CASE REPORT

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A Diagnostic Conundrum in Liddle Syndrome: A Case Report from Nepal

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Abstract

Liddle syndrome is a rare genetic disorder presenting with hypertension, hypokalemia, and hypoaldosteronism . We report a 33-year-old male with recurrent lower limb weakness, hypertension, and severe hypokalemia. Initial treatment with spironolactone, losartan, and amlodipine was ineffective, and epithelial sodium channel (ENaC) blockers were unavailable. Persistent hypertension and hypokalemia despite spironolactone raised a high index of suspicion for Liddle syndrome. This case underscores diagnostic challenges and therapeutic limitations in resource-limited settings, adding to the scarce literature from Nepal.

Key words: Liddle syndrome, Nepal, resource-limited settings

INTRODUCTION

Liddle syndrome is a rare autosomal dominant form of monogenic hypertension characterized by early-onset hypertension, hypokalemia, metabolic alkalosis, and suppressed plasma renin and aldosterone levels.[1] It was first described in 1963 by Grant Liddle as a distinct clinical entity of pseudoaldosteronism.[1,2] The syndrome results from gain-of-function mutations in *SCNN1A*, *SCNN1B*, and *SCNN1G* genes encoding the α, β, and γ subunits of the epithelial sodium channel (ENaC), causing increased sodium reabsorption and potassium excretion in the distal nephron.[3,4] Because the clinical picture overlaps with disorders such as primary hyperaldosteronism, Cushing's syndrome, and syndrome of apparent mineralocorticoid excess (SAME), establishing the diagnosis can be challenging. A key distinction from hyperaldosteronism is that both plasma renin activity and aldosterone are low in Liddle syndrome.[1] Treatment requires ENaC blockers such as amiloride or triamterene, while mineralocorticoid receptor antagonists are ineffective.[5] However, in resource-limited countries like Nepal, the unavailability, genetic testing and ENaC blockers complicates management.

CASE REPORT

A 33-year-old Nepalese hypertensive male presented to the emergency department with sudden onset, progressive paraparesis of two days' duration, without bladder involvement. He reported a similar episode of weakness 18 months earlier, which had resolved spontaneously. There was no preceding fever, trauma, or history suggestive of thyroid disease. Past medical history was otherwise unremarkable. There was no family history of hypertension, similar episodes of weakness, or hypokalemia.

On examination, his blood pressure was 162/104 mmHg. Neurological evaluation revealed bilateral lower limb weakness (power 3/5), hypotonia, and diminished ankle and knee reflexes. Other systemic examinations were unremarkable.

Initial investigations showed severe hypokalemia (1.6 mEq/L) and metabolic alkalosis. Thyroid function, creatine kinase, and other biochemical parameters were within normal limits. He was admitted to the ICU, where intravenous potassium chloride was administered. His weakness improved significantly, though his hypertension persisted.

Further work-up for secondary hypertension revealed urinary potassium excretion of 19 mEq/L with a transtubular potassium gradient (TTKG) >5, consistent with renal potassium wasting. Plasma aldosterone concentration was suppressed (4.8 ng/dL), as was plasma renin activity (0.21 ng/mL/hr). Overnight dexamethasone suppression testing excluded Cushing's syndrome, and CT imaging showed no adrenal mass. Based on low renin and low aldosterone, Liddle syndrome and SAME were considered.

