A Rare Case Report of Glucocorticoid Remediable Aldosteronism in a Young Femal Presenting as Areflexic Quadriparesis

Dr. S. Manohar[*], Dr. R. Siddeswarir[**], Dr. Karthik [**]

[*] M.D., Professor & HOD of Medicine
[**] M.D., Professor of Medicine

Abstract- Familial hyperaldosteronism type 1, also called glucocorticoid – remediable aldosteronism (GRA) is a rare autosomal dominant disorder associated with variable degrees of hyperaldosteronism, high levels or hybrid steroids (e.g., hydroxycortisol, 18 – oxocortisol), that are suppressed with administration of glucocorticoids. A 14 year old female presented with weakness of sudden onset in all four limbs. On examination she is found to be hypertensive and investigations revealed hypokalemia with elevated aldosterone levels and suppressed plasma renin activity leading to a diagnosis of GRA. Suppression of ACTH release with exogenous dexamethasone is a useful diagnostic and therapeutic strategy. Treatment with the mineral corticoid receptor antagoinsts spironolactone and epleronone is also efficacious.

I. INTRODUCTION

GRA is a rare monogenic autosomal dominant disorder characterized by early onset moderate to severe refractory hypertension. It is caused by a genetic crossover that allows the ACTH – driven 11β – hydroxylase promoter to drive aldosterone synthesis instead of cortisol synthesis. Hypertension frequently has its onset during childhood and is usually refractory to standard anti-hypertensives such as ACE inhibitors and b-blockers. Hypokalemia can develop in those treated with a potassium – wasting diuretic, but random potassium levels are usually normal, (1). These patients may have a family history of hemorrhagic stroke at a young age. Early recognition of this disorder and treatment with steroids controls the hypertension and prevents its complications. One such case is reported here and there are no other case reports of the GRA from India.

II. CASE REPORT

History

A 14 year old female patient came with a chief complaint of generalized weakness associated with myalgias from one month duration & sudden onset of weakness of all 4 limbs since 2 days. H/o of head ache, not associated with vomiting, h/o polyuria & increased thirst, No h/o of cranial nerve of bladder / bowel involvement. She is not a smoker or alcoholic. She has been diagnosed as hypertensive one month back and started on Tab. Amlodipine 5 mg and Atenolol 50 mg O.D.

Examination

Patient is moderately built, moderately nourished, No pallor, clubbing, cyanosis, pedal edema and lymphadenopathy. No cushingoid or acromegalic features No goiter & no neuro cutaneous markers.

PR 90 / min regular rhythm normal volume all peripheral pulses felt equally on both sides. BP- 200 / 110 mm Hg in right upper limb in supine posture and 220 / 110 mm Hg in right lower limb. Respiratory rate and temperature normal and JVP normal. Hypotonia in all 4 limbs, Power 3/5 in both upper limbs, 1/5 in both lower limbs, Superficial reflexes corneal abdominals reflex + Plantars, DTR absent, Sensory examination normal, No signs of meningeal irritation, skull and spine are normal, Other systems examination normal.

Investigation

CBP Hb% 12 gm / TLC 8100/mm3, ESR – 20mm 1st hr, CUE normal, ECG – ST depression and T inversion in all precordial leads, Prominent U waves present, S/o hypokalemia, glucose – 126 md/dl; urea 26 md/dl; creatinine 1.0 md/dl ; sodium 155 meq/1, potassium 2.8 meq / l, Ultrasound abd : with grade I renal parenchymal changes normal sized kidneys. Thyroid profile normal, Serum ANA negative, Ds dna negative, Echocardiography normal, Fundus examination macular stippling, **Visual acuity 6/6 both eyes, 24 hr urine, Urine Volume 6 lt, metanephrines 1.98 ng/dl, Doppler of renal artery normal, 24 hr Urine k + 30 meq/d (elevated), proteins 150 mg/d, Urine volume 5000 ml, ABG analysis Ph 7.41, hco3 – 19 meq/l, pCO2 30 mm hg, Na +, 150 meq/l, K+ 2.5 meq/l.**

In view of increased urinary potassium loss and high blood pressure of the patient, plasma aldosterone levels and renin activity are measured, Plasma renin activity <0.1 ng / ml / hr, (normal value), Plasma aldosterone – 28.2 ng/dl, ARR - > 280, Important clinical point is that PRA is suppressed (< 1.0 ng/ml/hr) in almost all patients with primary aldosteronism. To confirm the hyperaldosteronism, Confirmatory saline infusion test done. After 4 hr of loading 2 litres of normal saline plasma aldosterone concentration was estimated, plasma aldosterone concentration after saline infusion is 30 ng/dl (<5 ng/dl normal), Hence primary hyperaldosteronism has been confirmed.

