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Rare Case of Adult-Onset Gitelman Syndrome in a Patient With Multiple Comorbidities: A Case Report

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ABSTRACT

Gitelman Syndrome (GS) is a renal tubulopathy transmitted in an autosomal recessive manner. Its primary cause is mutations Of SLC12A3 (Solute Carrier Family 12 Member 3) gene that encodes the sodium-chloride co-transporter and is characterized by hypokalemia, hypocalciuria, hypomagnesemia, and metabolic alkalosis. It appears in most cases in adolescents or early adulthood, but with end-organ disease in later adulthood with other comorbid conditions. The patient was a 55-year-old woman with refractory electrolyte disturbances comprising low potassium, calcium, and metabolic alkalosis, history of NASH (non-alcoholic steatohepatitis) cirrhosis, benzodiazepine poisoning, and gastric polyps. Persistent electrolyte abnormalities were most likely worsening renal failure before improvement with the addition of spironolactone. Urinary magnesium/creatinine ratios above 1 were indicative of GS. Electrolyte imbalances were recurring in both her and her late mother, which even existed throughout her childhood. Persistent electrolyte abnormalities in this patient's chronic NASH cirrhosis would probably worsen due to secondary hyperaldosteronism. Supplementation of potassium, calcium, and magnesium failed to address the refractory hypokalemia and hypocalcemia, and hypomagnesemia. So spironolactone was initiated, which resulted in a successful resolution of the condition. Clinical diagnosis of GS made based on biochemical markers due to an existing strong familial pattern of similar electrolyte manifestations since a genetic test for the condition was unavailable. This case shows the issue of disease synergy and how various diseases relate and need specific methods of treatment. The patient's status requires constant observation and the investigation of the possible hereditary renal –tubular disorders.

1 | Introduction

Renal tubules have exquisite control of the renal patient's homeostasis in terms of fluid and electrolyte content [1], as well as acid–base balance, where appropriate changes in reabsorption and excretion of solutes occur [2]. It makes it possible for the kidneys to be self-regulating, and so they are able to adjust to pleasures and demands put on them by the diet or metabolism, or prevailing environmental situations [3]. Because this system can fail, tubulopathies arise, a cluster of diseases that characterize the renal shedding of crucial solutes [4]. These disorders may be caused by genetic mutations of transport proteins in the renal tubules, and their clinical manifestations will depend on the specific electrolyte and acid– base disturbance involved [5]. Of these, the salt-wasting tubulopathies such as GS and BS (Bartter syndrome) stand out, both with distinct biochemical and genetic features [6]. Gitelman syndrome (GS) (Figure 1), an autosomal recessive disorder, is due to mutations in the SLC12A3 gene, which encodes the DCT (distal collecting tubule) of the kidney, making the sodium chloride co-transporter thiazide sensitive [7]. This transporter controls

the reabsorption of sodium and chloride: when reabsorption is impaired, distinctive features that may be observed include hypokalemia, hypocalciuria, hypomagnesemia, and metabolic alkalosis [8]. GS is generally diagnosed during adolescence or early adulthood but can develop at other ages; clinical manifestations are variable and relate to the degrees of electrolyte depletion [9]. The most frequent symptoms are fatigue, muscle weakness, and cramps; in chronic hypokalemia-hypomagnesemia cases—the fatal outcome is possible due to severe cardiac arrhythmias [10]. Molecular confirmation can only be reached by identifying mutations in the SLC12A3 gene [11], but biochemical diagnosis includes low serum potassium, hypocalciuria, and hypomagnesemia, with renal potassium and magnesium wasting being suggestive of GS [12]. The differential diagnosis of GS from other renal tubulopathies such as Bartter syndrome (BS) may not always be possible because some similar features are present; however, this usually occurs in children who present with more manifestations, and BS is characterized by hypercalciuria instead of hypocalciuria [13].

