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Case Report

A 100-year old patient presented with profound diuretic-induced hypokalemia as first indicator of primary aldosteronism: a case report

Like Zhao[1], Wei Liu[2], Xue Yu[2], Hongyi Li[2]

[1]Department of Rheumatology, Beijing Hospital, Beijing, China; [2]Department of Cardiology, Beijing Hospital, Beijing, China

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Abstract: A 100-year-old man with a 30-year history of hypertension was admitted to our institution because of pneumonia. As he had gradually improved by antibiotic therapy, his blood pressure was getting uncontrolled. Laboratory examinations showed hypokalemia (diuretic-induced), hyperkaliuria, metabolic alkalosis, suppressed plasma renin activity, increased aldosterone to renin ratio. Abdominal computed tomography revealed a nodular mass (14 mm in diameter) in the right adrenal gland. Primary aldosteronism was considered and spironolactone was put on the patient. After treated with spironolactone, the patient had a good clinical and biochemical response.

Keywords: Hypokalemia, aldosteronism, spironolactone

Introduction

Primary aldosteronism (PA) is characterized by excessive, autonomous secretion of aldosterone by the adrenal cortex with subsequent suppression of renin secretion. Usually it produces few symptoms. The diagnosis of PA is usually made in patients who are in the third to sixth decade of life. We herein report the case of a 100-year-old patient with a 30-year history of hypertension, who presented resistant hypertension and diuretic-induced hypokalemia. Moreover, the patient had a good clinical and biochemical response to the high dose of spironolactone after he was diagnosed with PA.

Case report

A 100-year-old Chinese man was admitted to the hospital because of pneumonia. He was diagnosed primary hypertension at the age of 70 and had a history of dementia, coronary atherosclerotic heart disease (old myocardial infarction), cerebrovascular sequelae, type 2 diabetes mellitus, stage III chronic kidney disease and chronic heart failure. Because of repeated aspiration pneumonia, the patient was receiving enteral nutrition. The patient also took spironolactone (20 mg/d) for chronic heart failure and 15% potassium chloride (50 ml/d). His blood pressure was well controlled and his serum potassium level was at an average of 4 mEq/L.

He was treated with intravenous administration of antibiotic and got improved. However his blood pressure was elevated gradually. He was initially treated with lacidipine (4 mg/d), isosorbide dinitrate (15 mg/d) and atenolol (12.5 mg/d). Despite titration to the maximal doses, his blood pressure remained elevated with his systolic pressure between 180 and 210 mmHg and his diastolic pressure between 70 and 80 mmHg. Dyspnea and increased heart rate (100-120 beat per minute) also presented with the increased blood pressure. Urapidil hydrochloride injection, glyceryl trinitrate injection and sodium nitroprusside were added respectively, and the systolic pressure lowered between 180 and 200 mmHg. Because of the remained high blood pressure and the history of stage III chronic kidney disease, angiotensin converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) were not considered and indapamide sustained release tablet (1.5 mg/d) was added to control blood pressure. To the

