

Hypokalemia Masks Primary Aldosteronism: Diagnostic Pitfalls and Rural Challenges

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ABSTRACT

Objective: Primary aldosteronism (PA) is a common but frequently underdiagnosed cause of secondary hypertension, particularly in low-resource settings where access to hormonal assays and confirmatory testing is limited. Hypokalemia, although traditionally associated with PA, is absent in most cases and may suppress aldosterone levels, further complicating diagnosis. This report describes a patient with recurrent hypokalemia and long-standing resistant hypertension, illustrating the diagnostic challenges encountered in rural clinical environments.

Case Report: A 43-year-old woman with a ten-year history of uncontrolled hypertension presented with fatigue and repeated episodes of severe hypokalemia requiring hospitalization. Despite multiple antihypertensive medications and continuous potassium supplementation, her blood pressure remained markedly elevated at 195/99 mmHg, and serum potassium was 2.2 mmol/L. Electrocardiography and chest radiography were unremarkable. Contrast-enhanced abdominal computed tomography demonstrated a 20 mm enhancing lesion in the left adrenal gland. Endocrine evaluation revealed markedly elevated aldosterone levels (78.40 ng/dL) with normal cortisol concentrations. A diagnosis of primary aldosteronism due to an aldosterone-producing adenoma was established. The patient underwent laparoscopic left adrenalectomy, and histopathological examination confirmed adrenal cortical adenoma. Following surgery, her blood pressure normalized without the need for antihypertensive therapy, and potassium levels remained stable.

Conclusions: This case underscores the importance of recognizing primary aldosteronism in patients with resistant hypertension and recurrent hypokalemia, particularly in settings with limited diagnostic resources. Early identification and timely surgical intervention can prevent prolonged disease, reduce cardiovascular risk, and offer the possibility of complete clinical cure.

Keywords: Primary aldosteronism; adrenal adenoma; hypokalemia; resistant hypertension; endocrine hypertension; adrenalectomy.

INTRODUCTION

Hypertension impacts 25% of the adult population globally, with 5% to 20% of these individuals presenting a treatable condition known as primary aldosteronism (PA). Patients with primary aldosteronism exhibit a 2- to 3-fold increased risk of cardiovascular events, renal failure, and diminished quality of life. Furthermore, patients with unilateral primary aldosteronism may achieve resolution of hypertension through adrenalectomy. Recent studies indicate that fewer than 2% of at-risk patients undergo screening. Estimates may be further reduced in resource-limited settings, particularly in lower-middle-income countries (Sukor et al., 2024).

Primary aldosteronism (PA), or Conn's Syndrome, is the predominant etiology of secondary hypertension and results from excessive adrenal synthesis of aldosterone despite inhibited renin levels. Initially regarded as rare and confined to individuals with hypokalaemia, emerging evidence indicates that the frequency of primary aldosteronism (PA) among primary care patients with hypertension ranges from 3.2% to 12.7%, with the majority of patients exhibiting normokalemia (Nainani et al., 2022).

The Endocrine Society guidelines for managing primary aldosteronism (PA) advocate for a series of tests, including screening, confirmatory, and subtyping assessments, prior to determining the appropriate treatment, which may involve mineralocorticoid-receptor antagonists (MRAs) or unilateral adrenalectomy. Biochemical tests for aldosterone and renin are generally not accessible in most standard clinical laboratories. Computed tomography (CT) is frequently unreliable for subtyping primary aldosteronism (PA), and adrenal vein sampling (AVS) is advised for the majority of patients pursuing curative surgery. AVS presents technical challenges, with overall success rates around 80% even in specialized centers. In low- and middle-income countries with constrained medical resources, there is a prevalent tendency to prioritize emergency services over the development of medical care for less urgent conditions, such as PA. Consequently, elective procedures,

including AVS and adrenalectomy, are likely assigned lower priority. Despite the availability of these health care facilities, patients may lack the financial means to access these investigations or treatments (Sukor et al., 2024). This case report details a patient who arrived at our hospital with history of uncontrolled hypertension. She exhibited undetectably low potassium levels, which is uncommon for this cause, and was later diagnosed with primary hyperaldosteronism.

