Symptomatic Hypokalemia in a 19-Year-Old Student

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ABSTRACT

Primary hyperaldosteronism (PA) is the most common cause of secondary arterial hypertension and is frequently undiagnosed. It affects all ages but is more frequent between 20 and 60 years old. The clinical presentation is variable, and the diagnosis is based on screening and, in equivocal cases, confirmatory tests. A 19-year-old student presented with complaints of extreme fatigue, arterial hypertension, hypokalemia and metabolic alkalosis, raising a high index of suspicion for PA. Screening tests were performed and its expressiveness excluded the need of confirmatory tests. CT-scan showed a unilateral adrenal adenoma and the patient was submitted to laparoscopic adenectomy without complications. Prompt diagnosis and treatment are essential to avoid long term complications of PA.

KEYWORDS

primary hyperaldosteronism; hypokalemia; hypertension; aldosterone-producing adenomas; Conn syndrome

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INTRODUCTION

Primary hyperaldosteronism (PA) is the most common cause of secondary arterial hypertension and is frequently undiagnosed. The two most common causes of PA are aldosterone-producing adenomas (Conn syndrome) and bilateral idiopathic hyperplasia. Less common causes of PA include unilateral adrenal hyperplasia, carcinomas and ectopic tumors (Table 1) (1).

Tab. 1 Types of primary hyperaldosteronism.

Type of primary aldosteronism	Cases
Aldosterone-producing adenoma	30%
Bilateral idiopathic hyperplasia	60%
Primary (unilateral) adrenal hyperplasia	2%
Aldosterone-producing adrenocortical carcinoma	< 1%
Familial hyperaldosteronism (FH)	
Glucocorticoid-remediable aldosteronism (FH type I)	< 1%
FH type II	< 6%
FH type III (germline KCNJ5 mutations)	< 1%
FH type IV (germline CACNA1H mutations)	< 1%
Ectopic aldosterone-producing adenoma or aldosterone-producing carcinoma	< 1%

FH – Familial hyperaldosteronism

Patients of all ages may be affected, but the peak incidence is between 20 years and 60 years.

The most common presentation of the disease is normokalemic hypertension. The degree of hypertension is typically moderate but may be severe. In some cases, it may present as resistant hypertension or asymptomatic diastolic hypertension. Hypertension (as opposed to hypokalemia) is a prerequisite for PA diagnosis. Hypokalemia is only present in 9–37% of patients: in half of aldosterone-producing adenomas and in 17% of bilateral idiopathic hyperplasia. Thus, hypokalemia has low sensitivity and its absence has a low negative predictive value for the diagnosis of PA (2). Metabolic alkalosis is common.

Although in some cases the clinical presentation may be similar, patients with aldosterone-producing adenoma have higher aldosterone secretion rates, resulting in more severe hypertension and marked hypokalemia; patients with bilateral idiopathic hyperplasia have a milder disease with less hypersecretion of aldosterone and less hypokalemia. Also, patients with aldosterone-producing adenoma are generally younger (< 50 years) than those with bilateral idiopathic hyperplasia (3).

Hyperaldosteronism is associated with higher rates of cardiovascular and cerebrovascular morbidity and mortality as compared to patients with essential hypertension, matched for age, sex and blood pressure (1), so, early diagnosis is the key to prevent disease progression.

It is important to identify the high-risk population for PA. The screening must be considered if the patient meets one of the following criteria (2):

- sustained blood pressure greater than 150/100 mmHg on 3 measurements on different days,
- blood pressure > 140/90 mmHg resistant to 3 antihypertensive drugs (including a diuretic),
- need of 4 or more antihypertensive drugs to control blood pressure,
- hypertension and hypokalemia,
- hypertension and adrenal incidentaloma,
- hypertension and sleep apnea,
- hypertension and family history of early-onset hypertension or cardiovascular event under 40 years old, or first-degree relative diagnosed with primary aldosteronism.

