International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

Liddle it's A Riddle

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Abstract: ***64-year-old male presented with complaints of hypertension and proximal bilateral lower limb weakness and was found to be hypokalemic with metabolic alkalosis with hypothyroidism. Further evaluation of refractory hypokalemia were consistent of a rare reported case of Liddle's syndrome.***

Keywords: ENaC, Liddle's syndrome, hypertension, blood pressure, hyperaldosteronism

1. Introduction

Liddle's syndrome (a.k.a Pseudoaldosteronism or Pseudo primary hyperaldosteronism) is a genetic disorder characterized by hypertension with hypokalemic metabolic alkalosis, hyporeninemia and suppressed aldosterone secretion.[1,2]These features were first reported together in a 16-year-old female patient by Liddle et al in 1963[5]. Liddle's syndrome is caused by mutations to subunits of the Epithelial Sodium Channel (ENaC). Liddle syndrome is caused by mutations in the *SCNN1B* or *SCNN1G* gene.[3,4] Potassium-sparing diuretics such as amiloride and triamterene reduce ENaC activity, and in combination with a reduced sodium diet can restore normotension and electrolyte imbalance in Liddle's syndrome patients. In most cases, the condition becomes apparent at a young age but some affected people are not diagnosed until well into adulthood.[1,2]

2. Case

We reported, 64-year male patient admitted to our ward with complaints of bilateral proximal lower limb weakness without any sensory involvement.

Patient gave a history of COVID vaccination a day prior to onset of symptoms followed by slight myalgia of lower limbs. Patient complained of difficulty in getting up from squatting position. On admission patient was found to be hypertensive with a history of angioplasty. Detailed neurological evaluation was done and Proximal Myopathy was the provisional working diagnosis. ECG showed LV strain pattern and 2Decho was suggestive of concentric LVH.Lab workup was issued which showed normal RFTs with CPK-Nac -21022 IU/L, TSH- 35.31 mIU/L, serum potassium – 1.4mEq/l. ABG analysis showed metabolic alkalosis. We started the patient on Thyroxine 100mcg gave Infusion Kesol for hypokalemia. Patient had persistent hypokalemia with metabolic alkalosis but his muscle weakness improved on day 2 of treatment. This made us think of a renal involvement. Urine analysis showed no evidence of myoglobin, urine potassium – 22.1 and urine sodium- 49 (both on the lower sides). USG abdomen showed bilateral raised renal cortical echogenicity. We started the patient on low sodium diet and Aldactone 50mg was started. Primary hyperaldosteronism as a provisional diagnosis we also evaluated hypothyroidism. CT abdomen showed left adrenal hyperplasia with mild narrowing at the origin of bilateral renal artery. USG thyroid gland showed feature of thyroiditis and nodules in the thyroid gland. PET scan was advised to rule out any FDG avid occult primary. To confirm our diagnosis, we sent samples of plasma RENIN (<1.0 micro-IU/ml) and Serum Aldosterone (5.44 pg/ml) both being significantly low. Serum microsomal TPO antibodies titre (>1000) was high which supported the thyroid status along with positive Anti-SARS-CoV-2 spike protein (S1/S2) IgG levels (>400Au/ml). Primary hyperaldosteronism was less likely with this picture leaving Liddle's syndrome as a possible diagnosis, so we started the patient on Amiloride 5mg. Genetic study was not done as the patient had financial issues for the same.

3. Discussion

The clinical and biochemical features characteristic of Liddle's syndrome includes early-onset hypertension and hypokalemic metabolic alkalosis in the setting of suppressed plasma renin activity and low plasma aldosterone concentration. Although the condition may not be associated with any signs and symptoms initially. Complications of long-standing hypertension documented in Liddle's syndrome patients include renal insufficiency, cardiovascular disease, and cerebrovascular accidents[1,2]. Adults could present with hypokalemia, which can include weakness, fatigue, palpitations or muscular weakness. Increased sodium flux across the apical membranes of distal nephron principal cells also favours the secretion of potassium and acid into the collecting duct, resulting in hypokalemia and metabolic alkalosis. Elevated blood pressure and low serum potassium concentrations suppress the renin-angiotensin-aldosterone system, resulting in hyporeninemia. In the index case by Liddle et al in 1963, the disorder was distinguished from the provisional diagnosis of primary hyperaldosteronism by the lack of response to mineralocorticoid synthesis inhibitors and receptor blockers and response to the ENaC blockers triamterene and amiloride[5].

4. Conclusion

Liddle syndrome is an inherited form of hypertension. Patients are symptomatic early in life, often in childhood, although some affected individuals are not diagnosed until adulthood. Complications of long-standing hypertension documented in Liddle's syndrome patients include renal insufficiency, cardiovascular disease, and cerebrovascular

accidents. Potassium-sparing diuretics such as amiloride and triamterene reduce ENaC activity, and in combination with a reduced sodium diet can restore normotension and electrolyte imbalance in Liddle's syndrome. Liddle syndrome resolves completely after kidney transplantation.

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Author Profile

Dr. Ashish Nair received his MBBS degree from GMC Kozhikode Medical College and his MD Degree in Anaesthesiology from Bharti Vidyapeeth Hospital, Pune. Currently he is pursuing his Fellowship in Critical Care in Pune