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A TRIAD TO DIAGNOSIS- CONGENITAL ADRENAL HYPERPLASIA

Pediatrics

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ABSTRACT

Congenital adrenal hyperplasia due to deficiency of 17 α Hydroxylase is an autosomal recessive condition caused by mutation of the CYP17A1 gene. The following case report demonstrates a rare case of 16 year old female, who presented to the Emergency Department with dehydration and generalized weakness (in a state of shock) with hypertension. She had persistent hypokalemia and her mother gave a history of not attaining menarche. Keeping a triad of hypokalemia, hypertension, and delayed puberty we investigated her endocrine workup which led to the diagnosis of 17 α Hydroxylase deficiency. She was later started on steroids and estrogen, which showed improvement in her clinical condition on follow-up.

KEYWORDS

delayed puberty, hypertension, hypokalemia, prednisolone, estrogen

INTRODUCTION

Congenital Adrenal Hyperplasia an endocrine disorder is caused because of various deficiencies of enzymes like 21 α hydroxylase, 17 α hydroxylase, 11 β hydroxylase, and 3 β hydroxysteroid dehydrogenase which are involved in the production of cortisol from cholesterol [1]. 21-hydroxylase deficiency is the most common deficient enzyme in CAH, which accounts for 90-95% of the cases, while the least common form of the disorder is 17 α hydroxylase, which is less than 1% of all CAH cases [2]. It is an autosomal recessive defect that occurs at the cytochrome P450 17A1 enzyme level. In P450c17 deficiency, hormones like estrogens, androgens, and cortisol cannot be produced. There occurs a compensatory increase in the synthesis of adrenocorticotrophic hormone (ACTH), because of the failure in cortisol synthesis which stimulates the synthesis of 11-deoxycorticosterone and corticosterone, both of which have strong mineralocorticoid action [2]. In severe cases, patients have female phenotype and they usually present with primary amenorrhea and absence of secondary sexual characteristics [3]. Here, we report a case of a 16-year-old female, who presented to us with a triad of hypertension, hypokalemia, and delayed puberty due to 17 α Hydroxylase deficiency.

Case report:

A 16-year-old female, the first issue of a non-consanguineous marriage presented in an emergency hour with fever, vomiting, and generalized weakness for 10 days. There was no history of rash, joint pain, icterus, cough, urinary complaints, or joint pain. There is a significant history of excessive thirst over one month. She had not attained menarche yet.
On examination, she is thinly built, having a height of 158 cm (75th centile) and a weight of 34 kg (less than 3rd centile). According to Tanner's staging, her breast development had progressed to Tanner stage 1 and pubic hair was sparse/underdeveloped. She was anxious, and alert with excessive demand for water. She had tachycardia (140 b/m), peripheral pulses weak, and peripheries cold with the acidotic type of breathing. She was exhibiting other signs of dehydration like dry tongue, and buccal mucosa, and her skin turgor was impaired.

On admission to the emergency department, a clinical diagnosis of shock was made, paradoxically her NIBP was 124/83 mm HG (90-95th centile). On other systemic examinations, no abnormality was noted. On central nervous examination, her power was grade 2 in the pelvic and pectoral girdle and grade 3 in the distal group of muscles. Her deep tendon reflexes were absent.

After collecting the critical sample, she was managed by appropriate fluid therapy to which she responded.

Laboratory parameters-Critical samples are as follows:

RBS	CBC	Sodium	Potassium	ABG	WIDAL
110 mg/ dL	Hb- 12 g/dL TLC-3200 cells/cu.mm Platelet-1.36 lakh	134 mEq/ L	2 mEq/ L	Metabolic acidosis	Positive 1: 320

Date	30/4/20	1/5/20	2/5/20	4/5/20	7/5/20	11/5/20	16/5/20	26/5/20
Urea	26	26	-	30	-	32	-	-
Creatinine	0.89	0.76	-	1.57	-	1.68	1.6	0.9
Sodium	134	136	-	137	-	139	-	-
Potassium	2	2	2	1.8	2	2.9	2.6	3.9
Urinary Sodium	-	<30	-	-	-	-	-	-
Urinary Potassium	-	12	-	-	-	-	-	-

After appropriate fluid management and antibiotic therapy, her hydration improved and her fever was controlled but there was persistent hypokalemia despite potassium correction (up to 60 mEq/L). Late her BP readings were in the hypertensive range (above 99th centile).