The pathophysiology of GS resides in impaired NaCl cotransportation in the DCT, resulting in increased Na delivery to the C.D (collecting duct) that enhances K+ (Potassium ion) and H+ (Hydrogen ion) excretion that is related to aldosterone, hypokalemia, and metabolic alkalosis [14]. In GS, magnesium reabsorption is also reduced, and this is attributed to first effects on the renal magnesium channel, TRPM6 (Transient Receptor Potential Melastatin 6), which is established in the DCT, which explains the various cases of hypomagnesemia in the patients [15]. Standard treatment requires daily administration of electrolytes (potassium, calcium, magnesium) in addition to conventional care, mainly with potassium-wasting diuretics such as spironolactone [16, 17]. There is variation in clinical presentation, even within the same families, which has been attributed to the environment, other genes and modifiers, and lifestyle issues, making its diagnosis and management a challenge [18]. Although GS is defined as a "mild" type of renal tubulopathies, severe effects on the patients' quality of life were observed throughout electrolyte disorders observed in the patients, which may cause muscle cramps, fatigue, and predisposition to cardiac events [12]. The purpose of this case report is to highlight the challenges in the management of long-standing electrolyte abnormalities, with a focus on hypokalemia, hypocalcemia, and hypomagnesemia in the presence of chronic comorbidity and genetic factors. Moreover, it reasserts the need for a highly systematic approach to the management of these patients in limited resource centers for which genetic analysis and other sophisticated techniques may not be available.

Summary

- This case highlights the importance of considering Gitelman Syndrome (GS) in patients with persistent electrolyte imbalances unresponsive to conventional treatments.
- Patients with electrolyte deficiencies unresponsive to supplementation should be evaluated for GS through serum tests, along with genetic examinations when possible, and doctors should include Spironolactone in the treatment plan.

2 | Case Presentation

A case of benzodiazepine intoxication of a middle-aged woman with a long list of chronic diseases came to the emergency department. At the time of presentation, she was found to have features of CNS (central nervous system) depression due to the sedative toxicity of benzodiazepines. In addition to this

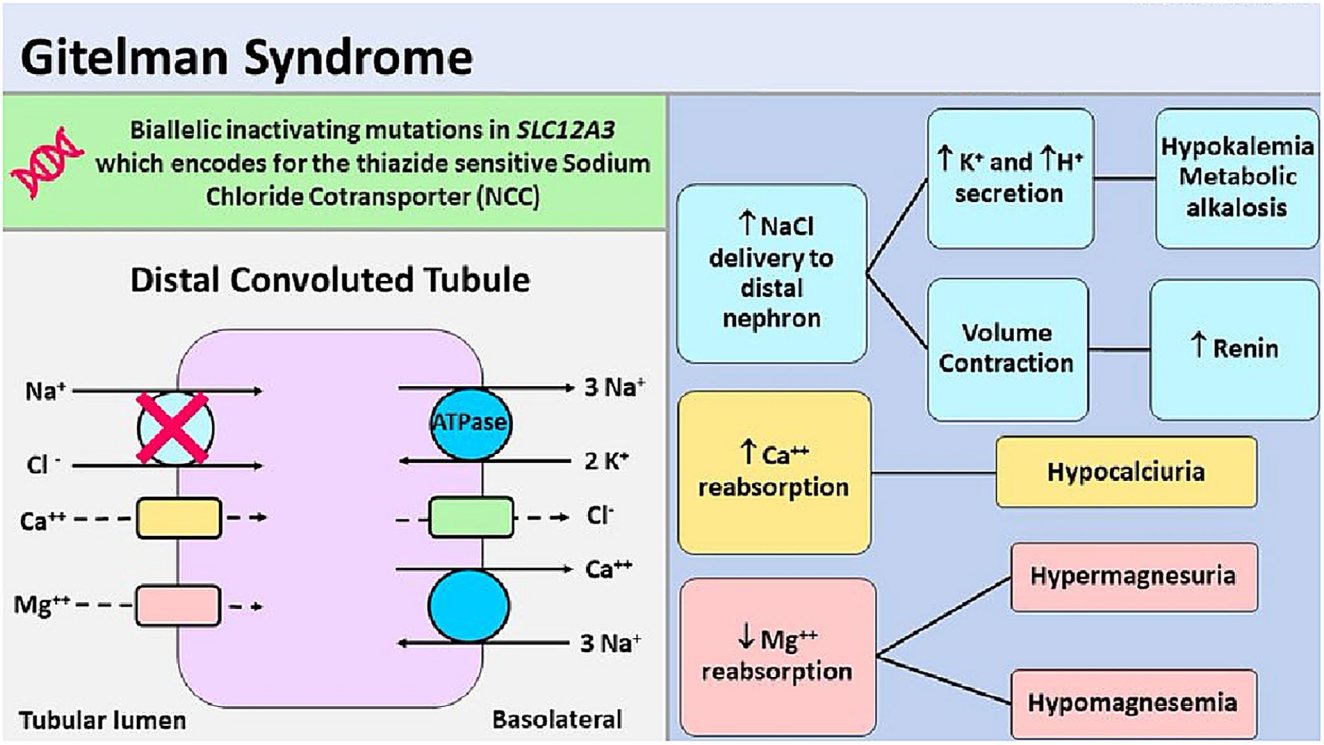

FIGURE 1 | Showing pathophysiology of Gitelman syndrome.