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The patient was initially treated for suspected SAME with spironolactone 50 mg daily, along with amlodipine 5 mg and losartan 50 mg. However, there was no meaningful reduction in blood pressure or improvement in hypokalemia. Over one year of follow-up, spironolactone was progressively titrated to 200 mg daily, while amlodipine and losartan were optimized to 10 mg and 100 mg daily, respectively. Despite these adjustments, his blood pressure remained above 140/90 mmHg and serum potassium did not exceed 3.5 mEq/L. The persistent hypertension and lack of meaningful increase in serum potassium levels despite high-dose spironolactone, together with suppressed renin and aldosterone levels and recurrent hypokalemic paralysis, increased suspicion for Liddle syndrome, in which mineralocorticoid receptor antagonists are ineffective.[6,7] The escalation of spironolactone reflected the persistence of hypertension while specific ENaC blockers were unavailable. Management was subsequently limited by the unavailability of amiloride and triamterene in Nepal. In their absence, sodium restriction and an angiotensin receptor blocker at the maximum tolerated dose were used to manage the patient's hypertension and clinical symptoms.

DISCUSSION

Liddle syndrome is a rare cause of resistant hypertension characterized by suppressed renin and aldosterone levels. Its prevalence is estimated to be 1.52–1.72% among young Chinese patients with early-onset hypertension of undetermined cause.[8,9] The condition follows an autosomal dominant inheritance pattern and is associated with mutations in the *SCNN1A*, *SCNN1B*, and *SCNN1G* genes, which encode the α, β, and γ subunits of ENaC.[3]

Patients typically present with early-onset hypertension, hypokalemia, and metabolic alkalosis, in the setting of suppressed plasma renin activity and low plasma aldosterone concentration.[1] Reports from India describe middle-aged hypertensive patients with hypokalemia and periodic paralysis who showed poor response to spironolactone.[10] Similar to these cases, our patient presented with hypertension, hypokalemia, and weakness, and demonstrated no meaningful biochemical or blood pressure response despite escalation of spironolactone therapy. The absence of a family history does not exclude Liddle syndrome because of variable phenotypic expression and the occurrence of apparently sporadic cases.[1]

Amiloride and triamterene, the ENaC blockers of choice, are not available in Nepal. In our case, spironolactone provided no meaningful control, and biochemical abnormalities persisted despite dose escalation during follow-up. The distinction of Liddle syndrome from other causes of apparent mineralocorticoid excess lies in its characteristic low renin and low aldosterone levels, and, when available, its response to ENaC blockade.[1,7] In the absence of genetic testing and ENaC blockers, management requires supportive measures. Dietary sodium restriction can reduce sodium-dependent blood pressure elevation and may enhance the effect of ENaC blockade when available.[1,6] Serum potassium should be monitored closely, with potassium supplementation considered when hypokalemia persists. Additional antihypertensive agents, such as calcium channel blockers, may be used to control blood pressure when specific ENaC blockade cannot be provided, although these do not correct the underlying renal sodium-channel defect.[7,11]

Diagnosing and managing Liddle syndrome in resource-limited settings remains challenging because both genetic confirmation and ENaC blockers may be unavailable. In such circumstances, persistent hypertension with hypokalemia, metabolic alkalosis, suppressed renin and aldosterone, and lack of response to spironolactone should raise a high index of suspicion.[7,11] Supportive measures, including dietary sodium restriction, correction and monitoring of hypokalemia, and use of additional antihypertensive agents when necessary, may help reduce complications while efforts are made to obtain specific ENaC-blocking therapy or genetic confirmation.[7,11] To our knowledge, this represents the first reported case of suspected Liddle syndrome from Nepal and underscores the importance of clinical suspicion in guiding diagnosis and management when definitive testing and targeted therapies are not accessible.

CONCLUSION

This case illustrates how Liddle syndrome can be overlooked in resource-limited settings. Recurrent hypokalemic weakness, hypertension, metabolic alkalosis, and suppressed renin and aldosterone levels should prompt consideration of Liddle syndrome, particularly when there is poor response to spironolactone. Although genetic testing was unavailable in this patient, the clinical phenotype and treatment response supported a high index of suspicion rather than definitive genetic confirmation. The unavailability of standard ENaC blockers further highlights the therapeutic challenges in Nepal. When specific therapy is unavailable, dietary sodium restriction, close potassium monitoring with supplementation when required, and appropriate additional antihypertensive therapy may provide supportive management while access to ENaC blockade or genetic testing is pursued.

