaCO₂ 42 mmHg). Ultrasonography of the abdomen and the pelvis showed absent uterus and ovaries. There was evidence of two well-defined hypoechoic structures with internal vascularity noted in bilateral inguinal regions likely to be testis, and also bilateral grade I/II renal parenchymal changes were noted. Renal biopsies was suggestive of hypertensive nephrosclerosis. Bilateral fundus examination revealed Grade I hypertensive retinopathy changes. 2D echo and renal artery Doppler were normal. Cytogenetic analysis was done by Giemsa (GTG) banding and the result was of a male karyotype (46XY). The patient’s clinical, hormonal, and metabolic characteristics were typical of 17 alpha hydroxylase deficiency. The patient was started on prednisolone (10 mg/day) and ethinyl estradiol 10 µg/day. Lifestyle modifications were advised and anti-hypertensives were continued. After 4 weeks, antihypertensives were tapered and stopped completely. Her blood pressure and potassium levels were normal at 6 weeks after discharge. She was continued on hormonal therapy and urologist opinion was taken regarding orchidectomy of both testes, as there is a chance of malignant transformation for which surgery was planned at a later date.

CAH is a spectrum that results from defects in various enzymes in the pathway of steroidogenesis. Pregnenolone, which is the common precursor for the steroid synthesis, is produced from the cholesterol. It is further metabolized by various enzymes to produce glucocorticoids, mineralocorticoids, adrenal androgens, and sex hormones. 17 alpha Hydroxylase helps in the metabolism of pregnenolone and progesterone through a chain of reactions to finally produce sex steroids and glucocorticoids. Its deficiency results in decreased production of the cortisol and the adrenal androgens and sex steroids. Genetic females (46XX) with complete deficiency of 17 alpha hydroxylase have primary amenorrhea and no pubertal development leading to hypoplastic breasts and lack of axillary and pubic hair. Genetically, male (46XY) patients have an absence of masculinization. However, normal Mullerian duct regression occurs because of normal production of Mullerian inhibitory factor from the testis. Thus, such patients have a blind vagina, absence of Mullerian structures (fallopian tubes and uterus, upper third of the vagina), and female external genitalia. Pregnenolone and progesterone increase the mineralocorticoid pathway resulting in an increase in 11-deoxycorticosterone, corticosterone, and 18-hydroxy corticosterone levels. In healthy individuals, decreased cortisol synthesis and the subsequent loss of feedback inhibition on pituitary ACTH release lead to an increase in ACTH release, in order to return cortisol production to normal levels. However, in CAH patients, overstimulation of the steroid synthetic pathway leads to the overproduction of mineralocorticoid precursors and hyperplasia of the adrenal cortex. High levels of mineralocorticoid precursors (11-deoxycorticosterone, corticosterone, and 18-hydroxy corticosterone) induce sodium and fluid retention, and loss of potassium and hydrogen, which consequently induces hypertension and hypokalemic alkalosis and flaccid paralysis. Hypertension was attributed to be the cause of renal failure in this patient, as biopsy showed that hypertensive changes and both eyes had grade 1 hypertensive retinopathy Recognition of 17OHD is difficult even after puberty; therefore, inappropriate managements are frequently encountered. Neonatal screening for CAH due to 21-α-hydroxylase deficiency can be done by measuring 17 alpha hydroxyprogesterone levels between 2 and 4 days after birth. However, the screening programs of 17-α-hydroxylase deficiency, which is relatively rare, have not been well described in the literature, but probably the levels of corticosterone, deoxycorticosterone, 18-hydroxy Deoxycorticosterone, Deoxycorticosterone and 18 hydroxycorticosterone can be tested as these are bound to increase in 17 alpha hydroxylase deficiency.

The mainstay of treatment is glucocorticoid therapy. Spironolactone is usually used as an antihypertensive agent and for the control of hirsutism in CAH; however, as our patient is a female phenotype (XY) with 17-α-hydroxylase

| Investigation | Result | Reference range |
|---------------|--------|-----------------|
| Creatinine    | 2.6 mg/dl | 0.7-1.2 |
| Sodium        | 146 mmol/l | 135-145 |
| Potassium     | 2.50 mmol/l | 3.5-5 |
| Cortisol      | 1.50 µg/dl | M: 6.2-19.4; E: 11.9 |
| Testosterone  | 0.03 ng/ml | 0.2-1 |
| FSH           | 91.50 mIU/ml | 1.5-12 |
| LH            | 74.60 mIU/ml | 1.7-8.6 |
| Prolactin     | 29.40 ng/ml | 3.4-24 |
| Aldosterone   | 9.2 ng/dl | At rest: 1-16, in motion: 3.5-30 |
| Plasma renin  | 0.04 ng/ml/h | |
| 11DOC         | 124 pg/dl | 3.76-4.20 |
deficiency, it can be used as an antihypertensive rather than for the control of hirsutism.