acute picture, she also suffers from a chronic condition of non-alcoholic steatohepatitis (NASH) cirrhosis, which raised administration difficulties in the initial period due to her low hepatic reserve.

The patient has a long medical history that includes multiple chronic diseases. She has also had a prolapsed lumbar intervertebral disc (PLID) and has been attending for chronic back pain and has had a sustained requirement for musculoskeletal care. Furthermore, she has major gastrointestinal complaints; she has had gastric polypectomy two times in 2016 and twice in 2020 and 2024 due to the subsequent gastric polyps. The patient had dysfunctional uterine bleeding after menopause, which was treated with Normens, a hormonal intervention to control the bleeding.

Non-alcoholic fatty liver disease (NAFLD) had been diagnosed since 2022, and this led to non-alcoholic steatohepatic hepatitis (NASH) cirrhosis. This organic affliction most probably has affected her general metabolism and predisposed her to the effects of alterations in the content of electrolytes. For the past 2 years, she has also had chronic melena, which may also be the cause of intermittent anemia and warrants continuous gastrointestinal follow-ups. Moreover, she has been diagnosed with hypokalemia five times in the last 5 years and has had to take potassium replacement to maintain normal levels.

At the time of her admission, her laboratory studies showed the following disturbances of electrolyte balance: hypokalemia, hypocalcemia, and metabolic alkalosis. In the first instance, an effort was made to correct her electrolyte imbalance using potassium and calcium, but only a small improvement was realized. Even after management efforts had been made, her electrolytes continued to fluctuate, which underlined the recalcitrant status to typical correction. Based on her results, it was expected that her metabolic alkalosis and the disturbance in electrolytes could worsen from her impaired hepatic metabolism due to chronic NASH cirrhosis.

Subsequent assessment of her renal function and electrolyte metabolism was therefore undertaken in order to identify the reason for the persistence of her electrolyte disturbances. Hypercalciuria was excluded as a cause of hypocalcemia based on the normal urinary calcium to creatinine ratio of less than 0.14. However, the urinary magnesium-to-creatinine ratio was significantly elevated, pointing towards renal magnesium wasting and towards an existing abnormality of renal magnesium metabolism.

And as always, the patient's family history helped explain a lot about her condition. Her mother had recurrent hypokalemia and hypocalcemia of unknown etiology that was the direct cause of her mother's death. The finding of electrolyte disturbance following this familial pattern indicated that the cause may be genetic or hereditary, in which a renal tubular defect as a cause of electrolyte wasting or a genetic predisposition to renal electrolyte was considered a possibility.

To ensure that she is able to possibly control her condition, magnesium supplements were added to the treatment regimen. The addition of magnesium did not correct her chronically low

TABLE 1 | Lab and clinical investigations findings of the patient.

Investigation	Result	Reference values
Hematology		
Hb	8.1 g/dL	12–16 g/dL (Female)
ESR	60 mm	< 20 mm (Female)
RBC	3.8 million/mm^3	4.2–5.4 million/mm^3 (Female)
PCV	32.9%	37%–47% (Female)
Platelet	3.7 lac/mm^3	1.5–4.5 lac/mm^3
MCV	85 fl	80–100 fl
Urine examination		
Physical exam:		
Color	Deep straw	Yellow
Appearance	Smoky	Clear
Sediment	Present	Absent
Chemical exam:		
Reaction	Acidic	pH: 4.5–8.0
Albumin	Trace	Negative
Microscopic exam:		
Epithelial cell	1–2	0–5/HPF
Pus cell	2–3	0–5/HPF
Serum electrolytes		
Na+	135 mmol/L	135–145 mmol/L
K+	2.1 mmol/L	3.5–5.0 mmol/L
Cl–	98 mmol/L	98–106 mmol/L
Calcium	5.9 mg/dL	8.5–10.5 mg/dL
Albumin	5.2 g/dL	3.4–5.4 g/dL
Mg	0.40 mmol/L	0.75–1.25 mmol/L
S. creatinine	2.1 mg/dL	0.6–1.2 mg/dL
Blood urea	35 mg/dL	7–20 mg/dL
Urine calcium creatinine ratio	0.11	< 0.14
Urine magnesium creatinine ratio	0.2	< 0.15
24-h urine calcium	150 mg/day	100–300 mg/day
24-h urine magnesium	350 mg/day	72–156 mg/day
PT	22 s	11–13.5 s

