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Case Report

Challenges in diagnosing and treating Liddle syndrome in resource-limited settings: A case report from Indonesia

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Abstract

Liddle syndrome, a rare form of monogenic hypertension, poses significant diagnostic and therapeutic challenges due to its phenotypic variability and the need for genetic testing. The rarity of the condition, coupled with the limited availability of first-line treatments such as epithelial sodium channel (ENaC) blockers, makes this case report particularly urgent and novel, highlighting alternative management strategies in resource-limited settings. The aim of this case report was to present the diagnostic challenges, therapeutic strategies, and clinical outcomes of a patient with Liddle syndrome who did not have access to ENaC blockers, emphasizing the importance of early recognition and personalized treatment. A 35-year-old female presented with resistant hypertension (190/100 mmHg) and bilateral limb weakness. Laboratory results revealed persistent hypokalemia, hypernatremia, and metabolic alkalosis. Low aldosterone levels, alongside clinical and family history, led to the diagnosis of Liddle syndrome. Genetic testing was not conducted due to resource limitations, and ENaC blockers were unavailable. The patients were managed with a combination of alternative antihypertensive agents, potassium supplementation, and a low-sodium diet. Although this approach led to modest improvements in blood pressure and motor strength, persistent hypokalemia and hypernatremia underscored the suboptimal control of the syndrome's underlying pathophysiology in the absence of ENaC blockers. This case highlights the challenges faced in resource-limited settings and the need for innovative strategies to manage rare conditions like Liddle syndrome. Liddle syndrome's diagnostic and therapeutic challenges underscore the critical importance of early recognition and access to targeted therapies. In the absence of ENaC blockers, alternative treatment strategies can provide some benefit, but they often fall short of optimal management. This case emphasizes the need for enhanced clinical awareness, improved access to genetic testing, and the development of personalized treatment approaches to achieve better patient outcomes.

Keywords: Liddle syndrome, diagnosis, treatment, genetic, challenge

Introduction

Hypertension, affecting nearly one billion people globally, is a prevalent modifiable risk factor for cardiovascular diseases and related disabilities [1]. Essential hypertension, influenced by both

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lifestyle and genetic factors, is common, whereas hereditary conditions such as Liddle syndrome, caused by epithelial sodium channel (ENaC) gene mutations, are rare, with a prevalence of 0.91% to 1.52% [2]. Liddle syndrome arises from genetic mutations in the *SCNN1B* or *SCNN1G* genes, which encode subunits of ENaC in the kidneys [3,4]. These mutations enhance sodium reabsorption and potassium excretion, leading to severe hypertension and hypokalemia [3–5]. Understanding these genetic mutations offers valuable insights into the molecular mechanisms regulating blood pressure and electrolyte homeostasis [2,3].

Liddle syndrome often mimics other forms of hypertension, such as primary hyperaldosteronism, but presents with distinct biochemical profiles [6-10]. Due to its rarity and subtle laboratory result differences, diagnosis is challenging [11]. Genetic testing is essential for distinguishing Liddle syndrome from other hypertensive disorders [4,11]. Understanding specific genetic mutations aids in developing targeted treatments for Liddle syndrome and other hypertensive forms, advancing personalized medicine with customized therapies based on genetic profiles. However, diagnosing Liddle syndrome requires specific genetic tests, which can be expensive and not widely available. The availability of medications can vary between healthcare centers, complicating access to the most effective therapies. Additionally, patient responses to treatment can differ significantly.

Liddle syndrome is intriguing due to its unique genetic basis, diagnostic challenges, and insights into hypertension and electrolyte balance [11]. This case report aims to present a case of Liddle syndrome, highlight diagnostic challenges, discuss genetic and clinical features, examine therapeutic strategies, and emphasize the importance of early detection. Previous case reports on Liddle syndrome predominantly highlight the use of ENaC blockers as the first-line therapy [8,12-15]. However, what sets this present case report apart is the significant challenge posed by the unavailability of ENaC blockers. Unlike previous cases where access to these medications facilitated more straightforward management [8,12-15], our case required exploring alternative therapeutic strategies due to the lack of access to these first-line treatments. This limitation necessitated using other antihypertensive agents, which may not address the root cause of the syndrome as effectively as ENaC blockers.