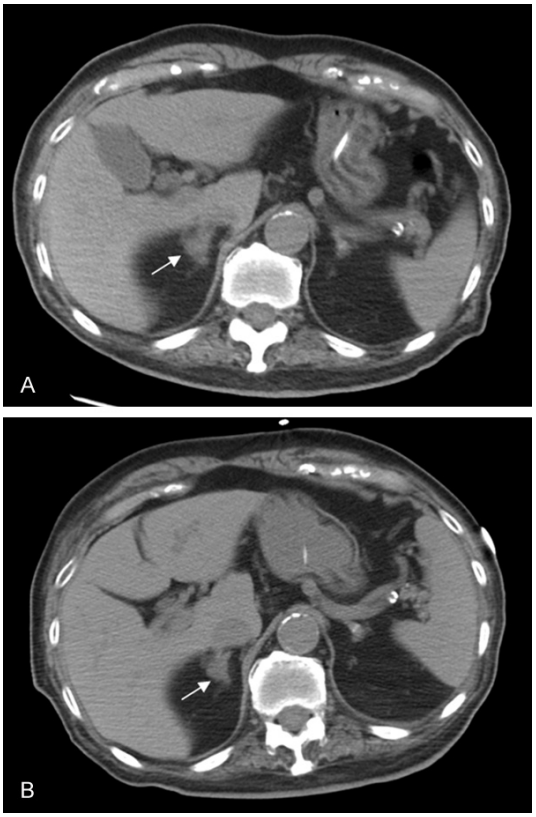

Figure 1. Abdominal computed tomography scan showed nodular mass on the right adrenal gland. A: CT was performed in 26th September 2013 and nodular mass was 16 mm in diameter (arrow). B: CT was performed in 20th October 2014 and nodular mass was 14 mm in diameter (arrow).

surprise, the patient showed profound hypokalmenia (serum potassium level decreased from 4.5 mEq/L to 2.57 mEq/L) three days later. The patient was immediately treated with intravenous administration of potassium and indapamide sustained release tablet was ceased. The combination of arterial resistant hypertension and diuretic-induced hypokalemia raised the suspicion of primary aldosteronism (PA). Reviewed his medical record recently, the abdominal computed tomography scan (CT) which performed two months and one year ago both revealed an almost same size nodular mass (14-16 mm in diameter) in the right adrenal gland (**Figure 1**). The function of adrenal adenoma was not evaluated one year ago because of well-controlled blood pressure. Our suspicion of PA was further supported.

The laboratory examinations were conducted and the results revealed hyperkaliuria (72.9 mmol/24 hrs, normal range: 20-30 mmol/24 hrs), metabolic alkalosis (arterial blood gasses: PH 7.416, PCO_2 45.7 mmHg, ABE 4.2 mEq/L, HCO3-28.1 mEq/L). Plasma concentrations of adrenocorticotropic hormone (ACTH) and cortisol were (20.2 pg/mL, normal range: 0-46 pg/mL) and (10.5 μg/dL, normal range: 5-25 μg/dL) respectively, which both were in normal limits. Moreover the plasma renin activity (PRA), plasma aldosterone concentration (PAC) and aldosterone to renin ratio (ARR) were detected (at supine position). Although the atenolol, lacidipine and spironolactone have the potential effect on renin measurements, considering the severity of the patient's hypertension and his age, we did not cease these medicines. The results showed that PRA was low (0.5 pg/ml, normal values: 4-24 pg/ml), PAC was at the high end of the normal range (155.1 pg/ml, normal values: 10-160 pg/ml) and the ratio PAC/PRA was 310.2, which suggests the presence of PA.

In view of the patient was not in good condition and his age was 100, confirmatory tests and subtypes tests were not performed to confirm the diagnosis of PA. Based on the clinical manifestation and laboratory tests which all suggest PA, the diagnosis of PA was made. Since the patient cannot tolerate the surgery, medication was the first and appropriate choice. The patient was put on spironolactone (40 mg per day with progressive dose titration up to 80 mg per day), which resulted in normalization of serum potassium (4.0 mEq/L) with 15% potassium chloride (20 mL/d) and improvement of blood pressure control (lacidipine 4 mg/d). His blood pressure level was at an average of 150/60 mmHg. One month later, we measure PRA, PAC and the ratio PAC/PRA again, which the values were improved (the values of PRA, PAC and the ratio PAC/PRA again, which the values were 1.9 pg/ml, 122.6 pg/ml and 66.2 respectively).

Discussion

Resistant hypertension is a common clinical problem. Although the exact prevalence is unknown, clinical trials suggest that it involves 20% to 30% of study participants [1]. The etiology of resistant hypertension is almost always multi-factorial, and epidemiological studies demonstrate that older age, obesity, impaired renal function, high dietary salt, refractory volume expansion, diabetes mellitus are all asso-