(Continues)

TABLE 1 | (Continued)

Investigation	Result	Reference values
INR	1.8	0.8–1.2
SGPT	80 U/L	< 40 U/L

Note: Therapeutic interventions: Administered intravenous potassium and magnesium supplements for electrolyte correction; Oral Spironolactone added as a potassium-sparing diuretic; regular monitoring of serum and urine electrolytes during follow-up.
Abbreviations: Cl−, chloride; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; INR, international normalized ratio; K+, Potassium; MCV, mean corpuscular volume; Mg, magnesium; Na+, sodium; PCV, packed cell volume; PT, prothrombin time; RBC, red blood cells; SGPT, serum glutamic-pyruvic transaminase.

serum magnesium values, most probably due to increased renal magnesium loss, as evidenced by high 24 h urinary magnesium and high magnesium/creatinine ratio (Table 1). Then, spironolactone was added, which is potassium-sparing diuretic with calcium, potassium, and magnesium supplements. The use of an aldosterone antagonist, spironolactone, was employed to balance any potassium loss due to mineralocorticoid activity and to enhance potassium conservation. This fact-oriented and 'high touch' approach thus culminated in stabilizing her electrolyte levels, despite taking the better part of days to fine-tune them.

The primary diagnostic procedure proposed to validate GS was genetic testing. Nevertheless, because of financial concerns, the proposed genetic testing could not be conducted. Therefore, the diagnosis was made based on clinical and biochemical assessments.

The following urine tests were carried out to substantiate clinical suspicion of normal urine calcium to creatinine ratio, increased urine magnesium to creatinine ratio, 24-h urinary calcium excretion test, and 24-h urinary magnesium excretion test. From the time of her admission to the hospital, she has had sufficient urinary output. She was getting enteral nutrition with thicker fluids around 2500 mL daily to maintain her hydration levels and at the same time eradicating the hitch of possible inaccuracies stemming from restricted fluid intake. These included offering a means to make initial clinical diagnosis even in the absence of molecular support.

3 | Differential Diagnosis

1. Drug-Induced Electrolyte Imbalances
2. Metabolic Alkalosis from Chronic Hypokalemia
3. Gitelman Syndrome

4 | Discussion

The aim of the following case report is to describe an atypical adult GS in the context of multiple comorbidities such as NASH cirrhosis, benzodiazepine intoxication, and resistant gastric polyps. This report seeks to identify diagnostic difficulties and therapeutic dilemmas of chronic electrolyte imbalances, especially hypokalemia, hypocalcemia, and hypomagnesemia, in light of such complications. Furthermore, it aims to stress the need for a multifaceted, individualized approach to the management of patients in LMICs (low- and middle-income countries) where genetic testing is often unavailable, as well as demonstrate the part of clinical suspicion and constant monitoring when managing complex disorders of electrolyte homeostasis.

That the patient was experiencing hypokalemia, hypocalcemia, and finally metabolic alkalosis, for which the vedoring was not successful, the sticky finger test result, and high bilirubin levels all pointed to renal or hepatic dysfunction coupled with some degree of genetic predisposition. NASH cirrhosis may lead to impaired electrolyte metabolism with prevalence for the situation of metabolic alkalosis and hypokalemia. These problems support her stable potassium and calcium levels with supplementation, combined with general metabolic disturbances that must be attributed to her liver disease.

The patient was found to have a high urinary magnesium to creatinine ratio and increased 24 h urinary magnesium levels implying renal magnesium wasting. These findings, together with her mother's previous episodes of recurrent hypokalemia and hypocalcemia, leading to death, wk. have certainly pointed to the possibility of hereditary renal tubular disorder, particularly GS in this case. GS, also known as hypokalemic metabolic alkalosis with hypocalcemia and hypomagnesemia, is a genetic disease of renal tubular pathogenesis.