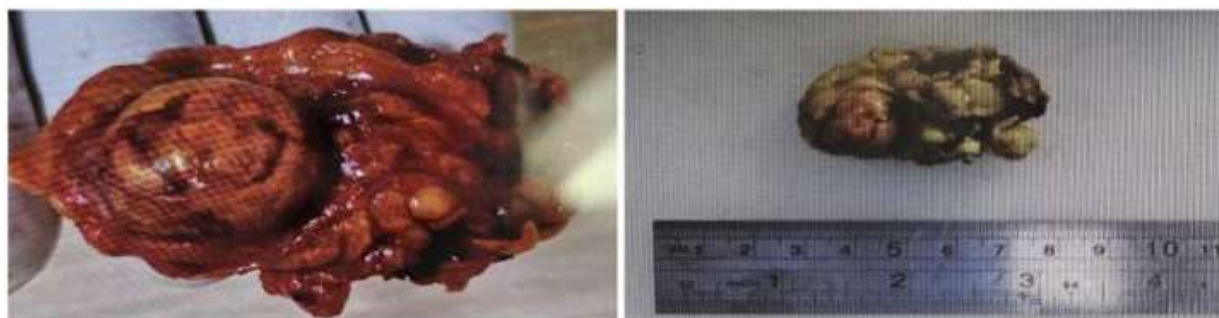
CASE PRESENTATION

Mrs. X 43 years old came to outpatient ward with chief complain of fatigue. Patient referred from a rural area with hypertension for possible 10 years' duration and already prescribed by several antihypertensive agents, including diuretics. The systolic reached up to 190 mmHg. Four years earlier, she was admitted to the ER with fatigue and paralysis at lower extremities. The patient was diagnosed with hypokalemia and received potassium chloride intravenous. This hypokalemia recurred about 4 times over 4 years. The patient received amlodipine 10mg, candesartan 16mg, and potassium slow release three times a day. She has a family history of high blood pressure; both of her parents had high blood pressure but infrequently took treatment. Her lifestyle history showed that she frequently ate salty meals, but she denied smoking, drinking alcohol, or taking herbal remedies. Physical examination revealed the patient with a Glasgow Coma Scale (GCS) score of 15 (E4 V5M6). Blood pressure was 195/99 mmHg in all extremities. Pulse rate was 75 beats per minute and regular, respiratory rate 20 breaths per minute, and temperature 36.4 °C. Examination of the head and neck showed no pallor. Jugular venous pressure was not elevated. Cardiovascular examination revealed the point of maximal impulse at the 5th intercostal space, left midclavicular line, with normal S1 and S2 and no murmurs or gallops. Pulmonary auscultation revealed vesicular breath sounds without added sounds. Abdominal examination was unremarkable, with no organomegaly or ascites. No peripheral edema or purpura was observed.

Laboratory revealed hemoglobin 10.8 g/dL, leukocytes 8,400/ μ L, and platelets 271,000/ μ L. Urinalysis showed clear yellow urine with pH 7.0, specific gravity 1.015, proteinuria and nitrites negative. Microscopic examination of the urine sediment demonstrated 1–2 erythrocytes/HPF, 2–4 leukocytes/HPF, a few epithelial cells, and no bacteria. Serum biochemistry results were: BUN 44 mg/dL, creatinine 1.13 mg/dL, albumin 4.62 g/dL, random plasma glucose 100 mg/dL, AST 20 U/L, ALT 18 U/L, potassium 2.2 mmol/L, sodium 144 mmol/L, chloride 104 mmol/L.

Electrocardiography demonstrated normal sinus rhythm at 85 bpm with a normal axis. Chest X-ray revealed no cardiopulmonary abnormalities. From the Abdominal MSCT Enhancing hypodense lesion in the left adrenal gland measuring 20.3x18.2x11.9mm supported the diagnosis of adrenal adenoma. Further endocrine evaluation showed elevated serum aldosterone at 78.40 ng/dL (reference range: 1.76-23.20) while morning cortisol was within normal limits at 15.1 μ g/dL (reference range: 3.7-19.4 μ g/dL). Based on clinical, laboratory, and imaging findings, the working diagnosis was primary hyperaldosteronism due to adrenal adenoma, with secondary diagnoses of stage 2 resistant hypertension, and recurrent hypokalemia. The patient underwent laparoscopic adrenalectomy sinistra. Histopathological examination confirmed an adrenal cortical adenoma measuring 5x3x1.5 cm.