Case

A 35-year-old female presented to the Emergency Department of Universitas Sebelas Maret Hospital, Surakarta, Indonesia, with bilateral limb weakness that had persisted for an extended period, with infrequent medical attention sought. The complaints initially began in the legs one month ago and gradually spread to all extremities. The weakness persisted throughout the day without worsening with activity or improving with rest. The patient infrequently sought medical attention. The intensity of the weakness progressively increased, and two days before admission, the patient experienced difficulty walking. No slurred speech, fever, vomiting, headache, or dizziness were reported. The patient also did not report any episodes of heart palpitations, excessive sweating, frequent urination, or body swelling. Additionally, there were no signs of drooping eyelids, blurred or double vision, difficulties with chewing or swallowing, or trouble breathing. The patient had a history of hypertension but had never consumed antihypertensive medication, as she had never experienced any significant symptoms before. The patient denied any history of hemiparesis, transient ischemic attack, or facial palsy. The family history revealed hypertension-related deaths in her mother. The patient does not smoke and has no history of alcohol consumption but has a diet high in salt and fat.

The vital signs showed blood pressure of 190/100 mmHg, a temperature of 36.4°C, a heart rate of 79 beats per minute, a respiratory rate of 20 breaths per minute, and oxygen saturation of 99% on room air. Physical examination showed no conjunctival pallor. Heart sounds were normal, with no murmurs, gallops, or rubs. Breath sounds were clear bilaterally, with no wheezing, rales, or rhonchi. Mild tenderness was noted in the right hypochondriac region, but no guarding or rebound tenderness was present. The liver was not palpably enlarged. The extremities were warm, with a capillary refill time of fewer than two seconds, and there was no edema. Neurological examination revealed symmetrical motor weakness in all four extremities, graded as 2/5 in each limb, with physiological reflexes diminished in both upper and lower

extremities. There were no pathological reflexes observed. Sensory examination was normal, and cranial nerve function was intact. No signs of fasciculations or muscle atrophy were present.

Haemoglobin, leukocytes, platelets, random blood glucose, triglycerides, free T4, thyroid-stimulating hormone (TSH), creatinine, and blood urea nitrogen were all within normal limits. Elevated levels were documented for aspartate aminotransferase (AST) at 81 units/L (normal range: 0–34 units/L) and alanine aminotransferase (ALT) at 192 units/L (normal range: 0–34 units/L). Low-density cholesterol (LDL) was also elevated at 247 mg/dL (normal range: 57–130 mg/dL). The patient had hypokalemia at 21.27 mmol/dL (normal range: 25–125 mmol/dL) and hypernatremia at 54.14 mmol/L (normal range: 40–220 mmol/L). Suppressed aldosterone level was 18 pg/mL (normal range: 20–230 pg/mL).

Blood gas analysis indicated metabolic alkalosis, with pH at 7.48 (normal range: 7.35–7.45), pCO_2 at 38 mmHg (normal range: 35–45 mmHg), pO_2 at 94 mmHg (normal range: 80–100 mmHg), HCO_3 at 28 mmHg (normal range: 22–26 mmHg), tCO_2 at 25 mmHg (normal range: 23–27 mmHg), base excess (BE) at 6 (normal range: -2 to +3), and SpO_2 at 99% (normal range: 95–99%).

An electrocardiogram revealed bigeminy premature ventricular contractions (PVCs) with periods of multifocal couplet PVCs (**Figure 1A**). Echocardiography indicated mild left ventricular (LV) chamber dilatation, with a normal LV ejection fraction of 58.7% and normal right ventricle (RV) systolic function (tricuspid annular plane systolic excursion (TAPSE)) of 2.61 cm), along with mild mitral valve regurgitation (**Figure 1B**). Abdominal ultrasonography revealed grade 1 fatty liver (**Figure 1C**).

The patient was given antihypertension medications, including ramipril 10 mg/24 hours and bisoprolol 1.25 mg/24 hours. The therapy was adjusted into ramipril 10 mg/24 hours, furosemide 40 mg/24 hours, clonidine 0.15 mg/12 hours, diltiazem 200 mg/24 hours, and bisoprolol 10 mg/24 hours. Despite this adjustment, resistant hypertension was observed, with blood pressure ranging from 150/90 mmHg to 170/100 mmHg. On the first day, the patient continued to experience weakness in all four limbs. However, motor strength improved to 3/5 by the second day, and by the third and fourth days, it further improved to 4/5.