Also, her liver disease upgrades from NAFLD to NASH cirrhosis, enhancing her electrolyte imbalances as well. Another complication of liver dysfunction is that it leads to secondary hyperaldosteronism, and therefore further potassium loss. This was the case of spironolactone, a potassium-sparing diuretic used to control her potassium disorder; hence, the need and value of a case-specific management. Her past surgical history with resection of gastrointestinal polyps and chronic melena creates more confounding electrolyte disturbances, as consistently observed anemia and low electrolytes may result from GI loss.

As a result of family history, she may benefit from a genetic workup that would explain the nature of the electrolyte disorder. The primary diagnostic procedure proposed to validate GS was genetic testing. Nevertheless, because of financial concerns, the proposed genetic testing could not be conducted. Therefore, the diagnosis was made based on clinical and biochemical assessments. However, in this low-resource setting, the patient will actually receive constant monitoring of her electrolyte levels, renal function, and liver status, as well as adequate management of her symptoms. This case points up the necessity of teamwork and a non-diagnostic approach to multiply connected cases indicating further multiyear strict patient-descent focus and care. Financial restrictions prevented genetic testing, which restricted the capability to validate the GS diagnosis. The decision to diagnose GS primarily based on clinical signs and biochemical tests resulted in uncertainty because low-resource environments have limited options to confirm genetic causes of complex health conditions that remain the major limitations of this study. It is hypothesized that the main cause of the patient's electrolyte disturbances stems from a hereditary renal tubular disorder (GS) while NASH cirrhosis with liver complications plays a secondary contributing role.

This particular case is remarkable because the patient was severely obese with comorbidities, unresponsive to conventional oral electrolyte supplements, and had biochemical abnormalities markedly unusual for GS. It also underlines the comprehensibility of the patient's tailor-made approach to management and indicates that genetics may influence electrolyte abnormalities. This case illustrates the critical role of comprehensive history and approaches for resistant electrolyte disorders and can be used for framing experiences in similar complex cases.

5 | Conclusion

The specified case emphasizes the challenging process of treating electrolyte imbalances in patients who have multiple medical issues under low-resource condition healthcare systems. When patients display long-lasting resistant electrolyte imbalance disorders, medical practitioners should think about GS as a possible diagnosis since diagnostic tools like genetic testing often remain inaccessible. Healthcare providers operating in these environments should display constant suspicion about genetic conditions while using clinical and biochemical data for therapeutic decisions.

Primary takeaway lesson in this case report is that healthcare professionals must detect genetic conditions in patients who display unexplained electrolyte problems and demonstrate why specific care is vital for low-resource medical settings and prove the necessity of better diagnostic tools. This case demonstrates the importance of robust clinical competence and complete management in low-and middle-income countries because these locations commonly lack molecular testing facilities for diagnosis.

Author Contributions

Md. Deluwar Hussen: conceptualization, data curation, formal analysis, methodology, project administration, resources, supervision, visualization, writing – original draft, writing – review and editing. **Fareha Rezwana:** methodology, resources, software. **Merazul Islam Ony:** data curation, resources, software, writing – review and editing. **Fariha Sultana:** data curation, software, visualization, writing – original draft. **Fabeha Akter Joba:** data curation, resources, validation. **Zareen Tabassum:** data curation, resources, software, validation, visualization, writing – review and editing.

Disclosure

For the paraphrasing of citations and the basic structure of the outline, actually, very limited use of Quillbot has been made, and all have been edited properly after review.

Ethics Statement

We have no compliance as per IRB, as we did not do any research on human/animal models. However, there is no conflict of interest regarding this article, and all ethical rules are followed. The research paper here has been reviewed, and all the data used in this work have been referenced appropriately.

Consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

As for the accessibility of the data of this study, the datasets are available from the corresponding author on reasonable request. In view of the case report, informed consent to use identifiable data was sought from the patient, and in the exceptional circumstance that data is to be disclosed, it will only be done after the patient's details are anonymized. Users' requests should be combined with a declaration of the reasons why such requests are made, as well as a declaration of how the data is to be utilized. The data will be spread out in compliance with all the ethical scenarios from the study and the corresponding institutional guidelines.

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