CT Abdomen : Bulky kidneys with grade II renal parenchymatous changes, No adrenal masses found, MRI abdomen – Normal.

Urine 18 Oxy cortisol and 18 hydroxy cortisol levels were elevated.

Treatment

Patient started on dexamethasone 0.5 mg at bed time and the hypertension controlled well and the atenolol is stopped and the patient is now only on amlodipine 2.5 mg with dexamethasone. The therapeutic goal of normotension is achieved.

III. Discussion

Primary aldosteronism (PA) is the most frequent cause of secondary hypertension, and patients display an increased prevalence of cardiovascular events compared with essential hypertensives. To date, 3 familial forms of PA have been described and termed familial hyperaldosteronism types I, II and III (2).

FH type 1, or glucocorticoid – remediable aldosternoism, (GRA) is autosomal dominant in inheritance and is associated with variable degrees of hyperaldosteronism, high levels of hybrid steroids (e.g. 18-hydroxycortisol, 18-oxocortisol), and suppression with exogenous glucocorticoids. FH type II refers to the familial occurrence of Aldosterone – producing adnoma (APA) or bilateral idiopathic hyperaldosternism (IHA) or both. (3).

A rare cause of aldosterone excess is glucocorticoid – remediable aldosteronism (GRA), which is caused by a chimeric gene resulting from cross – over of promoter sequences between the CYP11B1 and CYP11B2 genes that are involved in glucocorticoid and mineral corticoid synthesis, respectively. This rearrangement brings CYP11B2 under the control of ACTH receptor signaling; consequently, aldosterone production is regulated by ACTH rather than by renin. This is a rare example of a hormone – over producing, syndrome without an increase in the number of cells making the hormone (4). Normally, angiotensin II stimulates aldosterone production by the adrenal zona glomerulosa, whereas ACTH stimulates cortisol production in the zona fasciculate. Owing to chimeric gene on chromosome 8, Mineralocorticoid production is regulated by corticotropin instead of by the normal secretagogue, angiotensin II in these patients. Therefore, aldosterone secretion can be suppressed by glucocorticoid therapy. In the absence of glucocorticoid therapy, this mutation results in overproduction of aldosterone and the hybrid steroids 18 – hydroxycorticsol and 18- oxycortisol, which can be measured in the urine (20-30 times normal in these patients) to make the diagnosis. Clinically GRA presents with early onset HT, with the mean age of onset being 13 years. HT is moderate to severe in most cases but can be mild or normal depending on the hereditary factors controlling HT and dietary salt intake. Hence, a positive family history is always not forthcoming. Patients with GRA are more prone to develop cerebrovascular accidents, especially fatal cerebral hemorrhage from rupture of intracranial aneurysms. Left ventricular wall changes are also common, indicating excess of aldosterone in the blood and may be independent of the degree of HT. Growth is typically not affected in children with GRA unlike Apparent Mineralcorticoid excess (AME) and congenital Adrenal hyperplasia (CAH). (5)

The Dexamethasone suppression test (DST) should be used in patients with biochemical primary hyperaldosteronism, who have a suggestive clinical history, and negative CT imaging of the adrenals. However, a positive DST should not displace the primacy of direct genetic testing in the diagnosis of GRA (6). For establishing the diagnosis, genetic testing for the chimeric gene is done with either Southern blotting or polymerase chain reaction (PCR) based technology.

FH type II autosomal dominant and may be monogenic. The hyperaldosteronism in FH type II does not suppress with dexamethasone, and GRA mutation testing is negative. FH type II is more common that FH type I, but it still accounts for fewer than 2% of all patients with primary aldosteronism. The molecular basis for FH type II is unclear, although a recent linkage analysis study showed an association with chromosomal region 7p22 (7).

IV. CONCLUSION

Primary aldosteronism is being increasingly diagnosed in the current era and the diagnosis of familial forms of hyperaldosteronism like GRA facilitates directed therapies and screening of at – risk individuals and kindreds.

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Authors

First Author – Dr. S. Manohar, M.D., Professor & HOD of Medicine
Second Author – Dr. R. Siddeswari, M.D., Prof. of Medicine
Third Author – Dr. Karthik, M.D., M.D., Prof. of Medicine