

Case Report



Long-Standing Hypokalemia and Hypomagnesemia in a 61 Year-Old Woman: A Delayed Diagnosis of Gitelman Syndrome

Shin Young Lee , Sang-Woong Han , Jiwon Lee , Mi-Yeon Yu

Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine, Guri, Republic of Korea



Received: Jun 3, 2026
Revised: Jun 18, 2026
Accepted: Jun 18, 2026
Published online: Aug 13, 2026

Correspondence:

Mi-Yeon Yu

Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine, 153 Gyeongchun-ro, Guri 11923, Republic of Korea.
Email: pure8203@gmail.com

Copyright © 2026 Korean Society for Electrolyte and Blood Pressure Research
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Shin Young Lee
<https://orcid.org/0009-0006-1936-9416>
Sang-Woong Han
<https://orcid.org/0000-0003-3658-7248>
Jiwon Lee
<https://orcid.org/0000-0001-7568-9285>
Mi-Yeon Yu
<https://orcid.org/0000-0001-5112-6955>

Funding

None.

ABSTRACT

Background: Gitelman syndrome (GS) is an autosomal recessive renal tubular disorder characterized by a distinct biochemical profile, including hypokalemia, metabolic alkalosis, hypomagnesemia, and hypocalciuria. Due to its often mild or nonspecific clinical presentation, GS is frequently misdiagnosed as idiopathic hypokalemia, leading to prolonged symptomatic treatment without a definitive etiologic diagnosis.

Case Presentation: We report the case of a 61-year-old female with a one-year history of unexplained, refractory hypokalemia and hypomagnesemia. The diagnosis had been delayed as clinical efforts were primarily focused on escalating electrolyte supplementation. Systematic evaluation of renal electrolyte handling revealed inappropriate urinary potassium and magnesium wasting in conjunction with marked hypocalciuria. In addition, a symptom-oriented family history, documenting chronic fatigue and muscle cramps in her sibling, served as a critical diagnostic clue. Genetic testing confirmed the diagnosis by identifying compound heterozygous variants in the *SLC12A3* gene. Following diagnosis, the patient was enrolled in the Korean National Medical Expense Support Program for rare diseases, ensuring structured long-term management.

Conclusions: This case underscores the importance of an etiologic approach over a purely treatment-focused one in patients with recurrent electrolyte imbalances. GS may be more prevalent than currently recognized, particularly among adults receiving empirical therapy for hypokalemia. Early clinical suspicion, grounded in urinary electrolyte indices and careful family history, is essential for timely diagnosis.

Keywords: Gitelman syndrome; Hypokalemia; Magnesium; Renal tubular transport; Inborn errors; Solute carrier family 12, member 3

INTRODUCTION

Gitelman syndrome (GS) is an inherited renal tubular disorder caused by loss-of-function mutations in the *SLC12A3* gene, which encodes the thiazide-sensitive Na-Cl cotransporter

Conflicts of interest

All authors have no conflicts of interest to declare.

Data sharing statement

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

Authors' contributions

Conceptualization: SYL, MYY; Supervision: MYY; Writing - original draft: SYL; Writing - review & editing: SWH, JL, MYY.

(NCC) in the distal convoluted tubule [1,2]. Dysfunction of NCC leads to impaired sodium and chloride reabsorption, resulting in a characteristic biochemical profile, including hypokalemia, metabolic alkalosis, hypomagnesemia, and hypocalciuria [2,3].

Despite these distinctive laboratory findings, its diagnosis is frequently delayed in clinical practice. Patients often present with nonspecific symptoms such as fatigue, muscle cramps, or gastrointestinal complaints, or are incidentally found to have electrolyte abnormalities during evaluation for unrelated conditions. This diagnostic delay is particularly common in adult patients, in whom GS often presents with subtle or nonspecific manifestations. In many cases, hypokalemia is managed with repeated electrolyte replacement without sufficient effort to identify the underlying cause, leading to prolonged symptomatic treatment and delayed etiologic diagnosis [2,3].