Figure 1. Gross pathology of adrenal tumor. Gross appearance of the excised specimen showing a 5 × 3 × 1.5 cm



exophytic adrenal mass removed from the left suprarenal region. The tumor is sharply circumscribed, non-necrotic, and displays a characteristic yellow coloration attributable to abundant intracytoplasmic lipid content. Figure 2. Histopathology of adrenal cortical adenoma (10× magnification) (A) and histopathology of adrenal cortical adenoma (40× magnification) (B)

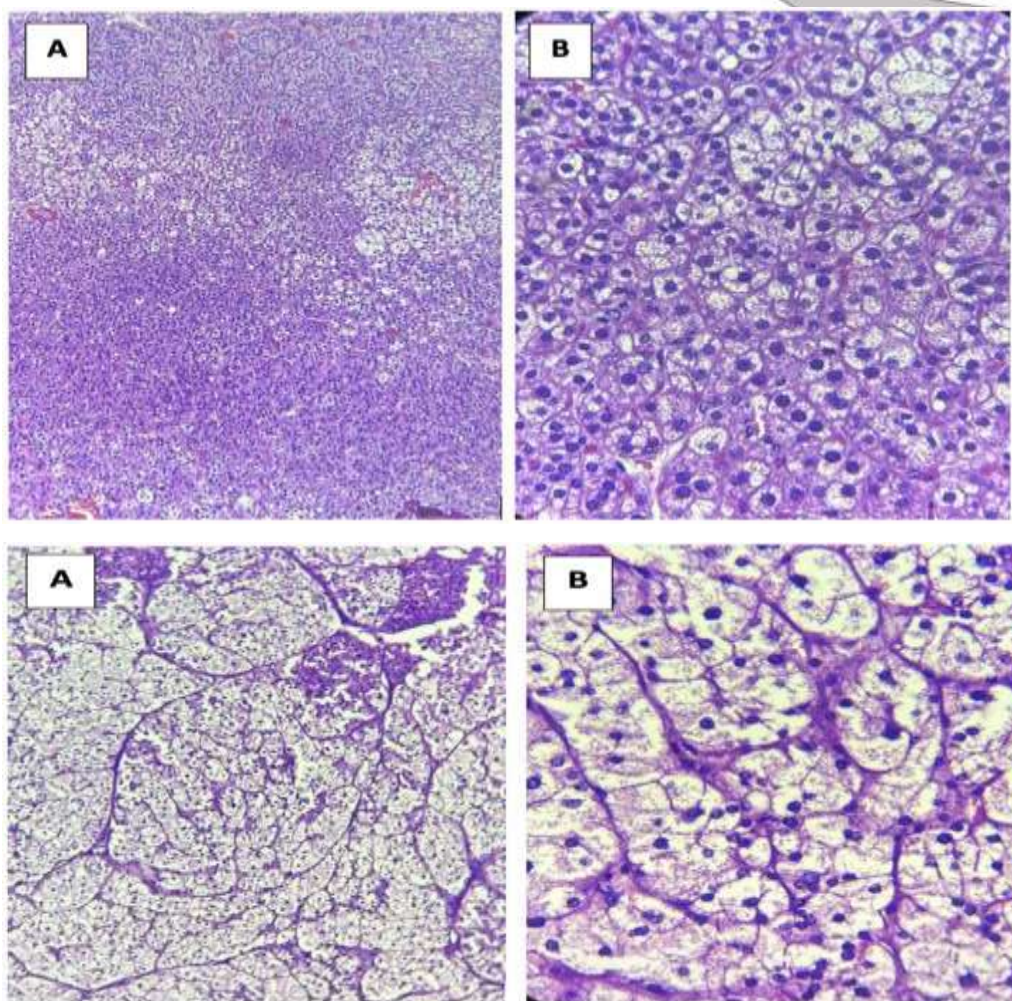


Figure 3. Histopathology section (10× magnification) (A) and histopathology section (40× magnification) (B)

Two days after surgery patient remained asymptomatic, with blood pressure 115/78 mmHg and pulse rate 70 bpm. She was discharged in stable condition without antihypertension medication.

DISCUSSION

Primary hyperaldosteronism (PA) is the predominant endocrine etiology of secondary hypertension, with reported incidence in the literature reaching as high as 11% among hypertensive patients. About two-thirds of cases result from unilateral adrenal adenoma, one-third from bilateral adrenal hyperplasia, and less than 1% from adrenocortical cancer. The majority of primary aldosteronism cases exhibit normokalemia, while hypokalemia is observed in about 9-37% of patients. Two variables contribute to hypokalemia in patients with primary hyperaldosteronism: elevated aldosterone levels, which promote potassium excretion via the kidneys, and a sufficient quantity of sodium and water in the distal nephron. In patients with primary aldosteronism, hypokalemia frequently sustains steady potassium levels due to the potassium-retaining influence of hypokalemia counteracting the effects of elevated aldosterone levels. Severe hypokalemia in the context of primary aldosteronism typically occurs in patients with an additional contributing component of hypokalemia (Sameer et al., 2025).