The diagnosis is based on laboratory tests. The aldosterone-to-renin ratio (ARR) has higher sensitivity and lower variability than other measures, so it should be the first to perform. ARR is the ratio of plasma aldosterone and plasma renin activity or direct plasma renin collected in the morning (more than 2 hours after awakening), in sitting position for 5 to 15 minutes, with normal dietary salt intake (urinary sodium 100–200 mmol/24h), normal serum potassium level and without intake of angiotensin converting enzyme inhibitors or angiotensin receptor blocker for at least 2 weeks (4). If the ARR is higher than laboratory threshold, PA should be suspected.

In case of spontaneous hypokalemia, plasma renin below detection levels and plasma aldosterone concentration > 20 ng/dL, confirmatory tests are not needed (2). In the other scenarios it must be performed.

Nowadays, there are four confirmatory tests approved in America and Europe for the diagnosis of PA: oral sodium loading, saline infusion test, fludrocortisone suppression test, and captopril challenge (5, 6). There is not a gold standard confirmatory test, as each has advantages and disadvantages that should be assessed case by case. In Japan, the furosemide upright test is used, although it is not approved by Endocrine Society as a confirmatory test of PA (6).

All patients with suspicion PA should undergo adrenal computer tomography (CT) scan in the initial study to determine subtype (adenoma versus hyperplasia) and exclude adrenal carcinoma. When surgical treatment is indicated, adrenal venous sampling (AVS) should be performed by an experienced team, to distinguish between unilateral adenoma and bilateral hyperplasia. In some cases, AVS is not necessary, especially in younger patients (< 35 years), with spontaneous hypokalemia, high aldosterone levels, and unilateral adrenal lesions with radiological features consistent with a cortical adenoma on adrenal CT scan (2). In these cases, AVS is not routinely indicated as it is expensive, technically demanding and carrying a tiny risk of adrenal vein rupture, and so, unilateral adrenalectomy may be safely performed.

Treatment depends on whether it is unilateral or bilateral disease. In case of unilateral adenoma hyperplasia, curative surgery, such as laparoscopic unilateral adrenalectomy performed by an experienced surgeon, is considered

the treatment of choice. In case of bilateral disease, medical management with mineralocorticoid receptor antagonist is usually used as the first-line treatment modality.

CASE REPORT

We report a case of a 19-year-old student with arterial hypertension (first time documented in 2015: systolic blood pressure of 130–140 mmHg and 150 mmHg in 2018) and longstanding complaints of fatigue and headache.

He was referred to the Emergency Department by his Family Physician for assessment of symptomatic hypokalemia (K+ 1.9 mEq/L) detected in a routine blood test. He had no significant past medical history and was not taking any medications. On admission he denied headache and fatigue, was afebrile, a blood pressure of 156/91 mmHg and heart rate of 73bpm. The remainder of the physical examination was unremarkable.

Investigations (shown in Table 2) revealed hypokalemia (serum potassium of 1.4 mEq/L) and arterial blood gas analysis on room air showed alkalemia with metabolic alkalosis. The electrocardiogram showed normal sinus rhythm, a heart rate of 67 bpm and prominent U-wave in the precordial leads (Figure 1). During electrocardiographic monitoring, atrial and ventricular extrasystoles were noted.

Tab. 2 Laboratory data, blood gas analysis and hormonal examination.

Laboratory data	
Hemoglobin	16.9 g/dL (N 13–18)
Hematocrit	46.6% (N 40–52)
Platelets	281 × 10^3/uL (N 130–450)
Leucocytes	9.36 × 10^3/uL (N 4.5–13)
Creatinine	0.75 mg/dL (N 0.4–1.2)
Sodium	142 mEq/L (N 136–145)
Potassium	1.4 mEq/L (N 3.5–5.1)
Magnesium	2.2 mg/dL (N 1.8–2.5)
Reactive C Protein	< 0.1mg/dL (N 0.02–0.75)
Blood gas analysis	
pH	7.54 (N 7.35–7.45)
pO_2	91 mmHg (N 80–100)
pCO_2	51 mmHg (N 35–45)
HCO_3^-	43.6 mmol/L (N 22–26)
Sodium	143 mEq/L (N 136–145)
Potassium	1.6 mEq/L (N 3.5–5.1)
Lactate	1.7 mmol/L (N <2.0)
Hormonal examination	
Plasma aldosterone (supine)	32 ng/dL (N <15)
Plasma renin activity	< 0.5 ng/mL/hour (N 0.7–3.3)
ARR	65.44 (N < 30)