The laboratory results up to day four indicated the following trends: (1) sodium level was consistently high, exceeding the normal range, suggesting hypernatremia; (2) potassium level was critically low throughout the period, showing a slight increase but still significantly below the normal range, indicating severe hypokalemia; (3) chloride levels fluctuated, mostly below or just reaching the lower end of the normal range, suggesting an electrolyte imbalance; and (4) calcium level was consistently below the normal range, indicating hypocalcemia (**Table 1**). To address these issues, the patient received intravenous potassium (100 mEq per day) and was advised to adhere to a sodium-restricted diet (under 2 g NaCl daily).

Table 1. Patient's laboratory results trends over the four days of hospitalization

Laboratory test	Hospital admission day				Normal range
	1st day	2nd day	3rd day	4th day	
Sodium	143	146.35	145.66	149.89	135–145 mmol/L
Potassium	1.00	1.28	1.72	2.05	3.5–5.5 mmol/L
Chloride	87.3	95.70	98.30	93.91	96–106 mmol/L
Calcium	0.75	0.82	1.12	0.85	1.1–1.35 mmol/L

The patient was subsequently discharged after a four-day hospital stay and was prescribed outpatient medications, including ramipril 10 mg/24 hours, furosemide 40 mg/24 hours, clonidine 0.15 mg/12 hours, diltiazem 200 mg/24 hours, bisoprolol 10 mg/24 hours, and potassium supplementation 600 mg/8 hours. Seven days after discharge, the patient reported persistent mild weakness in all limbs, with motor strength of 4/5. The patient was also given spironolactone 60 mg three times a day for two weeks, but no significant change in blood pressure was observed, which remained between 150/90 mmHg and 170/100 mmHg. Due to the lack of response to spironolactone, it was discontinued after two weeks.

