A Patient with Primary Aldosteronism

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Primary aldosteronism resulting from an adrenocortical adenoma is a common cause of secondary hypertension, and also one of the few causes that are potentially curable. Aldosteronoma is the most common cause of primary aldosteronism and may result from a functional adenoma or adrenal carcinoma. With the routine use of abdominal computed tomography (CT), adrenal masses are a common incidental finding; only rarely are these masses malignant. This article reports a case of a patient with longstanding hypertension who was found to have primary aldosteronism resulting from a functional adrenal adenoma. The clinical features and diagnosis of primary aldosteronism are reviewed.

CASE PRESENTATION

History and Physical Examination

A 64-year-old man sought endocrine assessment after being referred by his primary care physician for hypertension and hypokalemia. He had a 10-year history of hypertension, currently poorly controlled on 4 antihypertensive medications. He was taking potassium chloride tablets for persistent hypokalemia that caused recurrent leg cramps. He mentioned that fatigue and lethargy had recently been bothering him excessively.

The patient denied any recent weight gain, abdominal pains, headaches, palpitations, or chest pain. His past medical history was significant for hypercholesterolemia, gastritis, and a rotator cuff repair 2 years ago. His current medications included lisinopril 20 mg daily, atenolol 100 mg daily, nifedipine 90 mg daily, terazosin 5 mg daily, ranitidine 150 mg daily, simvastatin 20 mg daily, aspirin 81 mg once daily and potassium chloride 8 mEq 3 times daily. He denied taking any over-the-counter medications. He stated that one of his two brothers had hypertension, but knew of no one in his family who had had an adrenal or endocrine tumor. He smoked tobacco for the past 40 years. He was currently retired.

Physical examination revealed a blood pressure of 141/83 mm Hg, a pulse of 77 bpm, and a respiratory rate of 18 breaths/min, His height was 5 ft 9 in and he weighed 194 lb. Results of examination of the heart and lungs were unremarkable. The abdominal examination was benign, without any striae, hepatosplenomegaly, or abdominal bruits on auscultation. Extremities examination showed no edema or bruises.

Laboratory Findings

Results from an evaluation performed by the primary care physician for persistent hypokalemia (potassium level, 2.5–3.9 mEq/L) and hypertension revealed a low renin level of 1.22 ng/mL/h (normal, 0.15–3.95 ng/mL/h) along with a high aldosterone level of 100 ng/dL (normal, 1–16 ng/dL). The aldosterone: renin ratio was high at 83 (normal, < 20). Subsequently, a CT scan of the abdomen with contrast ordered by the primary care physician showed a 2-cm left adrenal mass. The patient was referred for endocrinological assessment to confirm the presence of aldosteronism and rule out production of other hormones by the adrenal adenoma. Blood chemistry tests ordered by the endocrinologist are shown in the **Table**.

Because angiotensin-converting-enzyme inhibitors can "falsely elevate" plasma renin activity, lisinopril was stopped for further work-up of the patient. His terazosin dose was escalated to 10 mg daily to compensate. After 2 weeks of this medication regimen and an unrestricted sodium diet, 24-hour urine studies were obtained to confirm aldosterone oversecretion and rule out any other hormonal abnormalities. The results of a 24-hour collection for urinary catecholamines were normal, with values as follows: metanephrine, 139 μg/24 h (normal, 35–460 μg/24 h), normetanephrine, 470 μg/24 h (normal, 110–1050 μg/24 h), epinephrine, 0 μg/24 h (normal, 0–24 μg/24 h), norepinephrine, 75 μg/24 h (normal, 0–140 μg/24 h), and vanillylmandelic acid, 4.1 mg/24 h (normal, 1.8–6.7 mg/24 h). Another 24-hour urine collection showed a normal free cortisol concentration (22 μg/24 h; normal range, 10–105 μg/24 h). However,

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Table. Serum Laboratory Values for Case Patient After Presentation to Endocrinologist

Variable	Result	Normal Range
Potassium (mEq/L)	3.5	3.6–5.2
Sodium (mEq/L)	141	140–148
Chloride (mEq/L)	103	98–107
Bicarbonate (mEq/L)	29	22–29
Urea nitrogen (mg/dL)	23	7–18
Creatinine (mg/dL)	1.1	0.6–1.3
Calcium (mg/dL)	9.4	8.8–10.5
Glucose (mg/dL)	102	70–110

24-hour urinary aldosterone was elevated at 83 μg/24 h (normal range, 6–25 μg/24 h).

The patient subsequently was admitted to the hospital for a postural aldosterone test and a saline infusion test. The saline infusion test reconfirmed the suspicion of aldosteronism. The postural aldosterone test did not show any difference between supine and upright aldosterone levels, also supporting a diagnosis of aldosteronoma. After confirmation of the diagnosis of an aldosteronoma, he was started on spironolactone. The patient had a successful laparoscopic excision of the adrenal tumor 4 weeks later.

Pathologic Findings

On intraoperative examination, a tan-yellow, nodular mass was identified adjacent to the adrenal gland that measured 2.0 × 1.5 × 1.2 cm in its greatest dimensions. The mass appeared soft, and no necrosis or hemorrhage was noted. The adrenal gland appeared unremarkable. Histologically, the tumor was identified as an adrenal cortical adenoma. Following surgery, the patient's hypertension was adequately controlled with terazosin only.

