Journal of
Medical Case Reports

CASE REPORT Open Access

Concomitant pheochromocytoma and hyperaldosteronism in a 47-year-old man: a case report

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Abstract

Background The coexistence of pheochromocytoma and hyperaldosteronism is a rare and clinically significant finding with diagnostic challenges that need to be considered in the workup of patients with hypertension.

Case presentation This case report describes a 47-year-old Iranian man who initially presented with cold symptoms, chills, and headaches. Despite being diagnosed with panic disorder, his symptoms worsened, leading to a systolic blood pressure crisis. The results indicated elevated levels of 24-hour urine vanillylmandelic acid, metanephrine, and normetanephrine, suggesting increased catecholamine levels. An increase in serum aldosterone was also observed. Further evaluation revealed a 4 cm left adrenal mass and subsequent tests confirmed the diagnosis of pheochromocytoma and hyperaldosteronism. The patient underwent left adrenal gland resection, resulting in complete resolution of symptoms and normalization of test results.

Conclusion This case highlights the importance of considering rare coexisting endocrine disorders in patients presenting with hypertension. Appropriate diagnosis and management of concomitant pheochromocytoma and hyperaldosteronism are crucial for favorable outcomes and may offer insights into potential overlaps in disease pathways.

Keywords Pheochromocytoma, Hyperaldosteronism, Hypertension, Case report

Introduction

In terms of etiology, hypertension can be primary without a known cause or secondary (with a known cause). Despite the higher prevalence of the primary type (90–95%), evaluating the secondary type is particularly important owing to differences in treatment approaches and variable prognoses [1, 2]. Although factors such as renovascular disease, renal parenchymal disease, and obstructive sleep apnea can cause secondary hypertension, the most common causes of secondary hypertension are endocrine disorders [3]. Approximately 63% of secondary hypertension cases are caused by primary hyperalderonism [4]. Aldosterone is a hormone secreted from the cortical part of the adrenal gland that plays a role in regulating blood pressure by controlling sodium stored in the bloodstream and potassium output. Hyperalderonism can be primary (disorder in the adrenal glands) or secondary (disorder in other parts of the body). Primary hyperalderonism can cause serious cardiovascular complications such as atrial fibrillation, stroke, and myocardial infarction [5]. The treatment of choice for unilateral disease is surgery, while mineralocorticoid receptor

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antagonists (MRAs) are available for treating bilateral lesions [6].

Pheochromocytoma is an adrenal medulla tumor that occurs in 0.2–0.6% of hypertensive individuals and can arise from nonadrenal tissue in 10–15% of patients [7]. Approximately 95% of patients with pheochromocytoma develop hypertension due to elevated levels of catecholamines, which can be either short term or long term. Hypertensive paroxysms (episodic hypertension) may occur in individuals despite the presence of constant hypertension [8]. Other symptoms of this disease include headache, sweating, palpitations, abdominal discomfort, vomiting, extreme fatigue, indigestion, right hypochondrial pain, and increased liver enzymes [9–11]. Screening for pheochromocytoma is performed by measuring 24-hour urine levels of catecholamines, total and fractionated metanephrine, and vanillylmandelic acid (VMA). Visualization of the mass by imaging with computed tomography (CT) scan scan or magnetic resonance imaging (MRI) can also be used for diagnostic evaluation [7]. A review of studies revealed that the simultaneous presence of two causes of secondary hypertension is not as rare as expected [12, 13]. However, the coexistence of pheochromocytoma and hyperalderonism is still rare. We present a patient with pheochromocytoma and hyperalderonism.

Case report

A 47-year-old man (Iranian ethnicity) with a history of cold symptoms from 4 days prior, including fever, chills, sweating, and headache, was referred to the neurology unit with a headache complaint.

Following a medical evaluation with a brain MRI that did not show any pathological findings, he was diagnosed with panic attack disorder and received appropriate medication.

The next day, he presented with worsening headache, agitation, and sweating without fever, nausea, or vomiting. A systolic blood pressure crisis of up to 250 mmHg was reported. The patient's blood pressure did not improve with nitroglycerin (TNG) but decreased with labetalol.

His 12-lead electrocardiogram (ECG) revealed a normal sinus rhythm, no axis deviation, and no significant ST-segment or T-wave changes (Fig. 1). He then underwent echocardiography to exclude the possibility of coarctation of the aorta.