Here, we report a case of genetically confirmed GS in a patient with long-standing, unexplained hypokalemia and hypomagnesemia. This case underscores the importance of clinical suspicion and systematic diagnostic reasoning in patients with recurrent electrolyte abnormalities.

CASE PRESENTATION

A 61-year-old woman presented to the emergency department with abdominal pain and diarrhea. She had experienced abdominal discomfort for 3 days prior to presentation and developed up to seven episodes of watery diarrhea on the day of admission. She had a known history of dyslipidemia and hypothyroidism, for which she had been taking levothyroxine (50 µg/day), but had no prior use of diuretics, laxatives, or herbal medicines.

Blood pressure was 102/58 mmHg, and other vital signs were within normal limits. Physical examination was unremarkable, and electrocardiography showed no abnormal findings. Initial laboratory evaluation revealed hyponatremia (serum sodium 123.4 mmol/L), hypokalemia (2.5 mmol/L), hypochloremia (85.4 mmol/L), hypomagnesemia (1.4 mg/dL), and mild metabolic alkalosis, reflected by a serum total CO₂ level of 27 mmol/L. Renal function was preserved, with a serum creatinine level of 0.63 mg/dL and an estimated glomerular filtration rate of 97.1 mL/min/1.73 m².

Mild hypophosphatemia (3.0–3.9 mg/dL) and low-normal serum uric acid levels (3.5–3.8 mg/dL) were also observed. Serum calcium, liver function tests, and inflammatory markers were within normal ranges. Thyroid function tests revealed markedly elevated thyroid-stimulating hormone (87.5 µIU/mL) and low free thyroxine (0.7 ng/dL), consistent with inadequately controlled hypothyroidism. Accordingly, the dose of levothyroxine was increased from 50 to 100 µg/day during hospitalization. Although hypothyroidism may have contributed to the hyponatremia, it does not account for the persistent hypokalemia and hypomagnesemia observed in this patient.

Given her diarrhea, gastrointestinal potassium loss was initially considered, and the patient was admitted for electrolyte correction and monitoring. However, medication reconciliation revealed that she had been taking high-dose oral potassium chloride (4,800 mg/day) along with oral magnesium supplementation (magnesium lactate hydrate 470 mg per tablet, 4 tablets twice daily). She also reported intermittent diarrhea during magnesium supplementation. Further history taking confirmed that she had experienced intermittent

fatigue for 2 years. Fourteen months prior to admission, she was evaluated at a local nephrology clinic and started on potassium and magnesium supplementation. Despite progressive dose escalation over the following year, serum potassium and magnesium levels remained persistently low.

In addition, family history revealed that her younger sister had experienced chronic fatigue and recurrent muscle cramps, requiring multiple medical visits and ongoing follow-up at a neurology outpatient clinic for similar symptoms. No prior laboratory data were available at the time of initial assessment.

Given the long-standing electrolyte abnormalities and the suggestive family history, further etiologic evaluation was pursued rather than continued symptomatic correction alone.

A 24-hour urine study revealed low urinary calcium excretion (101 mg/day), consistent with hypocalciuria. Urinary potassium (70.7 mmol/day) and magnesium (273 mg/day) excretion remained inappropriately elevated despite hypokalemia and low-normal serum magnesium levels. The fractional excretion of potassium and magnesium, calculated from the 24-hour urine collection, were 20.7% and 18.4%, respectively. Additionally, spot urine analysis demonstrated an elevated transtubular potassium gradient (5.2), supporting inappropriate renal electrolyte wasting due to an intrinsic tubular defect rather than extrarenal loss.

Based on these findings, genetic testing was performed. Next-generation sequencing identified 2 heterozygous variants in the *SLC12A3* gene: a pathogenic splice-site variant, *c.964+1G>A*, and a likely pathogenic missense variant, *c.403C>T* (*p.Arg135Cys*). These findings were consistent with autosomal recessive GS.