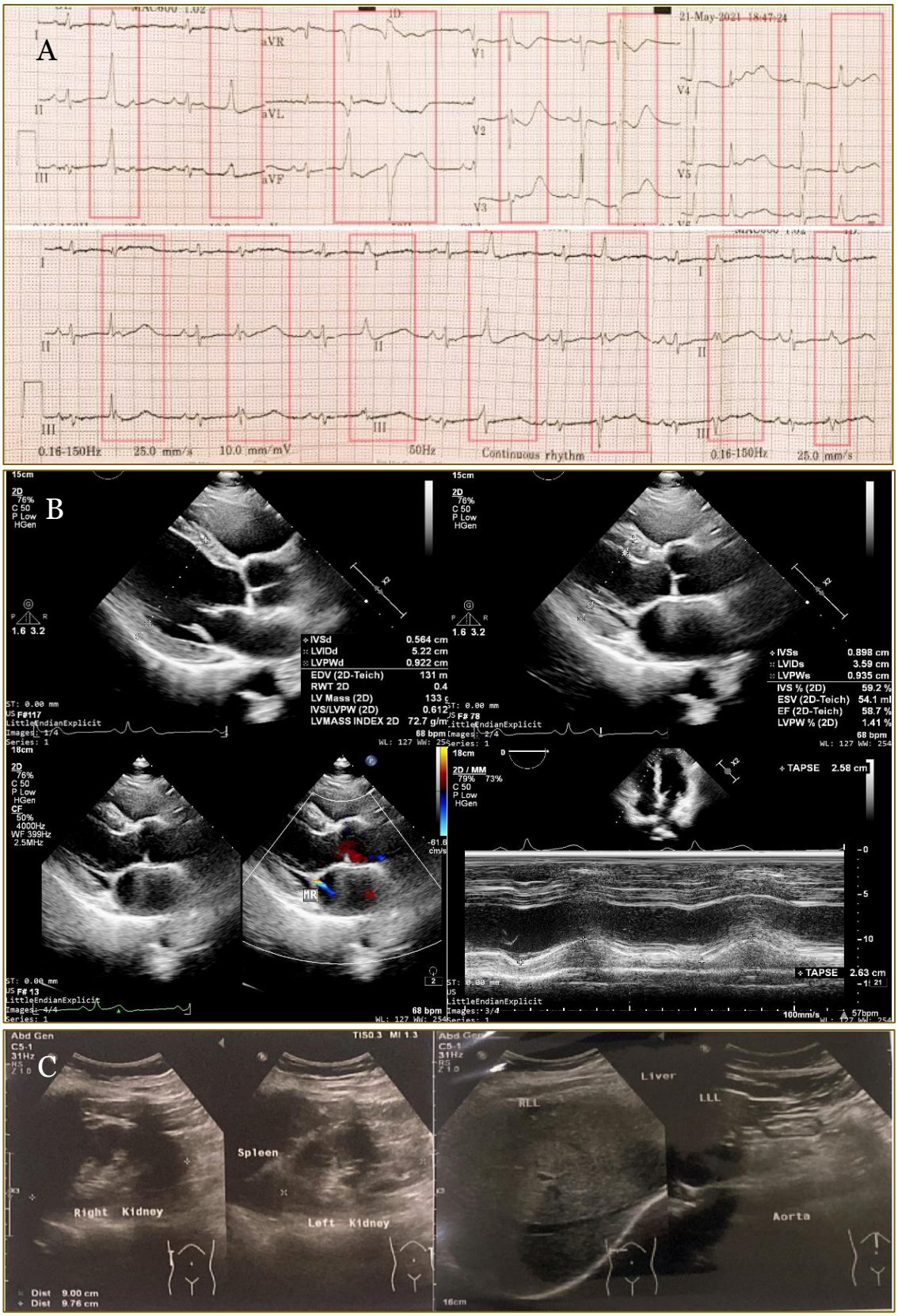

Figure 1. Electrocardiogram (ECG) of the patient revealed bigeminy premature ventricular contractions (PVCs) with periods of multifocal couplet PVCs (red boxes) (A). Echocardiography indicated mild left ventricular chamber dilatation, tricuspid annular plane systolic excursion (TAPSE) of 2.61 cm, and mild mitral valve regurgitation (B). Abdominal ultrasonography (USG) indicated a normal liver size (13.3 cm), with diffusely increased echostructure, sharp angles, regular edges, normal intrahepatic bile duct (IHBD) and extrahepatic bile duct (EHBD), a normal portal vein/hepatic vein, no nodules/cysts/masses suggestive of fatty liver (C).

Subsequently, the patient was diagnosed with Liddle syndrome, as detailed in **Figure 2**. Genetic testing was not conducted in this case. The patient had early-onset resistant hypertension, a family history of hypertension, and a combination of clinical, physical, and laboratory findings (metabolic alkalosis, hypernatremia, normal urinary potassium, low aldosterone level), imaging findings and lack of response to spironolactone, led to the diagnosis of Liddle syndrome after ruling out other diagnoses. The patient did not receive ENaC blockers because they were unavailable at our healthcare facility.