His blood sugar was 400 mg/dL. Serum electrolyte assessment revealed that the sodium (141.3 mmol/L), potassium (4.20 mmol/L), and chloride (102 mmol/L) concentrations were within normal limits. His arterial blood gas (ABG) was unremarkable (pH: 7.43; $PaCO_2$: 37 mmHg; HCO_3: 23 mEq/L). He was a smoker (one pack per year for 10 years) without any other past medical history, such as diabetes mellitus or hypertension. The patient's family history revealed left adrenal gland cancer

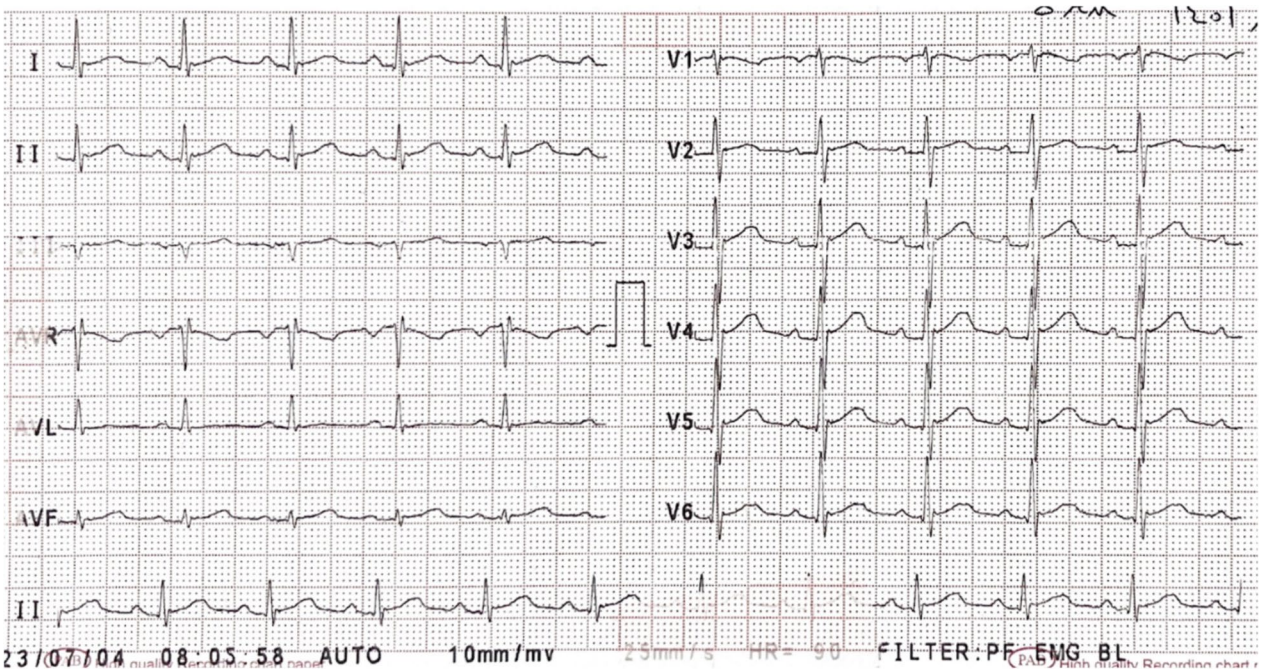

Fig. 1 First-day electrocardiogram that showed normal findings without any rhythm disorder, axis deviation, or ST-segment or T-wave changes

in his aunt, which resulted in her death at a young age, and a history of diabetes mellitus in his family members. An abdominal CT scan was requested owing to the suspicion of an adrenal tumor, and a 4 cm left adrenal mass was observed without any other pathological findings, such as pancreatic lesions (Fig. 2).

Following the observation of the adrenal mass, additional tests were conducted, revealing the following results: a 24-hour urine cortisol level of 172.5 g/24 hours (within the normal range of 50–190 g/24 hours), a 24-hour urine vanillylmandelic acid (VMA) concentration of 18.35 mg/24 hours (elevated compared with the normal limit of 13.6 mg/24 hours), 24-hour urine metanephrine levels exceeding 2000 µg/24 hours, and a 24-hour urine normetanephrine level of 1731.9 µg/24 hours. The findings revealed an increase in catecholamine levels in the 24-hour urine sample. Regarding microalbuminuria and creatinine, the test findings indicated normal results; however, the 24-hour urine volume was 2500 mL, which is considered elevated. The notably high serum aldosterone level of 24.70 ng/dL was of particular significance. Subsequent assessment was conducted to investigate the presence of multiple endocrine neoplasia (MEN) syndromes. The results of his thyroid and parathyroid ultrasound and thyroid function tests were normal, ruling out the presence of medullary thyroid carcinoma and parathyroid adenoma or hyperplasia, as well as hypothyroidism/hyperthyroidism, including thyroiditis. His brain MRI did not show any abnormal findings, such as pituitary gland adenoma. These findings made the diagnosis of MEN syndromes unlikely.

