CLINICAL VIGNETTE

A Patient with Hypokalemia and Hypertension

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Case Report

A 33-year-old healthy woman with no significant past medical history presented to establish care. She had no complaints except for chronic yeast infections. Her physical exam was significant for elevated BP of 147/99 attributed to being nervous around doctors. Her comprehensive metabolic panel and fasting glucose were checked and revealed a potassium of 2.6, which was confirmed on repeat draw.

Further questioning of the patient was unrevealing. She denied laxative use, diuretic use, chronic diarrhea, weakness, supplement use, prior electrolyte imbalance, kidney disease, or nephrolithiasis. She referenced occasional fatigue and periods of increased urination, but otherwise endorsed an active lifestyle and excellent exercise tolerance. Her EKG was normal. The rest of her metabolic panel was otherwise unremarkable as were her thyroid, calcium, and phosphorus levels. The patient was started on potassium supplementation.

Initial workup included urine electrolytes, serum aldosterone, and renin levels. A calculated trans-tubular potassium gradient was inappropriately elevated, and the patient's serum aldosterone to plasma renin activity (PRA) was greater than 90. A CT abdomen with and without contrast/Adrenal protocol was obtained and showed a 3 cm adenoma. To confirm the adenoma was functional, renal vein sampling was obtained. The test was performed twice with suboptimal results but felt overall to imply primary hyperaldosteronism. She underwent an uncomplicated adrenalectomy; pathology revealed an adrenal cortical adenoma. Her post-operative labs included an aldosterone level of less than 1.0. On subsequent office visit with her PMD, her blood pressure was 120/75 and her potassium level was normal.

Discussion

Primary aldosteronism (otherwise defined as renin-independent, primary hypersecretion of aldosterone) accounts for an underestimated 5-13% causes of hypertension and has been recently acknowledged as the most common form of secondary hypertension.[1] The most frequent causes of primary aldosteronism are bilateral idiopathic hyperaldosteronism (60-70%) and unilateral aldosterone-producing adenomas (30-40%). Other forms include unilateral or primary adrenal hyperplasia, familial hyperaldosteronism, pure aldosterone-producing adrenocortical carcinomas, and ectopic aldosterone-secreting tumors. The path to diagnosis has become streamlined and should be considered for those patients who present with 1) hypertension and hypokalemia, 2) treatment-resistant hypertension as defined by suboptimal control despite three agents, severe hypertension (>160mmHg systolic or >100mmHg diastolic), hypertension with a history of an incidental adrenal mass, early onset hypertension or CVA at age less than forty years, and all hypertensive first-degree relatives of patients with primary aldosteronism.[2]

The clinical presentation is mostly attributed to the effects of aldosterone on the kidney; aldosterone causes an increase in sodium reabsorption leading to an electrical gradient that promotes potassium-wasting. While hypokalemia is considered a classic sign, in clinical practice it can be an inconsistent finding.[3] The hypertension is attributed to the volume expansion that occurs with sodium and water retention. A mild hypernatremia can occur as can a metabolic alkalosis and mild hypomagnesemia. Other renal effects include an increase in renal perfusion pressure and increase in GFR. Finally, an increased risk of cardiovascular disease has been noted relative to patients with primary hypertension, pheochromocytoma, and Cushing's syndrome.[4,5] Patients report muscle weakness when the hypokalemia is severe enough (<2.5 meq/mL).

The first step to diagnose primary aldosteronism is to determine the plasma renin activity and the plasma aldosterone concentration (PRC). The PRA levels are typically very low or undetectable (as in this case < 1ng/mL per hour for PRA) and the PAC is > 15ng/dL. An elevated aldosterone-renin ratio (PAC/PRA) is required for the diagnosis (> 20-30 depending on laboratory normal). In most patients, further confirmatory testing is required with aldosterone suppression testing, which can be performed by oral sodium loading and measurement of urine aldosterone secretion or with a saline infusion test and PAC measurement.

Once the diagnosis of primary aldosteronism is confirmed, the subtypes, including bilateral adrenal hyperplasia, unilateral adrenal adenoma and rarely functional adrenal carcinoma must be distinguished. The 2008 Endocrine Society guidelines recommend that an adrenal CT be obtained to determine this subtype in addition to ruling out an adrenal carcinoma. But due to numerous limitations of the imaging modality[6], the Endocrine Society has established that adrenal vein sampling be the criterion standard test to distinguish between subtypes. If unilateral disease is present, an increase in PAC up to four times is measured on that side while no difference is noted in a patient with bilateral hyperplasia.

Goals of treatment are targeted at prevention of the deleterious effects of hypokalemia, hypertension, renal, and cardiovascular toxicity. Treatment itself is dependent upon the subtype. For unilateral adrenal adenoma, hyperplasia or carcinoma, surgery is the preferred therapy for most patients. Preoperatively, one can utilize a mineralocorticoid receptor antagonist (spironolactone or eplerone) or potassium supplementation to manage the hypertension and hypokalemia. Following unilateral laparascopic adrenalectomy aldosterone secretion is dramatically lowered resulting in correction of hypokalemia and resolution of hypertension. For patients with bilateral adrenal hyperplasia, medical therapy is considered the standard of care per the Endocrine Society's 2008 guidelines given the suboptimal blood pressure control after subtotal adrenalectomy and the risks associated with bilateral adrenalectomy.[7]

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