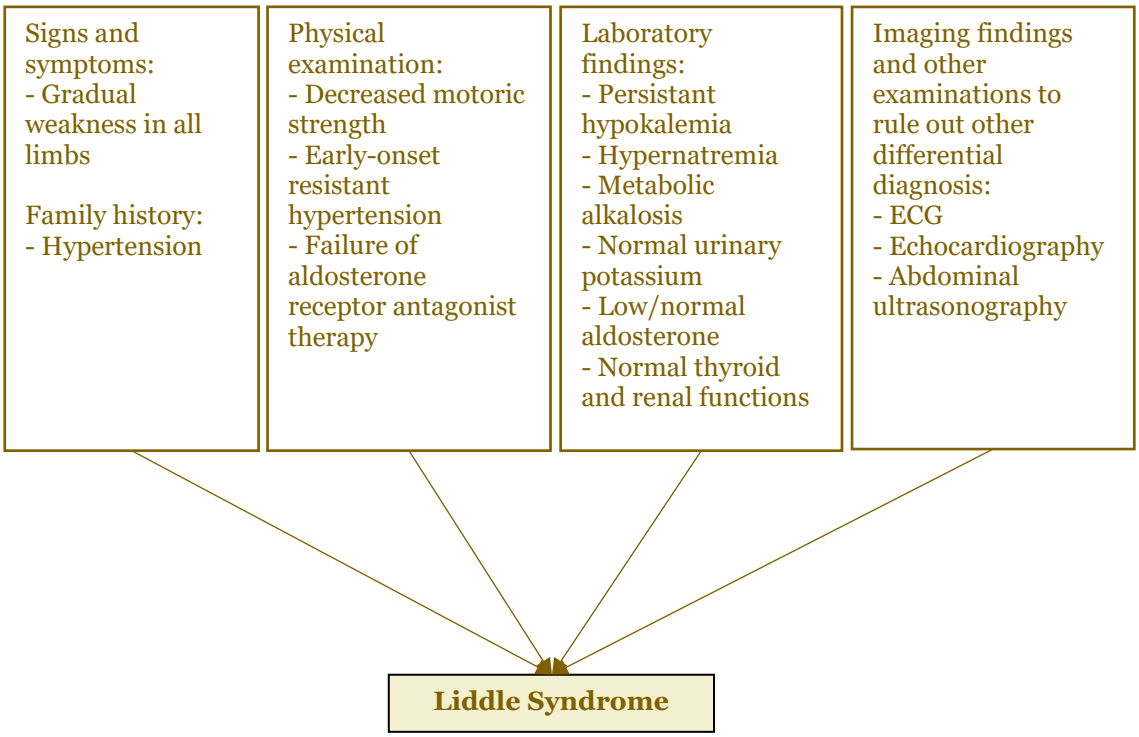

Figure 2. Diagnostic process of the patient. ECG: electrocardiography.

Discussion

Recent genetic research has improved the diagnosis of Liddle syndrome, highlighting key mutations associated with sporadic and familial cases [5]. However, genetic profiling remains a challenge in resource-limited settings like Indonesia, where access to such testing is often constrained by cost and availability. In these situations, alternative diagnostic approaches using clinical assessment combined with hallmark laboratory findings, spironolactone testing, and performing other examinations to rule out other differential diagnoses become essential.

In the present case, a 35-year-old woman presented with bilateral limb weakness and hypertension (190/100 mmHg). A study found that 92.3% of patients with Liddle syndrome experience hypertension [2]. Another study reported an average onset of hypertension at 15.5±3.3 years and peak blood pressures of 196±22 mmHg systolic and 121±16 mmHg diastolic [3]. Clinical acumen in recognizing Liddle syndrome's hallmark characteristics was pivotal in the present case. Persistent hypokalemia, hypernatremia, metabolic alkalosis, and resistant hypertension raised clinical suspicion despite the absence of genetic testing. A family history of hypertension further supported the genetic basis for the symptoms.

In Liddle syndrome, hypokalemia is present in about 71.8% of cases [6]. Hypoaldosteronism affects 58.2% of survivors, distinguishing it from hyperaldosteronism due to low aldosterone level [6]. When investigating early-onset hypertension and hypokalemia, especially in patients with a family history of resistant hypertension, stroke, or sudden death, it is imperative to consider Liddle syndrome after excluding other potential causes [5]. Normal findings in urinary potassium excretion, renal function, thyroid function, and suppressed aldosterone levels ruled out secondary

causes such as hyperaldosteronism and thyroid dysfunction, confirming Liddle syndrome as the likely diagnosis in the present case [3,7].

Diagnosing Liddle syndrome relies heavily on genetic sequencing, particularly when clinical suspicion is high [4,7,11]. Phenotypic variability underscores the need for thorough genetic screening to avoid misdiagnosis [5]. Enhancing healthcare professionals' awareness is vital to address underdiagnosis, emphasizing timely consideration and genetic testing in cases of resistant hypertension for early identification and better patient outcomes [2].

Genetic mutations in ENaC subunit genes underlie Liddle syndrome, leading to aldosterone-independent sodium reabsorption in the kidneys [7,16-21]. ENaC facilitates sodium movement across epithelial cell membranes, which is crucial for regulating sodium balance in extracellular fluid and kidney function, impacting extracellular fluid volume and blood pressure regulation [13,16]. Metabolic alkalosis in Liddle syndrome results from increased sodium absorption in the principal cell, leading to H^+ production in the distal nephron [16,22,23]. Hypokalemia exacerbates this metabolic alkalosis by disrupting renal acidification processes, affecting glomerular filtration rate, H^+ secretion in tubules, and ammonia synthesis [22,23]. Potassium depletion also impairs aldosterone secretion, further influencing sodium absorption and acid-base balance [23].