On the basis of these results, the diagnosis of pheochromocytoma combined with hyperaldosteronism was confirmed. Following the management of blood pressure with alpha-blockers, the patient underwent surgical resection of the left adrenal gland. The renin levels were not measured to determine the classification of hyperaldosteronism (primary or secondary), as the decision to proceed with adrenal gland resection had already been made, and it would not have altered the treatment plan.

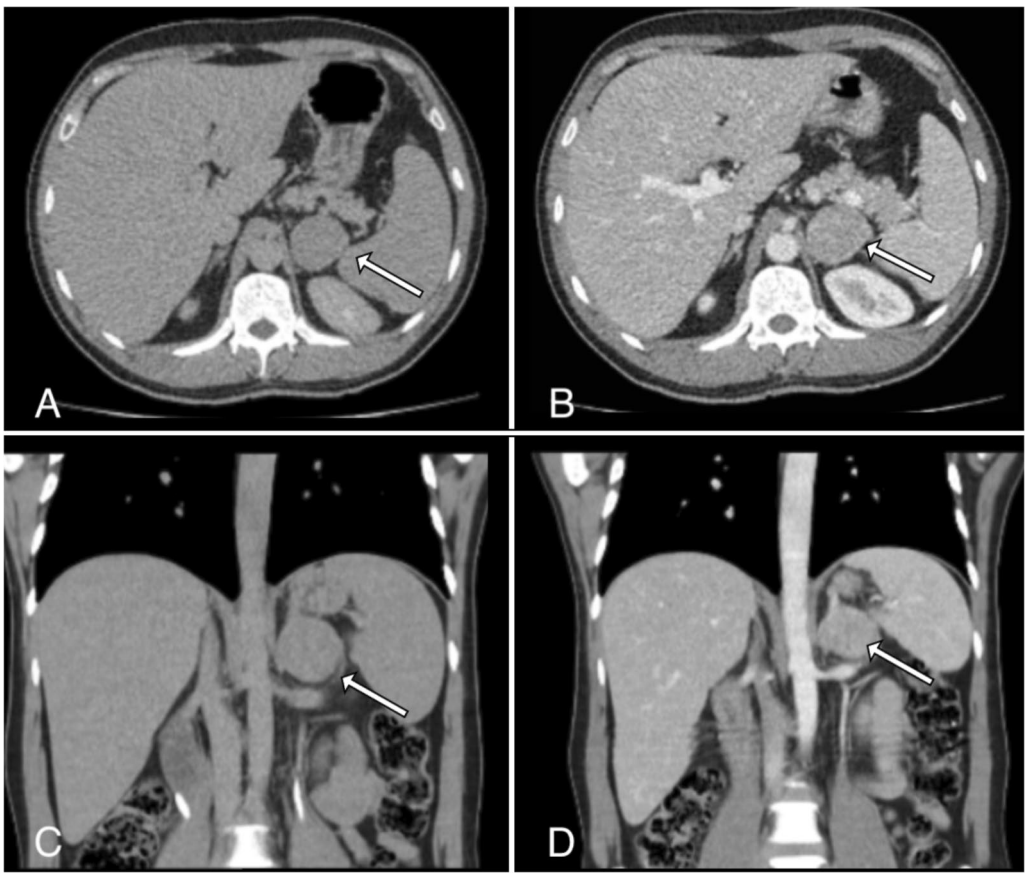

Fig. 2 Abdominopelvic computed tomography scan with and without contrast. **A** Axial view of pre-contrast abdominopelvic computed tomography scan. **B** Axial view of abdominopelvic computed tomography with contrast. **C** Coronal view of pre-contrast abdominopelvic computed tomography scan. **D** Coronal view of abdominopelvic computed tomography with contrast. **A** and **C** demonstrated a 4 cm mass in the left adrenal gland (arrow). **B** and **D** showed mass enhancement with contrast (arrow)

Following surgery, the patient's symptoms were completely resolved, and all test results returned to within normal ranges without hemodynamic instability or hypoglycemia (systolic blood pressure: 133 mmHg; potassium: 4.25 mmol/L; fasting blood sugar: 113 mg/dL). A 24-hour urine analysis, performed 3 weeks after surgery, demonstrated normal results, suggesting complete resection (metanephrine: 293 µg/24 hours; normetanephrine: 452 µg/24 hours). In the last follow-up at 1 year post-surgery, he was still asymptomatic; his blood pressure was 125/70 mmHg, and his blood sugar was 96 mg/dL with HbA1c of 5.7% (without taking any diabetic drugs). His 24-hour urinary metanephrine (235 µg/24 hours), normetanephrine (383 µg/24 hours), serum aldosterone (3.5 ng/dL), and potassium (4.30 mmol/L) levels were all within normal limits.