ARR – aldosterone-to-renin ratio; N – normal

Potassium chloride replacement therapy was started, and patient was transferred to the Intermediate Care Unit due to severe hypokalemia with arrhythmogenic potential.

On admission to the Intermediate Care Unit, patient was hemodynamically stable but with tendency to develop hypertension peaks and frequent atrial and ventricular extrasystoles.

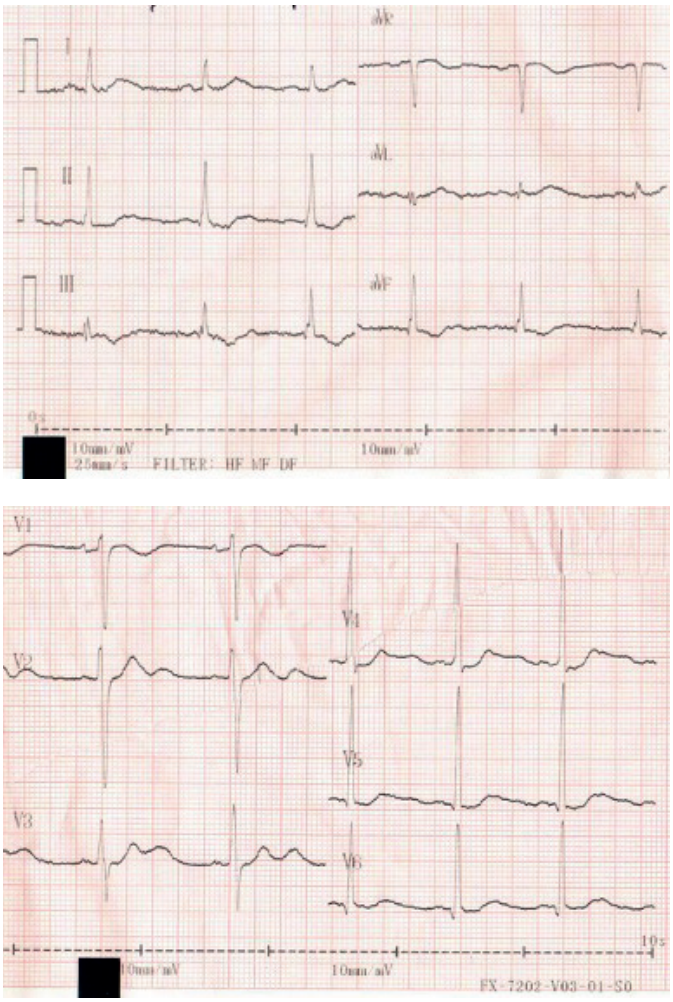

Fig. 1 12-lead Electrocardiogram.

Potassium chloride and magnesium sulphate were administered by subclavian central venous catheter. Serum aldosterone and Plasma Renin Activity (PRA) were evaluated once serum potassium level was corrected. Hypertension was managed with drugs that do not interfere with renin-angiotensin-aldosterone system.

The ARR was 65.44, excluding, in this setting, the need for confirmatory test of PA.; Urinary 24-hour excretion of metanephrine and normetanephrine were normal.

Non-contrast adrenal CT scan revealed a small regular hypodense nodule in the left adrenal gland, approximately 1.5 by 1.2 cm, with a CT attenuation of 11.3 Hounsfield units, suggestive of a benign cortical adenoma (Figure 2).