ciated with resistant hypertension. Secondary hypertension is detected in 5% to 10% of all patients with resistant hypertension. However, several secondary forms of hypertension are more prevalent in resistant hypertension than in uncomplicated hypertension: obstructive sleep apnea (in 60% to 70% of patients with resistant hypertension), primary aldosteronism (in 7% to 20%), renal artery stenosis (in 2% to 24%), renal parenchymal disease (in 1% to 2%), drug-induced or heavy alcohol use (in 2% to 4%) and thyroid disorders (less than 1%) [2]. For the patient with uncontrolled blood pressure, before diagnosing resistant hypertension, clinicians must exclude medication non adherence and the white coat syndrome, which were the common causes of pseudoresistant hypertension. Moreover, all patients with resistant hypertension should be counseled about lifestyle modification, such as sodium intake is a major factor contributing to resistant hypertension. In this patient, he also has history of coronary atherosclerotic heart disease (old myocardial infarction), cerebrovascular sequelae, type 2 diabetes mellitus, chronic kidney disease and chronic heart failure and his blood pressure were well controlled in last thirty years. We did not consider secondary cause of hypertension until the diuretic-induced hypokalemia was presented. After the diagnosis of PA was made and the treatment was performed, the blood pressure of was lower, but antihypertensive regimen was still needed, which suggests PA combined with hypertension may responsible for the resistant hypertension in this patient.

PA is the most common form of endocrine hypertension secondary to excessive or inappropriately elevated aldosterone production from the adrenals that is partially or completely autonomous of the renin-angiotensin system (RAS) [3, 4]. According to recent studies, PA is seemingly a much more common cause of hypertension than has been thought historically, with a 10% prevalence of general hypertensive populations and approximately 20% of subjects with resistant hypertension [5]. Furthermore, the prevalence raised to 30% when ARR was used as a screening test in randomly selected hypertensive patients by general practitioners [6]. The diagnosis of PA is usually made in patients who are in the third to sixth decade of life. Hypertension and hypokalemia are the hallmarks of PA in most physicians' minds, but, on the contrary, hypokalemia is not as common as was previously suspected in PA patients. Although the optimal timing to test for PA is still an unresolved issue, a consensus endorsed by the Endocrine Society indicates that testing should be performed in patients with the following features: stage 2 and stage 3 hypertension; drug-resistant hypertension; hypertension with spontaneous hypokalemia or diuretic-induced hypokalemia; hypertension with adrenal incidentaloma; hypertension and a family history of early-onset hypertension, or cerebrovascular accident at a young age and patients with first degree relatives diagnosed with PA [7].

The optimal treatment strategy depends upon the subtype of PA. The mainstays of treatment for PA continue to be unilateral adrenalectomy for most patients with unilateral forms and medications that antagonize aldosterone action (for example, spironolactone, eplerenone, or amiloride) for most with bilateral PA. Both treatment approaches can result in marked blood pressure lowering in patients with hypertension, including those with resistant forms [8]. If patients are unwilling or unable to receive surgery, medical treatment with aldosterone antagonist should be attempted and high doses might be necessary in order to be effective. Spironolactone has been the treatment of choice for PA for more than four decades. Dosages of spironolactone have varied from 25 to 400 mg per day [9]. Although spironolactone effectively controls blood pressure and hypokalemia in the majority of cases, its use is often associated with considerable side effects, especially at high doses (>100 mg per day). Eplerenone is a more selective mineral corticoid receptor antagonist, with minimal antiandrogen and progesterone agonist effects and lower incidence of adverse effect. Because the patient cannot tolerate surgery and surgery is not to be contemplated, he was treated medically with spironolactone. Due to he is 100-year old and there was no recommendation management for elderly patient, we used 80 mg per day in combination with antihypertensive agents. One month after starting spironolactone, his blood pressure decreased to 150/60 mmHg, allowing for the discontinuation of intravenous antihypertensive drugs and lowering of lacidipine to 4 mg/d.

In summary, this report presents a rare case of a 100-year-old patient under antihyperten-

sive treatment the last thirty years for essential hypertension, who presented with profound diuretic-induced hypokalemia as first indicator of PA due to unilateral adrenal nodule. In addition, although the patient is already 100 years old, the screening test is still positive. Furthermore, the patient had a good clinical and biochemical response to the high dose of spironolactone (80 mg/d), which provide some clinical experience for the therapy of elderly patient with PA.

Disclosure conflict of interest

None.

Address correspondence to: Wei Liu, Department of Cardiology, Beijing Hospital, Beijing, China. E-mail: liuweibjyy@163.com

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