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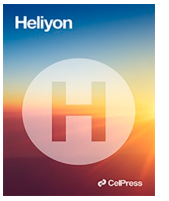

Case report

Successful treatment of resistant hypertension and severe complications in a 63-year-old man with primary aldosteronism without adrenalectomy: A case report

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ABSTRACT

Primary aldosteronism (PA), often due to aldosteronoma, commonly causes secondary hypertension and typically requires surgery. We present a case of an elderly man with longstanding hypertension, complicated by cerebral hemorrhage and myocardial infarction. Enhanced CT imaging identified a right-sided aldosteronoma and left adrenal gland fullness. Combined with upright supine aldosterone ratio, captopril challenge test, bilateral adrenal venous sampling, and CYP11B1/CYP11B2 fusion gene testing, the diagnosis of PA was confirmed. Despite the absence of surgical intervention in this patient, pharmacotherapy effectively managed hypertension and enhanced cardiac function, thereby underscoring the advantageous utilization of aldosterone antagonists in non-surgical candidates diagnosed with PA.

1. Introduction

Primary aldosteronism (PA) is a form of endocrine hypertension characterized by excessive secretion of aldosterone by an adrenal adenoma or hyperplasia, leading to sodium and water retention, hypertension, and hypokalemia. The pathophysiology of PA is characterized by dysregulated aldosterone production, which is independent of renin and is not fully suppressed by volume and/or sodium loading, often despite hypokalemia. PA in the general hypertensive population have a prevalence of 5–15 % [1,2]. Compared to patients with essential hypertension of similar age and blood pressure, PA especially those with concomitant and hypokalemia demonstrate a heightened prevalence of adverse cardiovascular and renal outcomes, including stroke, cardiac hypertrophy, atrial fibrillation, coronary artery disease, and heart failure, kidney disease (decline in glomerular filtration rate and/or albuminuria) [3,4]. In the context where screening for PA often transpires belatedly [5] early diagnosis and treatment of these conditions become crucial. This is because the underlying cause can frequently be rectified, thus averting disease progression.

In this report, we delineate a case of profound cardiovascular complications attributed PA, wherein pharmacological intervention effectively regulated blood pressure and elicited improvements in cardiac function, thus negating the necessity for adrenalectomy.

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1.1. Case presentation

A 63-year-old man with a 30-year history of uncontrolled hypertension (peaking at 210/130 mm Hg) was admitted to the hospital for treatment. He had been diagnosed with acute myocardial infarction 5 years ago and acute cerebral hemorrhage 1 year ago. The coronary angiography indicated a 70 % stenosis in the distal RCA with unstable plaque, with TIMI 3 flow. One stent was implanted at the lesion site. Recurrent hypokalemia had occurred 5 years prior. Prior to admission, his medication regimen included nifedipine (30 mg, twice daily), amlodipine/hydrochlorothiazide (20 mg/12.5 mg, 1 tablet daily), metoprolol succinate (47.5 mg, once daily), urapidil hydrochloride (30 mg, three times daily), rosuvastatin calcium (10 mg, once daily), ezetimibe (10 mg, once daily), and potassium chloride (1 g, three times daily) orally.

The patient did not exhibit hirsutism, moon face, buffalo hump, pendulous abdomen, central obesity, or purple striae. He denied any history of smoking or alcohol consumption. Both of his parents had a history of hypertension, and his father passed away at the age of 57 due to ischemic cerebrovascular disease. He has one 34-year-old son with no history of hypertension.

The patient's measurements indicated a height of 176 cm, weight of 80 kg, and body mass index of 25.83 kg/mˆ2. His vital signs included a pulse rate of 64 beats/min, respiratory rate of 17 breaths/min, and heart rate of 64 beats/min with a regular rhythm. No murmurs were detected upon auscultation. An enlarged heart border was observed at the left sternal border.

Blood cell analysis, blood transaminase, and blood creatinine levels were within normal range. Thyroid function and D-dimer levels were also within normal ranges. The patient's fasting plasma glucose was 5.24 mmol/L, and the glycated hemoglobin was 5.7 %, both within the normal range. Urine protein was negative. The B-type natriuretic peptide level was elevated (151.6 pg/mL). However, there was slight hypokalemia observed: K^+ (2.96 mmol/L). After potassium supplementation to normalize levels, an upright and supine aldosterone ration (ARR, using radioimmunoassay) was calculated, with results detailed in Table 1. Our institution's cutoff for ARR was ≥30 % [(ng/dL)/μg/(L·h)], with no exclusion of PA. Further confirmatory testing was performed using a captopril suppression test. The patient underwent overnight supine positioning and fasting blood collection. Results of the captopril challenge test are detailed in Table 2, indicating a positive result.