Following stabilization of hypokalemia and blood pressure profile, patient was started on spironolactone 300 mg/day, potassium chloride 600 mg 3id and amlodipine 5 mg/day, with frequent monitoring of potassium levels and dose adjustment. Amlodipine was suspended as soon as blood pressure control was achieved.

Following multidisciplinary team discussion, patient was referred for surgical treatment once stabilization of the potassium levels and blood pressure profile were achieved. The patient underwent a left laparoscopic adrenalectomy without complications. Histopathological examination confirmed features of adrenal adenoma.

Post operatively patient had recovery of his fatigue, his headaches became occasional and was not requiring

any antihypertensive drugs to control his blood pressure profile. Serum potassium and ARR on follow-up were normal.

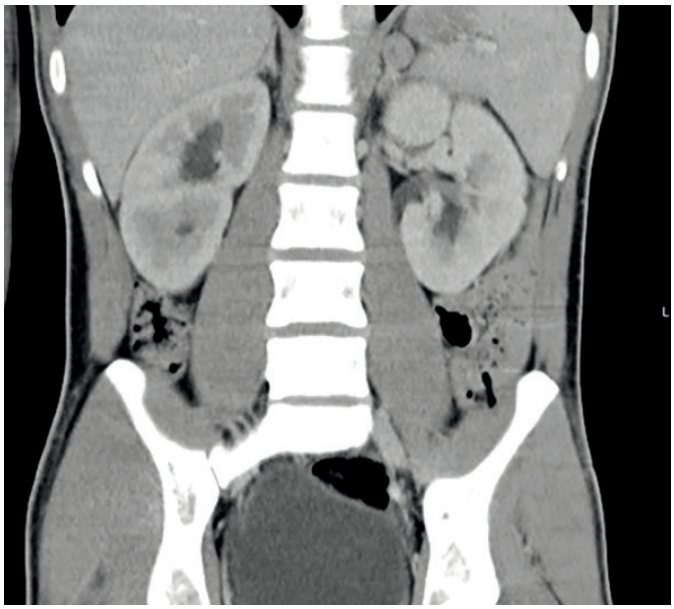

Fig. 2 Abdominal-pelvic CT scan showing a small regular hypodense nodule in the left adrenal gland (1.5 × 1.2 cm).

DISCUSSION

In PA there is an inappropriate (i.e. renin-independent) increase in aldosterone secretion. Under influence of high levels of aldosterone, there is an excessive sodium retention, volume expansion and plasma renin suppression, leading to hypertension. Thus, hypokalemia results from the urinary loss of potassium, in exchange for sodium in the distal renal tubule.

In this case, there was a high suspicion for the diagnosis of PA because the patient presented with hypertension, hypokalemia and metabolic alkalosis, typical presentation of aldosterone-producing adenoma subtype. He also exhibited neuromuscular symptoms related to severe hypokalemia, as well as longstanding complaints of extreme fatigue.

We followed a rational diagnostic approach. The confirmatory test for PA was omitted, due to the expressiveness of the screening test result (high levels of aldosterone and suppressed renin level), assessed in standard conditions, making the presence of adrenocortical tumor clear. Also, the confirmation of laterality by AVS was not performed before proceeding to the left adrenalectomy. The patient was young, clinically had a typical aldosterone-producing adenoma subtype, a marked aldosterone excess, as well as a unilateral adrenal lesion with radiological features consistent with cortical adenoma on adrenal CT scan, therefore not needing AVS (2).

The surgical treatment solved the symptoms and the arterial hypertension. Until now, he has not developed cardiac or cerebrovascular disease, namely new-onset diabetes mellitus, metabolic syndrome, stroke, atrial fibrillation, coronary artery disease, left ventricular hypertrophy or heart failure, which are more common in longstanding PA (1).

CONCLUSION

The diagnosis of PA is essential and should be made early in the course of the disease because proper treatment may prevent the progression of cardiovascular and cerebrovascular disease, offering patients a better quality of life, with less morbidity and mortality.

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