

CLINICAL VIGNETTE

Primary Hyperaldosteronism Presenting with Severe Hypokalemia

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Case Presentation

A 56-year-old Asian male with severe chronic hypokalemia presented to establish care as his previous primary care provider was retiring. The patient was diagnosed with hypertension and hyperlipidemia at age 40. At that time, he was requiring 10 to 20 mEq of potassium supplements daily. He cannot recall the name of his first anti-hypertensive agent. However, he states that approximately 7 years ago, he required massive amounts of potassium supplements and since has been on 120 mEq of potassium/day. At the time of initial presentation, he met criteria for resistant hypertension as he was on 3 anti-hypertensive agents. These agents were started by his previous primary care provider and included amlodipine 10 mg daily, hydrochlorothiazide 12.5 mg daily and olmesartan 40 mg daily. He was also taking atorvastatin 20 mg daily for hyperlipidemia. His surgical history was only significant for plantar wart excision. He was adopted and unaware of family history.

On initial physical exam, blood pressure was well controlled at 130/80. He was mildly obese, well nourished and in no acute distress. He provided a good history but did appear somewhat anxious. Head and neck exam was normal; there were no suggestions of Cushing's features. Lungs were clear to auscultation. Heart examination revealed a soft II/VI systolic murmur at the left upper sternal border. Abdominal exam was normal without any evidence of striae. Examination of lower extremities revealed 3+ pitting edema of right leg and trace to 1+ pitting edema of left leg.

Initial laboratory on current medications was noticeable for sodium of 144, potassium of 2.4, chloride 99, bicarbonate of 34, bun of 17 and creatinine of 1.2. CBC, liver transaminases and albumin were normal. Plasma renin activity was normal at 2.8 and aldosterone level was normal at 54. Plasma ACTH was normal at 12 and cortisol was normal at 19. Bilateral venous Doppler ultrasounds of bilateral lower extremities were negative for deep venous thrombosis.

His potassium was repleted and daily potassium supplement was increased to 200 meq daily and he was referred to Nephrology and Endocrinology for work-up of excess mineralocorticoid activity given resistant hypertension and hypokalemia. The patient denied any chronic gastrointestinal symptoms that could explain hypokalemia or surreptitious use of diuretics. Initially, hydrochlorothiazide was discontinued as hypokalemia results from increased urinary potassium loss. Initial plasma renin activity and serum aldosterone levels were obtained on olmesartan, an angiotensin receptor blocker (ARB). Given normal levels and a high suspicion of a state of excess mineralocorticoid activity, repeat levels were obtained off ARB as this can interfere with lab results. The patient was started on calcium channel blocker, nifedipine as the patient was off ARB for 2 weeks for blood pressure control. Repeat labs off olmesartan demonstrated a plasma renin activity of 1.20 and aldosterone level of 100. The calculated plasma aldosterone concentration/plasma renin activity (PAC/PRA) ratio was 83.

The patient presented with the classic triad of hypertension, hypokalemia and metabolic alkalosis along with the PAC/PRA ratio was strongly suggestive of the diagnosis of primary hyperaldosteronism. The patient's nifedipine was replaced with spironolactone 25 mg and his potassium supplement was weaned down from 120 mEq to 60 mEq/day. With this regimen, patient's blood pressure and potassium remained in the normal range. To identify the source of primary hyperaldosteronism, CT abdomen/pelvis demonstrated a 2.4 cm left adrenal adenoma. He was referred to endocrine surgery, however, he refused and preferred to remain with medical management at this time.

Discussion

Primary hyperaldosteronism is a resistant-form of hypertension that is caused by inappropriately

elevated levels of aldosterone production. Primary aldosteronism can be caused by an adrenal adenoma, adrenal hyperplasia or rarely glucocorticoid-remediable aldosteronism. In the work-up of hypertension and hypokalemia all forms of primary mineralocorticoid excess should be evaluated including Liddle's syndrome.

Aldosterone is a key hormone in the regulation of hypertension and electrolytes. Normally, aldosterone is produced in the zona glomerulosa of the adrenal cortex of the adrenal gland. Aldosterone binds to the aldosterone receptor of the principal cell of the medullary collecting duct and increases activity of the apical epithelial sodium channel (ENaC), opening Na⁺ channels and increasing sodium reabsorption. In addition, aldosterone increases activity of Na⁺/K⁺-ATPase pump generating a lumen-negative potential and increases the apical potassium channel, ROMK, allowing additional opening of potassium channels. Hypokalemia is a result of urinary potassium wasting from increased ROMK activity. Metabolic alkalosis is a result of increased urinary hydrogen excretion from H⁺ excretion into lumen as a result of the favorable electrical gradient generated by effects of aldosterone. The net effect of aldosterone is sodium retention leading to volume expansion and hypertension. Both surgical and medical treatment

has been shown to improve both hypertension and cardiovascular complications. Surgery, the preferred treatment, has been shown to cure or improve hypertension in 90% of patients with an adrenal adenoma¹. Good prognostic factors for cure include younger age, lower pretreatment renin activity, and preoperative urinary aldosterone as well as lateralization in patients with hyperplasia. Medical management utilizing mineralocorticoid receptor antagonists is reserved for patients with bilateral hyperplasia or those who are not surgical candidates. In

a small study patients with aldosterone-producing adenomas managed pharmacologically, systolic blood pressure decreased from 175 to 129 mmHg, diastolic blood pressure decreased from 106 to 79 mmHg, and serum potassium increased from 3.0 to 4.3 mmol/L². Finally, basic lifestyle modification through dietary salt restriction has also been shown to improve hypertension, since sodium retention is the primary mechanism for hypertension.³

Further randomized trials are needed to compare the effects of surgery versus medical management on cardiovascular events in primary hyperaldosteronism patients.

REFERENCES

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