Echocardiography and abdominal ultrasonography in the present case revealed cardiac and hepatic involvement, complicating the diagnosis. Resistant hypertension increases the risk of vital organ damage, including myocardial infarction, transient ischemic attacks, stroke, pulmonary oedema, ventricular hypertrophy, renal issues, and death [6,13,24]. These complications underscore the importance of comprehensive genetic screening, especially in first-degree relatives, to identify mutation carriers [3]. Genetic testing should also be considered in patients with early-onset resistant hypertension in the context of suppressed plasma renin activity and plasma aldosterone concentration [7,14], or hypertension associated with hypokalemia [3,14].

Management of Liddle syndrome focuses on blood pressure control and electrolyte balance correction [14], and inhibition of ENaC activity [14,15]. Although genetic testing is the gold standard for diagnosis, clinical criteria often provide sufficient evidence to initiate treatment [14]. This multifaceted approach includes a sodium-restricted diet, ENaC blockers such as amiloride and triamterene, and potassium supplementation [9,24]. Amiloride and triamterene, as specific ENaC inhibitors, effectively control hypertension and correct biochemical abnormalities [7,15].

In the present case, the patient did not receive an ENaC blocker. However, the management strategy had to be adjusted without these specific medications. The patient was instead treated with alternative antihypertensive therapies due to ENaC blockers unavailability at the treatment center. As a consequence of not using ENaC blockers, the patient's hypertension remained only modestly controlled, with blood pressure levels still elevated despite the use of multiple antihypertensive agents. Additionally, the patient continued to experience persistent hypokalemia and hypernatremia, reflecting the suboptimal management of the electrolyte disturbances typically associated with Liddle syndrome.

In regions where ENaC blockers are unavailable, loop diuretics such as furosemide may be used, although they are less effective [16]. Furosemide increases urinary potassium excretion by enhancing distal sodium delivery, stimulating potassium secretion, and inhibiting sodium and chloride reabsorption in the proximal and distal tubules, as well as the thick ascending loop of Henle [25]. Spironolactone is ineffective in Liddle syndrome due to increased ENaC activity and low aldosterone levels, underscoring the need for targeted treatments [7,11,13,14].

Dietary sodium restriction effectively treats Liddle syndrome by modulating ENaC activity [15]. A low-sodium diet can reverse symptoms and prevent severe complications [9,24]. In the present case, the patient received outpatient therapy and education on adhering to a low-sodium diet. Outpatient management is crucial for improving clinical status and reducing complication risks of hypertension [26]. Follow-up of the patient in the present case showed modest hypertension improvements, but persistent hypokalemia and hypernatremia underscore the need for tailored approaches. Continuous monitoring and comprehensive care for this patient are essential to prevent complications, including end-organ damage.

Conclusion

Liddle syndrome presents significant challenges in diagnosis and treatment due to its rarity, phenotype variability, and the requirement for specialized genetic testing. In this case, the absence of first-line therapies such as ENaC blockers further complicated management. Despite these challenges, the patient's condition was managed with a combination of alternative antihypertensive therapies, potassium supplementation, and a low-sodium diet, which led to modest improvements in blood pressure and motor strength. However, the persistent issues of hypokalemia and hypernatremia emphasize the limitations of alternative therapies and the critical importance of ENaC blockers for effectively managing the syndrome. This case underscores the need for increased awareness and early recognition of Liddle syndrome, especially in patients with resistant hypertension and characteristic electrolyte imbalances. Overcoming these challenges requires timely clinical assessment and improved access to genetic testing and targeted therapies, which are essential for treatment and better patient outcomes. Continuous follow-up and comprehensive care are vital for managing complications and improving the quality of life in patients with Liddle syndrome.

Ethics approval

The patient provided written informed consent for publication as a case report.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

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References

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol 2020;16(4):223-237.
2. Tetti M, Monticone S, Burrello J, *et al.* Liddle syndrome: Review of the literature and description of a new case. Int J Mol Sci 2018;19(3):812.
3. Cui Y, Tong A, Jiang J, *et al.* Liddle syndrome: Clinical and genetic profiles. J Clin Hypertens 2017;19(5):524-529.
4. Yang Y, Wu C, Qu D, *et al.* Liddle syndrome misdiagnosed as primary aldosteronism is caused by inaccurate aldosterone-rennin detection while a novel *SCNN1G* mutation is discovered. Blood Press 2022;31(1):139-145.
5. Fan P, Zhang D, Pan XC, *et al.* Premature stroke secondary to severe hypertension results from Liddle syndrome caused by a novel *SCNN1B* mutation. Kidney Blood Press Res 2020;45(4):603-611.