Discussion

The patient in question initially presented to a neurologist with a chief complaint of headaches, leading to a consideration of panic attack as a potential diagnosis. In cases of pheochromocytoma, the presence of palpitations, often described as "my heart is coming out of the chest," and feelings of anxiety may lead the neurologist to initially suspect panic and anxiety disorders. These symptoms can be attributed to elevated levels of catecholamines in the patient's serum, which are also elevated in individuals experiencing panic and anxiety [14]. However, persistent headaches and elevated blood pressure prompted further investigation into potential endocrine disruptions. Therefore, it is crucial to be mindful of these two manifestations in patients who are initially suspected of having panic and anxiety disorders.

While there was no laboratory confirmation specifically indicating primary hyperaldosteronism, the normalization of all relevant parameters subsequent to the resection of the adrenal gland, coupled with the absence of symptom recurrence or hypertension for a duration of 1 year, allows for the inference that the elevated secretion of aldosterone was indeed attributable to the excised adrenal gland. This increased secretion may have resulted from either an excessive release of aldosterone from the adrenal cortex or the release of an aldosterone-stimulating factor originating from the pheochromocytoma. Furthermore, on the basis of the patient's response following surgical intervention, the possibility of a contralateral adenoma or bilateral adrenal hyperplasia can be effectively discounted.

Cases of simultaneous pheochromocytoma and primary aldosteronism are rare, and in a case series and literature review by Mao *et al*. in 2021, only 15 patients were identified and described [15]. Among these patients, high blood pressure emerged as the prevailing symptom, with 13 out of the 15 patients exhibiting this manifestation, according to the study. Notably, the prevalence of hypokalemia mirrors that of hypertension among patients presenting with pheochromocytoma and primary aldosteronism. Hypokalemia, attributable to the direct impact of aldosterone on serum potassium levels, constitutes one of the diagnostic findings of aldosteronism. While its prevalence remains relatively modest in primary aldosteronism cases (below 40% in the absence of concurrent conditions) [16], an approximate incidence of 87% has been reported in simultaneous cases of pheochromocytoma and aldosteronism [15]. However, in the specific patient under investigation, the patient's potassium level before any intervention was measured at 4.20 mmol/L, denoting a state of complete normalcy. Research has demonstrated that, in patients with concurrent pheochromocytoma and primary aldosteronism, the failure to administer adrenergic blockers prior to surgery can potentially lead to life-threatening blood pressure crises [17]. In our patient, upon suspicion of pheochromocytoma, standard diagnostic tests were conducted to confirm the presence of the tumor.

Additionally, aldosterone level testing was requested, and on the basis of the elevated aldosterone levels and the absence of contralateral adrenal masses, the proposed course of action involved unilateral adrenal gland resection following pretreatment with alpha-blockers. After surgery, the patient experienced remarkable improvement, and his symptoms disappeared. This highlights the favorable prognosis associated with adrenal gland resection in such cases.

Conclusion

The concurrent occurrence of pheochromocytoma and primary aldosteronism represents an infrequent yet manageable medical condition that necessitates prompt identification by physicians. Failure to detect pheochromocytoma in such patients may lead to unfavorable outcomes if surgical intervention targeting hyperaldosteronism is pursued without prior pretreatment. Notably, despite markedly elevated blood pressure in affected individuals, their potassium levels can remain within the normal range.

Abbreviations

VMA	Vanillylmandelic acid
MRAs	Mineralocorticoid receptor antagonists
CT scan	Computed tomography scan
MRI	Magnetic resonance imaging
ECG	Electrocardiogram
MEN	Multiple endocrine neoplasia

Acknowledgements

Not applicable.

Author contributions
FM conceptualized the study, collected data, and revised the manuscript. AS collected data, drafted the manuscript, and ensured the completion of the final draft. SN drafted the manuscript and participated in the review and editing of the manuscript. AM reviewed the literature and drafted the manuscript. All authors read and approved the final manuscript.

Funding
None.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval is not applicable, and patients' written informed consent to participate is present.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare that they have no competing interests.

Received: 9 July 2024 Accepted: 10 December 2024
Published online: 18 January 2025

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