Once stabilized, she was shifted to the ward. Keeping the triad of persistent hypokalemia which was resistant to treatment, hypertension, and delayed puberty; we further investigated her with a few endocrine and hormonal tests:

Test	Result	Normal Range
FSH	15.6 (high)	0.64-10
LH	51.6	0.04-10
Serum Cortisol	0.2	5-23
Serum Aldosterone	3.3	5-9
Corticosterone	4191	140-690
DHEA	4.93	15-133
Estradiol	15	26-165
17 OHP	3.8	16-183

High FSH and LH were suggestive of hypergonadotropic hypogonadism. The reports were suggestive of congenital adrenal hyperplasia due to 17 α Hydroxylase.

She was started on oral steroids- prednisolone (0.2 mg/kg/day), and gradually, she showed improvement. Her blood pressure was controlled with Aldactone and her potassium level was corrected with potassium supplementation.

On follow up she was continued on oral steroids and started on oral estrogen therapy. After 6 months her breast development was of stage 2

Tanner scale.

DISCUSSION:

Congenital adrenal hyperplasia due to 17α-hydroxylase deficiency forms 1% of all cases of CAH [2]. A 17α-hydroxylase deficiency was first described in a 35-year-old patient with raised blood pressure, sexual infantilism, and primary amenorrhea in 1966 who was phenotypically female [4]. 17α-hydroxylase deficiency occurs on chromosome 10q24.3 due to mutations of CYP17A1. It codes for the enzyme CYP17A1, and it buffers both 17α hydroxylase and 17,20-lyase activity, which is necessary for the production of hormones like cortisol, androgens, and estrogen. Due to the deficiency, the steroid precursor products proximal to the enzymatic block are converted to progesterone, deoxycorticosterone (DOC), and corticosterone. High level of DOC leads to sodium as well as fluid retention with loss of potassium and consequently increased blood pressure because of its mineralocorticoid effect [5]. A similar case was described by Rasha Ammar et al. in an 8-year-old female with delayed secondary sexual characteristics and primary amenorrhea. But her phenotype was 46 XY [6]. The first case in Oman of congenital adrenal hyperplasia was a 22-year-old female with no secondary sexual characteristics and primary amenorrhea. She responded to steroids well [7]. In the case of affected males, they have ambiguous or female external genitalia due to a deficiency in the synthesis of androgen. There was a lack of negative feedback mechanisms from sex steroids hence follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were high. A gonadectomy is required to prevent the chances of testicular cancer. Female patients have normal genitalia but they show immature sexual development and primary amenorrhea caused by to deficiency of estrogen in adolescence [2]. A 17-year-old female of 46 XX phenotype had a similar presentation to our case. A year later she had progressed to Tanner stage 2. The main aim of prednisolone is to reduce the ACTH level. Estrogen therapy is indicated in all patients who wish to continue as female. [8]

CONCLUSION:

In this case report, we present a female patient with delayed puberty, hypokalemia, and hypertension due to 17 a-hydroxylase deficiency. Early diagnosis is required to reduce the severity of the disorder. To acquire maximum health advantages in improving sexual development and fertility and lowering the negative effects of 17α-hydroxylase deficiency, therapies should be customized to each patient's needs. Most patients have a better prognosis if the illness is detected early through screening and treated promptly. Genetic testing plays an important role in the diagnosis. Treatment with glucocorticoids and in-vitro fertilization can lead to a successful pregnancy in such 46, XX patients.

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