Subsequent family evaluation confirmed that her sibling was also diagnosed with GS. The patient was enrolled in the Korean National Medical Expense Support Program for rare diseases and initiated on structured long-term management, including potassium and magnesium supplementation and potassium-sparing therapy. Following treatment initiation, serum potassium and magnesium levels gradually increased and remained stable (**Fig. 1**).

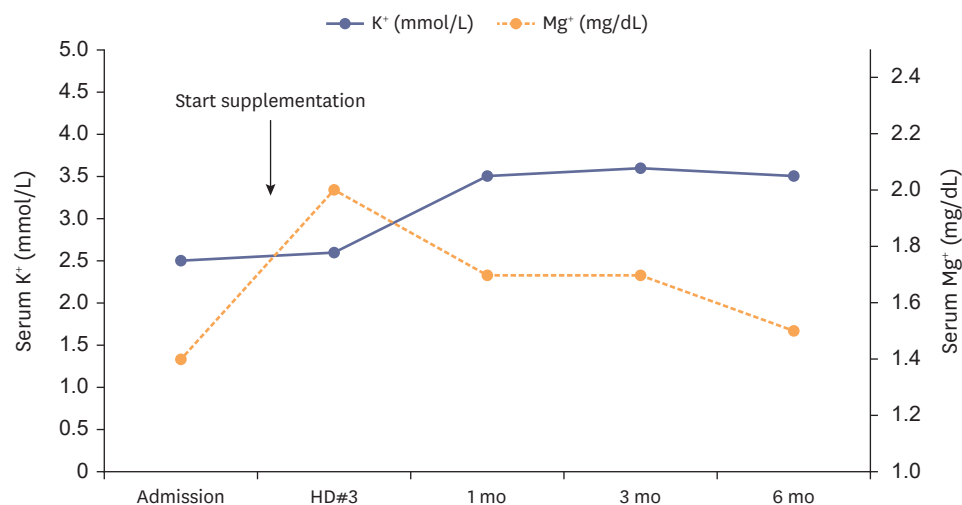


Fig. 1. Longitudinal trends in serum K⁺ and Mg²⁺ levels. HD, hospital day; K⁺, potassium; Mg²⁺, magnesium.

DISCUSSION

This case illustrates a common clinical pitfall in adult patients with chronic electrolyte disturbances, where hypokalemia is repeatedly treated without sufficient effort to determine its underlying cause. The diagnosis in this case was not prompted by worsening laboratory abnormalities but was made during evaluation for unrelated gastrointestinal symptoms.

At presentation, hypokalemia secondary to gastrointestinal potassium loss was appropriately considered in the acute setting. However, systematic reassessment redirected the diagnostic focus. Careful history taking revealed that hypokalemia and hypomagnesemia had clearly preceded the onset of diarrhea, concomitantly with magnesium supplementation. High-dose magnesium supplementation is a well-recognized cause of osmotic diarrhea and likely contributed to the patient's watery diarrhea. This may have further complicated long-term maintenance of electrolyte supplementation. More importantly, urinary electrolyte analysis demonstrated inappropriate renal potassium and magnesium excretion despite low serum levels, findings incompatible with extrarenal electrolyte loss. The presence of hypocalciuria further supported an intrinsic distal tubular defect, allowing differentiation from secondary hypokalemia and other tubulopathies.

Although metabolic alkalosis is a hallmark of GS, it may be milder in adult-onset or late-diagnosed patients than in classic pediatric presentations. Consequently, serum bicarbonate or total CO₂ levels may remain within the upper-normal range despite the presence of an underlying metabolic alkalosis. This case demonstrates the diagnostic value of simple urinary electrolyte assessment. Even without complex or invasive testing, basic urine studies, including urinary potassium, magnesium, and calcium excretion, can provide critical insight into renal tubular function. Early incorporation of urinary electrolyte analysis into the diagnostic workup of chronic or unexplained hypokalemia allows clinicians to suspect renal tubular disorders at an early stage and to pursue targeted etiologic evaluation.

Despite its characteristic biochemical profile, GS is frequently underdiagnosed because of its nonspecific and variable clinical presentation. Many patients experience only mild symptoms or remain asymptomatic for years, and chronic electrolyte abnormalities are often attributed to idiopathic or acquired causes [4].