The electrocardiogram depicted T-wave inversion in leads II, III, and aVF (Fig. 1). Echocardiography revealed segmental thinning of the left ventricular myocardium with abnormal motion, along with left ventricular enlargement (LA 53 mm, LV 62 mm), hypertrophy, and a mildly reduced left ventricular ejection fraction of 51 %. Renal artery Doppler showed no significant renal artery stenosis. The adrenal-enhanced CT scan revealed a 1 cm nodule in the outer aspect of the right adrenal gland and mild fullness in the left adrenal gland (Fig. 2). Adrenal venous sampling (AVS) revealed relatively balanced bilateral adrenal hormone levels, indicating bilateral equipoise. This is evidenced by the left Plasma Aldosterone Concentration (PAC) and Plasma Cortisol Concentration (PCC) ratio being comparable to the right PAC and COR ratio, calculated as 1.32 ng/ml/1250.00 nmol/l: 1.14 ng/ml/808.0 nmol/l = 0.973. Super-selective sampling was recommended but declined by the patient. Genetic testing was conducted, revealing that the sample did not amplify the fusion gene product CYP11B1/CYP11B2, indicating no homologous recombination or formation of a chimeric gene (Fig. 3).

The patient was diagnosed with PA. Adjusted medication regimen included: Eplerenone (50 mg, once daily); nifedipine (30 mg, once daily); valsartan (80 mg, once daily); atorvastatin calcium (20 mg, once daily); potassium chloride (0.5 g, three times daily) with regular monitoring of serum potassium levels. The patient underwent a follow-up upright PRA and Plasma Aldosterone Concentration (PAC) assessment one month after treatment initiation, with PRA measuring 1.76 ng/ml/h and PAC measuring 0.26 ng/ml. Despite an increase in both PRA and PAC from pre-treatment data (0.59 ng/ml/h and 0.19 ng/ml, respectively), the values remained within normal ranges, accompanied by normal blood pressure. One-year post-discharge, regular outpatient follow-up demonstrated good blood pressure control ranging between 120 and 135/70–85 mm Hg and normal serum potassium levels (4.31 mmol/L). Echocardiography revealed improved heart function, with a left ventricular ejection fraction of 53 %. Re-examination of adrenal CT revealed no significant enlargement of nodules. No adverse effects were reported by the patient.

2. Discussion

This case highlights the complexity of primary aldosteronism (PA), despite the patient's healthy lifestyle, absence of familial history, and normal BMI. Recurrent cardiovascular events, such as prior myocardial infarction and stroke, preceded the PA diagnosis, indicating potential target organ damage. Although overt symptoms were absent, refractory hypokalemia suggested underlying aldosterone excess. Adrenal imaging revealed nodular lesions, necessitating adrenal vein sampling (AVS) for diagnosis and management guidance. This underscores the importance of comprehensive evaluation in unraveling PA intricacies.

PA is the most common cause of secondary hypertension, affecting 17–23 % of patients with resistant hypertension [6,7]. Screening typically involves an aldosterone suppression test followed by a confirmatory captopril challenge test. Imaging examinations like CT or MRI are necessary to determine the type of PA. Unilateral adrenalectomy is a viable option for cases with a solitary unilateral macroadenoma (>1 cm) and a normal contralateral adrenal gland. However, imaging often shows normal adrenals or equivocal changes,

Table 1
Upright and supine aldosterone ratio test.

Test Position	Aldosterone (ng/ml)	Plasma renin activity (ng/ml/h)	Angiotensin II (ng/ml)	ARR (%)
Supine	0.16	0.36	30.1	44.4
Upright	0.19	0.59	55.42	32.2

Table 2
Results of captopril challenge test.