Hypokalemia is not a sensitive or specific marker for diagnosing primary aldosteronism. Hypokalemia may serve as an indicator of severe illness, thereby identifying patients at elevated cardiovascular risk. Furthermore, hypokalemia serves as an additional indicator of the underlying subtype of primary aldosteronism (Gruber et al., 2020).

The main screening test for primary hyperaldosteronism (PHA) is the serum aldosterone/renin ratio (ARR), which is deemed positive when ARR exceeds 30 ng/dL, accompanied by suppressed renin levels (<1.0

ng/mL/h) and aldosterone levels greater than 15 ng/dL. Three ARR sensitivity exhibits considerable variability, ranging from 10% to 100%, which undermines its reliability. Four Due to the diurnal variation of aldosterone levels, a single serum aldosterone measurement may not effectively exclude primary hyperaldosteronism (PHA). Recent studies indicate that a suppressed renin level may serve as a more sensitive indicator of primary hyperaldosteronism (PHA) than the aldosterone-to-renin ratio (ARR) or random serum aldosterone levels alone. Confirmatory testing typically occurs after a positive screening; however, it may be postponed if patients satisfy all three criteria: (1) spontaneous hypokalemia, (2) random aldosterone level exceeding 20 ng/dL, and (3) suppressed renin levels. The predominant confirmatory test is the oral salt suppression test, which entails a high-salt diet (>200 mmol/day) for four days to achieve maximal suppression of aldosterone. On day 4, a 24-hour urine sample is collected, with primary hyperaldosteronism (PHA) defined by a urine aldosterone level exceeding 12 µg/24 h.

The intravenous salt suppression test consists of administering 2 L of normal saline over a duration of 4 hours, followed by the measurement of plasma aldosterone concentration. A result exceeding 10 ng/dL is indicative of primary hyperaldosteronism (PHA). Excessive salt consumption can exacerbate hypertension and hypokalemia in PHA, necessitating meticulous monitoring of potassium levels and blood pressure during assessment. Aldosterone secretion is primarily regulated by angiotensin II, serum potassium, and ACTH. Hypokalemia can independently suppress aldosterone production; therefore, it is recommended to normalize serum potassium prior to diagnostic testing. To achieve optimal sensitivity, it is recommended to collect mid-morning samples from patients who have been out of bed for a minimum of 2 hours and seated for 5 to 15 minutes, considering the effects of ACTH (Lamba, 2023).

Screening tests for aldosterone and renin levels are essential for the diagnosis of primary aldosteronism. Most ASEAN countries depend on foreign laboratories for assays. This has numerous implications. This extends the test turnaround time, often exceeding three weeks at numerous centers. This leads to an extended diagnostic interval for both confirmatory tests and adrenal venous sampling, which depend on biochemical results. Third, screening tests utilizing ARR are often conducted exclusively by endocrine specialists, even when they are accessible. Given that a majority of patients with primary aldosteronism exhibit hypertension and frequently remain asymptomatic, it is essential to conduct screening in primary care settings. Consequently, numerous patients with PA remain undiagnosed (Sukor et al., 2024).

Primary care serves as the primary setting for the majority of patients with hypertension, making it essential to comprehend the perceptions of primary care providers regarding PA. A qualitative interview-based study of general practitioners participating in a physical activity screening research program in Australia identified several factors influencing screening, including knowledge, cost and convenience, risk conceptualization, and enhancement of clinical care. Numerous general practitioners encountered difficulties in discontinuing standard antihypertensive medications to achieve a more significant absolute risk reduction (Libianto et al., 2023).

Early detection and targeted treatment of PA are crucial for three reasons. Patients with primary aldosteronism exhibit poorer cardiovascular outcomes compared to those with essential hypertension matched for blood pressure. Second, targeted treatment of primary aldosteronism, through unilateral adrenalectomy or initiation of a mineralocorticoid receptor antagonist, can enhance blood pressure regulation, decrease cardiovascular risk, and reverse end-organ damage. Diagnosing PA at a younger age decreases the duration of untreated disease and correlates with improved treatment outcomes (Nainani et al., 2022).

CONCLUSION

Primary aldosteronism is common and clinically important among hypertensive patients. Current diagnostic pathways are complex and resource-intensive for many real-world settings, particularly rural and LMIC contexts. Simplifying and decentralizing screening, improving primary-care awareness, and ensuring access to definitive treatment could substantially improve outcomes by shortening the duration of untreated PA and preventing irreversible end-organ damage.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest

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