Due to the low incidence of adrenal crisis and other severe symptoms in untreated 17OHD, the diagnosis is often delayed. Patients usually present around adolescence or at the pubertal age and the awareness of the clinician about this condition is very important so that diagnosis should not be missed.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Anvesh Golla, Sreebhushan Raju, Krishna Prasad
Department of Nephrology, Nizams Institute of Medical Sciences, Hyderabad, Telangana, India
Address for correspondence:
Dr. Sreebhushan Raju,
Department of Nephrology, Nizams Institute of Medical Sciences, Punjagutta, Hyderabad - 500 082, Telangana, India. E-mail: Sreebhushan@hotmail.com

References
1. Oh YK, Ryoo U, Kim D, Cho SY, Jin DK, Yoon BK, et al. 17alpha-hydroxylase/17, 20-lyase deficiency in three siblings with primary amenorrhea and absence of secondary sexual development. J Pediat Adolesc Gynecol 2012;25:e103-5.
2. Miller WL. Congenital adrenal hyperplasias. Endocrinol Metab Clin North Am 1991;20:721-49.
3. Biglieri EG, Herron MA, Brust N. 17-hydroxylation in man. J Clin Invest 1966;45:1946-54.
4. Honour JW. Diagnosis of diseases of steroid hormone production, metabolism and action. J Clin Res Pediatr Endocrinol 2009;1:209-26.
5. Turcu AF, Aouchis RJ. The next 150 years of congenital adrenal hyperplasia. J Steroid Biochem Mol Biol 2015;153:63-71.
6. Larson A, Nokoff NJ and Travers S. Disorders of sex development: Clinically relevant genes involved in gonadal differentiation. Discov Med 2012;14:301-9.
7. Gungor O, Kiricelli F, Carrero JJ, Hur E, Dheir H, Simsir A, et al. Congenital adrenal hyperplasia: A rare cause of renal failure and a successful renal transplantation. Clin Nephrol 2012;78:145-8.
8. Speiser PW, White PC. Congenital adrenal hyperplasia. N Engl J Med 2003;349:776-88.

Hyperkalemia Unveiled: A Case of Barakat Syndrome
Here we present an interesting case of Barakat syndrome with resistant hyperkalemia due to hyporeninemic hypoaldosteronism (Type 4 renal tubular acidosis). Barakat or HDR syndrome is an autosomal dominant disorder that consists of triad of hypoparathyroidism, sensorineural deafness, and renal dysplasia. [1,2]

As per our knowledge, we report the first case of Barakat syndrome presenting with resistant hyperkalemia and convulsions.

A 39-year-old female was admitted with history of recurrent episodes of generalized seizures due to hypocalcemia despite being on oral calcium and sodium valproate and easy fatiguability for 3 months. Neuroimaging was normal. Further history revealed progressive hearing loss for last 6 years with bilateral moderate sensorineural hearing loss on audiometry. Laboratory parameters revealed blood urea of 60 mg/dl, serum creatinine 1.7 mg/dl, serum potassium 6.6 mEq/L, chloride 115 mEq/L serum calcium 3.9 mg/dl, albumin 4.6 g/dl, serum bicarbonate 18 mEq/L, serum anion gap 12 mEq/L (normal 8-16 mEq/L) and phosphorus 10.5 mg/dL. Electrocardiography demonstrated prolonged QT interval (0.52 sec) and tall T waves. Ultrasound abdomen showed a solitary right kidney with raised echogenicity. Further investigations yielded very low PTH of 0.23 pg/ml (normal range 15-65 pg/ml) by electrochemiluminescence immunoassay (ECLIA) and high TSH 22 miU/l (normal range 0.4-4 miU/l). Her urine examination revealed 770 mg of proteinuria in 24 hours urine collection. There was no history of diabetes, hypertension, fever, neck surgery or irradiation. There was no significant family history.