Time (hours)	Aldosterone (ng/ml)	Plasma renin activity (ng/ml/h)	Angiotensin II (ng/ml)
Baseline	0.16	0.51	40.94
1	0.18	1.55	45.94
2	0.17	1.66	43.73

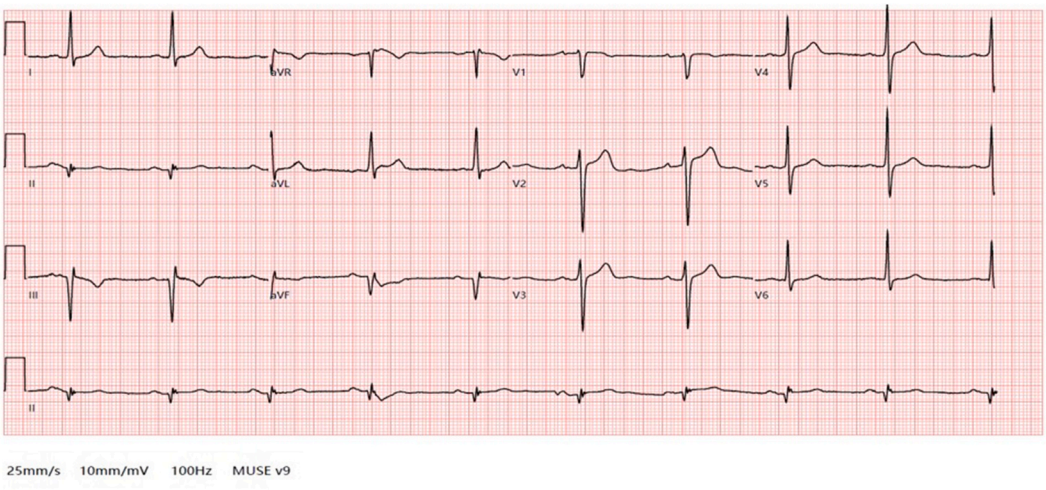

Fig. 1. The electrocardiogram depicts T-wave inversion.

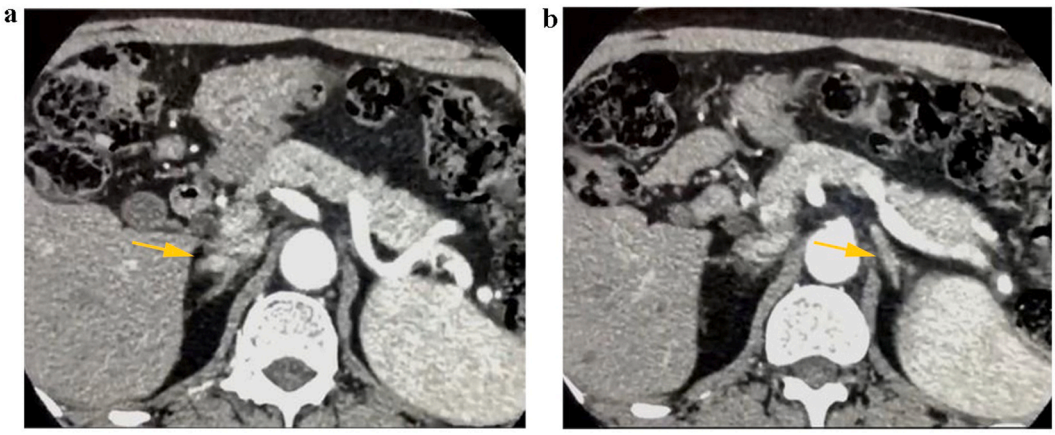

Fig. 2. a) Arrow indicates nodule on the right adrenal gland. b) The arrow highlights the fullness of the left adrenal gland.

complicating diagnosis [8]. AVS, considered the "gold standard," [9] accurately distinguishes unilateral from bilateral secretion and guides treatment decisions [10–12], particularly for patients with equivocal imaging findings or no identifiable adrenal lesions.

Patients with aldosterone overproduction may also have Cushing syndrome or subclinical Cushing syndrome, characterized by the coexistence of aldosterone-producing and cortisol-producing adenomas in the adrenal glands. Excessive secretion of both hormones can cause central obesity, moon face, buffalo hump, skin changes, metabolic abnormalities, hypertension, and other symptoms. Thus, further evaluation such as dexamethasone suppression test or gene test may be needed [1]. Most cases of PA are benign; however, somatic mutations in exon 3 of the CTNNB1 gene, detected in 2%–5% of sporadic aldosterone-producing adenomas (APAs), are implicated in tumorigenesis and cell proliferation [13]. To evaluate the risk of malignancy, this examination is recommended.

The management of PA significantly differs from essential hypertension. Treatment strategies are tailored based on etiology and patient response to medications. Goals include blood pressure control, correcting hypokalemia, reducing target organ damage, and minimizing aldosterone-induced injury. Guidelines recommend surgical adrenalectomy for unilateral lesions and medical therapy for bilateral disease, emphasizing the importance of AVS.

