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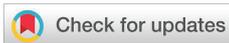
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Case Report

Apparent mineralocorticoid excess: A case of hypertension in a child with delayed diagnosis leading to stroke

echocardiography and electrocardiogram were normal. Serum 17 hydroxy progesterone was normal. Plasma free metanephrines, normetanephrines, serum cortisone and deoxycortisone were normal. Plasma aldosterone and plasma renin were low (Table 1). In view of the clinical picture of virilization and hypertension, provisional diagnosis of CAH was considered. Although Serum cortisol was normal and ACTH stimulation test was normal, patient was started on hydrocortisone orally and spironolactone was added. Genetic study for genome analysis was sent to confirm the diagnosis. After about 3 weeks, the child was rushed to emergency with right sided hemiparesis. MR venogram brain was suggestive of arteritis. Cerebrospinalfluid analysis was negative for any evidence

Introduction

Hypertension in pediatric patients, unlike adults, is mostly secondary to systemic disorders which may be renal, cardiovascular or endocrine, among others. Apparent mineralocorticoid excess (AME) is one such cause of hypertension. It occurs due to congenital deficiency of 11 beta hydroxysteroid dehydrogenase type 2 (11βHSD 2) which responsible for conversion of cortisol to cortisone [1]. Cortisol binds avidly to the mineralocorticoid receptors and due to higher circulating cortisol than aldosterone, this may cause increased mineralocorticoid activity leading to sodium retention, hypokalemia, hypertension. This is prevented by conversion of cortisol to cortisone, which is inactive at mineralocorticoid receptor, by 11βHSD2 [2].

Case Reports

A 7 year 6 month old male child, born out of consanguineous marriage, had hypertension for which he was being treated by a pediatric cardiologist with angiotensin receptor blocker and beta blocker but his BP was uncontrolled so, was referred to the department of pediatric endocrinology. His weight and height were 26.2kg and 126cm respectively (appropriate for age). On examination, blood pressure was 142/80mm of mercury which was more than 95th centile for age, sex and height. Systemic examination was normal except for penile length which was 9cm in presence of testicular volume of 2cm bilaterally (prepubertal). There was no other sign of virilization. On investigation, serum sodium and potassium were normal. His

Table 1: Biochemical Profile to rule out CAH (along with other causes of Hypertension) and Pubertas praecox vera.

S.no.	Tests	Report	Interpretation
1	S. Sodium	143mmol/l	N
2	S. Potassium	3.4mmol/l	N
3	pH	7.42	N
4	Bicarbonate	24.5mmol/l	N
5	Morning serum cortisol	6.60mic/dl	N
6	S.17 OH progesterone	2.29ng/ml	N
7	S. Aldosterone	1.03ng/dl	Low
8	Plasma Renin direct	0.5micIU/ml	Low
9	Plasma Aldosterone/renin ratio	2.060ng/dl/micIU/ml	
10	Corticosterone	6.11 nmol/l	N
11	Plasma ACTH	10.1pg/ml	N
12	ACTH stimulation test		N
	S. Cortisol		
	0min	6.6mcg/dl	
	30min	19mcg/dl	
	60min	22.4mcg/dl	
13	S. Deoxycorticosterone	18ng/dl	N
14	Plasma free metanephrines	42.5ng/l	N
15	Plasma free normetanephrines	80.3 ng/l	N
16	S. Testosterone	<7ng/dl	N
17	DHEAS	102ng/l	N
18	Androsetenedione	3.5ng/dl	N
19	FSH	1.1mIU/ml	N
20	LH	0.1IU/l	N
21	TSH	2.3 micIU/ml	N



of bacterial, viral or tubercular infection and autoimmune antibodies panel was negative. Meanwhile, the report of genetic study confirmed a homozygous missense variation in c.1099T>A in exon 5 of HSD11B2 gene (chr16:g.67470787T>A). It results in substitution of isoleucine for phenylalanine at codon 367 leading to apparent mineralocorticoid excess. The child was put on amiloride at 0.3mg/kg/day and he immediately responded with normalization of BP. Betablocker, ARB and spironolactone were gradually tapered to stop. Currently, the child is on oral amiloride only. He is growing well, BP is within normal limits, hemiparesis is improved and the size of penis is reduced to 7cm.

Discussion

Syndrome of AME is an uncommon form of low renin hypertension. It is an autosomal recessive disorder caused by homozygous or compound heterozygous loss of function mutation or deletion in 11 HSD2 gene, leading to decreased activity of enzyme 11 β HSD type 2. This enzyme is involved in conversion of cortisol to cortisone. As cortisol avidly binds to mineralocorticoid receptors, deficiency of the enzyme leads to excess cortisol being available at MCR causing sodium retention, hypokalemia and hypertension, in absence of excess circulating aldosterone [3]. This leads to a state of mineralocorticoid excess despite low aldosterone levels [1,2,4].

The typical features of AME are intrauterine growth retardation or low birth weight, hypokalemia, metabolic alkalosis, hypertension, low plasma renin, low serum aldosterone, increased cortisol to cortisone ratio in serum [5].

There is evidence of genotype phenotype correlation in AME [6]. When the genetic mutation leads to complete abolishment of enzyme activity, there is severe presentation of AME, while when there is residual activity of 11 beta HSD enzyme, the disease is in a milder form [4,7,8]. The above case report favours this correlation as the birth weight and serum potassium were normal and there was no alkalosis.

Stroke is a known complication of AME [9]. It can present with stroke at an early age [10]. Although hypertension is the cause of stroke in most cases, there have been studies elucidating the association of prolonged MCR activity with vascular wall integrity [11]. The short interval between presentation of hypertension and stroke in our case could probably be explained by the above hypothesis [5].

The presence of increased penile length was an inexplicable feature in this case. Despite extensive evaluation and literature search, we were unable to find a cause. It was an enigma for us, leading us to conclude that it might be an isolated feature unrelated to the primary diagnosis or a rare manifestation of AME due some unexplained interplay of adrenal steroids which is not reported till date. The possibility of peripheral precocious

puberty could not be ruled out although the investigations failed to confirm it.

Conclusion

Endocrine causes of hypertension in a child are not frequently evaluated due to low clinical suspicion and tedious workup. Although AME is a rare disorder, it should be suspected in a hypertensive child with low renin and poor response to conventional antihypertensives. High index of suspicion with genetic analysis is a key to diagnosis as the clinical presentation may be quite subtle with confusing features like the above case.

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