The key diagnostic step in this case was clinical suspicion based on the chronicity of electrolyte abnormalities, reinforced by structured evaluation including detailed history taking and urinary electrolyte analysis. Recognition of symptom-based family history, chronic fatigue and muscle cramps in the patient's sibling, provided an additional diagnostic clue. Family history should not be limited to confirmed diagnoses, but should also encompass symptom patterns suggestive of inherited disease.

GS is characterized by substantial intrafamilial phenotypic variability, such that affected individuals within the same family may present with different patterns and severities of electrolyte abnormalities. This variability is thought to result from differences in residual function of the thiazide-sensitive NCC due to distinct combinations of *SLC12A3* variants, modifier genes, hormonal factors, and environmental exposures [5,6]. For this reason, family history should include careful inquiry into a broad range of symptoms, such as fatigue, muscle cramps, weakness, or recurrent medical visits. A symptom-oriented approach to history taking may therefore raise clinical suspicion for GS even when biochemical presentations differ among family members.

In Korea, GS is classified as a rare disease and is included in the National Medical Expense Support Program. Diagnostic criteria require demonstration of characteristic electrolyte abnormalities on blood and urine testing and confirmation of loss-of-function mutations in the *SLC12A3* gene, making genetic testing essential for definitive diagnosis. Because GS is a lifelong, non-curable condition requiring chronic management, accurate diagnosis has important implications beyond academic interest, enabling access to structured medical surveillance and financial support. From this perspective, active diagnostic efforts are not only clinically meaningful but also beneficial for patients within the Korean healthcare system. While routine genetic testing is not warranted for all patients with hypokalemia, this case exemplifies the value of targeted genetic evaluation when clinical features strongly suggest an inherited renal tubular disorder. Furthermore, identification of GS has implications beyond the affected individual, as family members may benefit from clinical screening and genetic evaluation.

In summary, this case serves as a reminder that chronic hypokalemia should not be managed solely as a laboratory abnormality. Persistent hypokalemia warrants etiologic investigation, particularly when urinary electrolyte indices indicate inappropriate renal electrolyte wasting. Early recognition of inherited renal tubular disorders through systematic history taking, urinary electrolyte assessment, and targeted genetic testing can facilitate timely diagnosis, appropriate long-term management, and family screening.

REFERENCES

1. Simon DB, Nelson-Williams C, Bia MJ, et al. Gitelman's variant of Bartter's syndrome, inherited hypokalaemic alkalosis, is caused by mutations in the thiazide-sensitive Na-Cl cotransporter. *Nat Genet* 1996;12:24-30. [PUBMED](#) | [CROSSREF](#)
2. Blanchard A, Bockenhauer D, Bolignano D, et al. Gitelman syndrome: consensus and guidance from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. *Kidney Int* 2017;91:24-33. [PUBMED](#) | [CROSSREF](#)
3. Cruz DN, Shaer AJ, Bia MJ, Lifton RP, Simon DB; Yale Gitelman's and Bartter's Syndrome Collaborative Study Group. Gitelman's syndrome revisited: an evaluation of symptoms and health-related quality of life. *Kidney Int* 2001;59:710-717. [PUBMED](#) | [CROSSREF](#)
4. Knoers NV, Levchenko EN. Gitelman syndrome. *Orphanet J Rare Dis* 2008;3:22. [PUBMED](#) | [CROSSREF](#)
5. Lin SH, Cheng NL, Hsu YJ, Halperin ML. Intrafamilial phenotype variability in patients with Gitelman syndrome having the same mutations in their thiazide-sensitive sodium/chloride cotransporter. *Am J Kidney Dis* 2004;43:304-312. [PUBMED](#) | [CROSSREF](#)
6. Riveira-Munoz E, Chang Q, Bindels RJ, Devuyst O. Gitelman's syndrome: towards genotype-phenotype correlations? *Pediatr Nephrol* 2007;22:326-332. [PUBMED](#) | [CROSSREF](#)