Ethical Consideration
Patient consent form was obtained before manuscript submission.

Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

CRediT Author Statement
BA: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing – original draft preparation, Visualization, Project administration; **SS:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review and editing, Visualization, Project administration; **AT:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review and editing, Visualization, Project administration;

STL: Conceptualization, Methodology, Formal analysis, Investigation, Writing – review and editing, Visualization, Project administration; **RT:** Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing – original draft preparation, Writing – review and editing, Visualization, Supervision.

Data Availability Statement

No datasets were generated or analyzed for this study. All values are hospital records.

Author Disclosure

The authors declare no conflict of interest.

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References

1. Enslow BT, Stockand JD, Berman JM. Liddle's syndrome mechanisms, diagnosis and management. Integr Blood Press Control. 2019;12: 13-22. PMID: 31564964 PMCID: PMC6731958 DOI: 10.2147/IBPC.S188869
2. Liddle GW, Bledsoe T, Coppage WS Jr. A familial renal disorder simulating primary aldosteronism but with negligible aldosterone secretion. Trans Assoc Am Physicians. 1963;76:199-213.
3. Rolim ALR, Lindsey SC, Kunii IS, et al. Ion channelopathies in endocrinology: recent genetic findings and pathophysiological insights. Arq Bras Endocrinol Metabol. 2010;54(8):673-81. PMID: 21340151 DOI: 10.1590/s0004-27302010000800002
4. Hanukoglu I, Hanukoglu A. Epithelial sodium channel (ENaC) family: Phylogeny, structure-function, tissue distribution, and associated inherited diseases. Gene. 2016;579(2):95-132. PMID: 26772908 PMCID: PMC4756657 DOI: 10.1016/j.gene.2015.12.061
5. Botero-Velez M, Curtis JJ, Warnock DG. Brief report: Liddle's syndrome revisited -- a disorder of sodium reabsorption in the distal tubule. N Engl J Med. 1994;330(3):178-81. PMID: 8264740 DOI: 10.1056/NEJM199401203300305
6. Wang C, Chan TK, Yeung RT, Coghlan JP, Scoggins BA, Stockigt JR. The effect of triamterene and sodium intake on renin, aldosterone, and erythrocyte sodium transport in Liddle's syndrome. J Clin Endocrinol Metab. 1981;52(5):1027-32. PMID: 6262354 DOI: 10.1210/jcem-52-5-1027
7. Murphy L, Ansataspoulou C. Liddle syndrome (pseudohyperaldosteronism). In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025. PMID: 30725596. Bookshelf ID: NBK536911
8. Wang LP, Yang KQ, Jiang XJ, et al. Prevalence of Liddle syndrome among young hypertension patients of undetermined cause in a Chinese population. J Clin Hypertens (Greenwich). 2015;17(11):902-7. PMID: 26075967 PMCID: PMC8031848 DOI: 10.1111/jch.12598
9. Liu K, Qin F, Sun X, et al. Analysis of the genes involved in Mendelian forms of low-renin hypertension in Chinese early-onset hypertensive patients. J Hypertens. 2018;36(3):502-9. PMID: 28915228 DOI: 10.1097/HJH.0000000000001556
10. Mukhopadhyay J, Roy MK, Chatterjee A, et al. An interesting unusual case of hypokalemic quadriparesis in 48 years hypertensive male patient: A Liddle's syndrome. J Postgrad Med Educ Res. 2015; 49(3):143-5. DOI:10.5005/jp-journals-10028-1164
11. Prabowo NA, Putranto W, Myrtha R, et al. Challenges in diagnosing and treating Liddle syndrome in resource-limited settings: a case report from Indonesia. Narra J. 2024;4(3):e1000. PMID: 39816126 PMCID: PMC11731678 DOI: 10.52225/narra.v4i3.1000

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