DISCUSSION

Primary aldosteronism is the most common cause of secondary hypertension, with a prevalence of 1% to 2% in the hypertensive population.[1] Aldosterone regulates electrolyte excretion and intravascular volume mainly through its effects on kidneys by promoting sodium resorption and potassium excretion.[2] Aldosteronoma occurs more commonly in women than in men and occurs rarely in children.

Clinical Features of Aldosteronism

Patients with primary aldosteronism may be completely asymptomatic or have minimal symptoms. Symptoms may be related to hypertension (eg, headache), hypokalemia (eg, polyuria, nocturia, muscle cramps), or both.[3] Occasionally, severe symptoms from profound hypokalemia may be present and include serious muscle weakness, paresthesia, tetany, and paralysis; such features are more common in Asia, particularly China.[4] Severe retinopathy is rare.

Laboratory Evaluation of Aldosteronism

Identification of aldosteronism. Typical biochemical abnormalities include spontaneous hypokalemia with metabolic alkalosis, relative hypernatremia, and, in some cases, elevated serum glucose (from impairment of insulin secretion and action). Although spontaneous hypokalemia in a patient with hypertension is a strong indicator of aldosteronism, a substantial minority of patients (20% or more) have a potassium level that is in the low-normal range.[4] Causes of hypokalemia other than primary aldosteronism in patients with hypertension include diuretic therapy and licorice ingestion. Hypokalemia also may be a sign of secondary aldosteronism resulting from congestive heart failure or cirrhosis of the liver.

An increased ratio of plasma aldosterone concentration to plasma renin activity (aldosterone:renin ratio > 20) may differentiate patients with aldosteronism from those with essential hypertension.[5] However, in light of a study by Montori et al,[6] variation in the aldosterone:renin ratio may be inversely dependent on plasma renin activity. Many patients with hypertension, particularly elderly persons, African Americans, or patients with renal damage, have extremely low plasma renin activity levels, which would result in a high aldosterone:renin ratio. Thus, in relevant clinical settings, elevation of the aldosterone:renin ratio may be a reflection of low plasma renin activity rather than a sign of an inappropriately elevated plasma aldosterone level.[7]

Aldosteronism can be diagnosed definitively by measuring aldosterone and renin secretion in settings of sodium loading and sodium depletion. Patients with hypertension should be tested in an untreated state or after antihypertensive medication has been withheld for 2 weeks. A diagnosis of aldosteronism is established by (1) a high 24-hour urinary aldosterone excretion rate while on a high-sodium diet or (2) a high plasma aldosterone level after intravenous infusion of normal saline solution (2 L over a 4-hour period). Urinary aldosterone excretion of less than 14 μg/24 h after sodium loading rules out primary aldosteronism. Alternatively, a plasma aldosterone level of less than

8.5 ng/dL at the end of saline infusion (performed in the morning) also rules out primary aldosteronism.[4]

Differential diagnosis of aldosteronism. In a patient who has been found to have aldosteronism, a postural aldosterone test may help to determine whether the patient has an aldosteronoma. In a patient who has maintained an upright posture for 2 to 4 hours in the morning after overnight recumbency, a plasma aldosterone level that either decreases or fails to increase strongly suggests the presence of an aldosteronoma. Definitive diagnosis in some cases may require adrenal vein sampling, if available. Glucocorticoid-responsive aldosteronism is an uncommon type of aldosteronism that can be diagnosed by treatment with dexamethasone (at a dose of 0.5 mg every 6 hours for 2 days), resulting in lower blood pressure and fall in the plasma aldosterone level.[8,9]

Localization and Treatment of Aldosteronoma

Once the presence of an aldosteronoma has been diagnosed biochemically, the tumor can be localized using radiologic (CT or magnetic resonance imaging) or nuclear imaging techniques. The finding of large adrenal tumor (> 5 cm) should raise the possibility of adrenal cancer and surgery should be considered for tissue diagnosis after biochemical evaluation to rule out a hormonally active tumor. Malignant neoplasms of adrenal cortex account only for 0.02% of all cancers, with an approximate prevalence of 2 new cases per 1 million of population annually.[10]

Treatment for aldosteronoma is surgical. Unilateral adrenalectomy for an aldosteronoma results in improved blood pressure control and restoration of normal potassium levels in most cases.[4,11] Three to 4 weeks of spironolactone therapy prior to surgery minimizes sudden postoperative hypoaldosteronism and helps to restore potassium balance.

Evaluation of an Incidental Adrenal Mass

The finding of an adrenal mass in the course of abdominal imaging studies performed for other reasons poses an increasingly common problem. The prevalence of such incidentally recognized masses ranges from 0.6% to 1.3%.[12] These lesions should be assessed for hormonal activity for pheochromocytoma, excess glucocorticoids, mineralocorticoids, or sex steroids. Additional possibilities include adrenal cancer, simple adrenal cysts, myelolipomas, adrenal hemorrhage, and lymphoma (in cases of bilateral lesions).[12]

CONCLUSION

The case patient presented with a 10-year history of hypertension inadequately controlled on multiple antihypertensive medications as well as clinical symptoms of leg cramps and fatigue due to hypokalemia. He had mild metabolic alkalosis as shown by a high-normal serum bicarbonate level. Further biochemical studies confirmed a diagnosis of aldosteronoma.

Aldosteronism should be suspected in any patient with hypertension and unprovoked hypokalemia. It is the most common cause of secondary hypertension but is potentially curable. Biochemical diagnosis should be followed by radiologic studies. Surgery is the treatment of choice once the diagnosis is confirmed, but it may not alleviate hypertension in all cases. **HP**

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