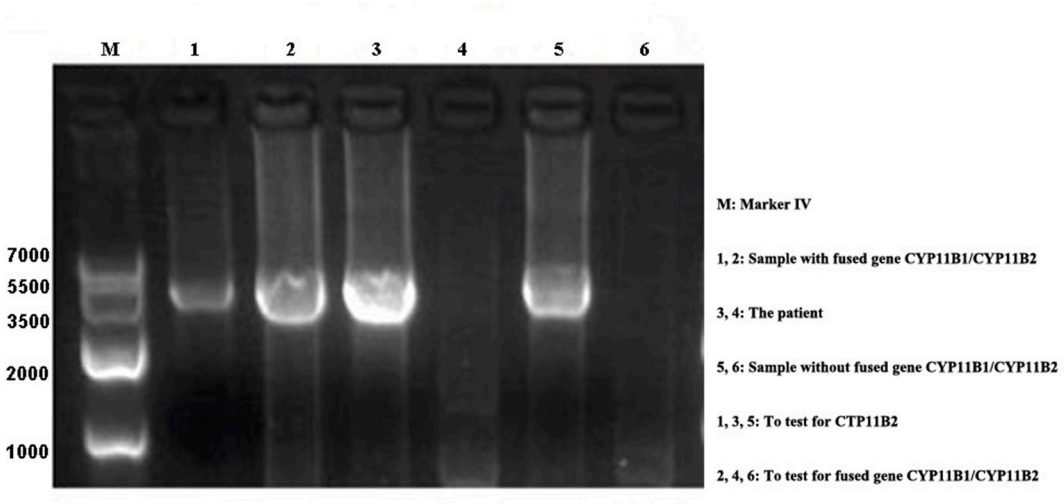

Fig. 3. Absence of CYP11B1/CYP11B2 fusion gene.

Recent research has revealed a close association between an elevated Aldosterone-to-Renin ARR and the development of hypertension and cardiovascular events [14–16]. For patients diagnosed with PA, even when blood pressure is well-controlled, the risk of cardiovascular events and mortality remains higher compared to those with essential hypertension [4,17]. Chronic hypokalemia, often overlooked for prolonged periods, may lead to cardiac, cerebral, and renal damage due to prolonged exposure to elevated aldosterone levels before a diagnosis of PA is established. Excessive aldosterone production reduces nitric oxide, impairs vascular elasticity, increases vascular resistance, and activates mineralocorticoid receptors in vascular tissues [18–20]. In this case, the patient's severe cardiovascular events are attributed to the combined effects of uncontrolled hypertension and aldosterone overproduction. Eplerenone suppress myocardial damage and improve l cardiac remodeling associated to improve prognosis [21]. The administration of eplerenone decreases mortality and cardiovascular incidents among patients experiencing left ventricular systolic dysfunction following myocardial infarction onset [22]. The patient is highly satisfied with blood pressure control and treatment outcomes, which alleviates his anxiety.

3. Key points

1. Adrenal vein sampling (AVS) is crucial post detection of unilateral adrenal nodules. AVS helps avoid unnecessary surgery, especially when imaging diagnosis is uncertain about true unilateral nodules.
2. When administered to patients with hyperaldosteronism, eplerenone not only effectively regulates blood pressure but also enhances cardiac function, thereby obviating the need for surgical intervention.
3. Although the majority of aldosteronomas are benign, it is still important to be vigilant for the possibility of malignancy. Apart from genetic testing, CT follow-up is also an option.

4. Conclusion

For PA, although surgery is the primary treatment approach, some patients may not be suitable or willing for surgical intervention. In such cases, pharmacological treatment with aldosterone antagonists alone can be a choice.

Ethics and consent

Written informed consent was obtained from all participants in the study. Additionally, consent to publish the findings was acquired from all authors. The study protocol received approval from the Ethics Committee. This case report adheres to the CARE guidelines.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Ai Wang: Writing – original draft, Software, Formal analysis, Conceptualization. **Qun Ma:** Validation, Investigation, Data curation.

Muisha B. Mbikyo: Writing – review & editing, Software. **Linlin Miao:** Validation, Project administration. **Nan Cui:** Methodology, Data curation. **Haoran Fu:** Visualization, Validation. **Jiahui Yu:** Visualization, Software. **Qiao Wu:** Visualization, Validation, Software. **Yingxian Sun:** Supervision, Conceptualization. **Zhao Li:** Supervision, Resources, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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