6. Mubarik A, Anastasopoulou C, Aeddula NR. Liddle syndrome (pseudohyperaldosteronism). In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.
7. Enslow BT, Stockand JD, Berman JM. Liddle's syndrome mechanisms, diagnosis and management. Integr Blood Press Control 2019;12:13-22.
8. Phoojaroenchanachai M, Buranakitjaroen P, Limwongse C. Liddle's syndrome: A case report. J Med Assoc Thail Chotmaihet Thangphaet 2015;98(10):1035-1040.
9. Pagani L, Diekmann Y, Sazzini M, *et al.* Three reportedly unrelated families with Liddle syndrome inherited from a common ancestor. Hypertension 2018;71(2):273-279.
10. Salih M, Gautschi I, Van Bemmelen MX, *et al.* A missense mutation in the extracellular domain of αENaC causes Liddle syndrome. J Am Soc Nephrol 2017;28(11):3291-3299.
11. Lu YT, Liu XC, Zhou ZM, *et al.* A novel frame-shift mutation in *SCNN1B* identified in a Chinese family characterized by early-onset hypertension. Front Cardiovasc Med 2022;9:896564.
12. Yamaguchi E, Yoshikawa K, Nakaya I, *et al.* Liddle's-like syndrome associated with nephrotic syndrome secondary to membranous nephropathy: The first case report. BMC Nephrol 2018;19(1):122.
13. Kozina AA, Trofimova TA, Okuneva EG, *et al.* Liddle syndrome due to a novel mutation in the γ subunit of the epithelial sodium channel (ENaC) in family from Russia: A case report. BMC Nephrol 2019;20(1):389.
14. Awadalla M, Patwardhan M, Alsamsam A, *et al.* Management of Liddle syndrome in pregnancy: A case report and literature review. Case Rep Obstet Gynecol 2017;2017:6279460.
15. Patel P, Kuriacose R. Liddle's syndrome: A case report. Saudi J Kidney Dis Transplant 2015;26(4):769.
16. Mashmoushi A, Wolf MTF. A narrative review of hyporeninemic hypertension-an indicator for monogenic forms of hypertension. Pediatr Med Hong Kong China 2022;5:21.
17. Burrello J, Monticone S, Buffolo F, *et al.* Is there a role for genomics in the management of hypertension? Int J Mol Sci 2017;18(6):1131.
18. Elliott MD, Rasouly HM, Gharavi AG. Genetics of kidney disease: The unexpected role of rare disorders. Annu Rev Med 2023;74:353-367.
19. Ding X, Jia N, Zhao C, *et al.* A family with Liddle's syndrome caused by a new c.1721 deletion mutation in the epithelial sodium channel β-subunit. Exp Ther Med 2019;17(4):2777-2784.
20. Suman S, Sudhir M, Nitin S, *et al.* A rare case of familiar hypertension presenting with hypertensive encephalopathy in an elderly patient: A diagnostic dilemma: A presentation of Liddle's syndrome due to novel mutation in *SCNN1G* gene. Saudi J Kidney Dis Transplant 2021;32(4):1163-1165.
21. Brower RK, Ghlichloo IA, Shabgahi V, *et al.* Liddle syndrome due to a novel c.1713 deletion in the epithelial sodium channel β-subunit in a normotensive adolescent. AACE Clin Case Rep 2021;7(1):65-68.
22. Emmett M. Metabolic alkalosis: A brief pathophysiologic review. Clin J Am Soc Nephrol 2020;15(12):1848-1856.
23. Do C, Vasquez PC, Soleimani M. Metabolic alkalosis pathogenesis, diagnosis, and treatment: Core curriculum 2022. Am J Kidney Dis 2022;80(4):536-551.
24. Nasser H, Nasser S, Said AZ, *et al.* Liddle's syndrome case report-unusual presentation with hypertension in children. Arch Clin Med Case Rep 2018;2(6):241-244.
25. Khan TM, Patel R, Siddiqui AH. Furosemide. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.
26. Moiz A, Zolotarova T, Eisenberg MJ. Outpatient management of essential hypertension: A review based on the latest clinical guidelines. Ann Med 2024;56(1):2338242.