Case Report

Intensive care management of Gitelman syndrome: A rare case

Subhankar Das[1], Silky Kumari[1], Sudha Kumari[1], Yuvika Kataria[2], Mohammad Sahanawaz[1]

From [1]Intern, Department of Pharmacy, [2]Consultant General Medicine, Department of Medicine, Institute of Medical Sciences and Research Centre, Jaipur National University, Jaipur, Rajasthan, India

ABSTRACT

Gitelman syndrome (GS) is an autosomal-recessive disorder distinguished by hypokalemia, hypomagnesemia, and hypocalciuria. Elderly people and women of childbearing age are highly affected by GC. Not much evidence is known about its effects on maternal and fetal outcomes. GS is caused by mutations in the thiazide-sensitive Na-Cl cotransporter gene. Due to its rarity and lack of knowledge, it is susceptible to misdiagnosis or being overlooked. In our case, the patient suffered from recurrent hypokalemia, hypomagnesemia, hypochloraemia, and hypocalciuria with hypotension. After taking proper medication, the patient recovered slowly, and during counseling, the patient was provided a diet chart by nutritionists to avoid recurrent electrolyte imbalances.

Key words: Hypocalciuria, Hypochloremia, Hypokalemia, Hypotension

Gitelman syndrome (GS) is a rare autosomal-recessive disorder first described in 1966 by Gitelman *et al*. GS, also known as Gitelman's version of Bartter's syndrome (BS), is a hereditary tubulopathy that runs in the autosomal-recessive family [1]. Even though Asians are more prone to this disease, estimated data from several genomic databases shows that GS affects around 1 in 40,000 individuals [2]. GS is characterized by hypokalemia, hypomagnesemia, metabolic alkalosis, and hypocalciuria [3]. Low serum potassium levels, or hypokalemia, occur when potassium levels fall below 2.5 m Eq/L, causing severe, life-threatening neurological and cardiac problems. Hypokalemia cannot be corrected just by lowering potassium levels, which may lead to recurrence and severe complications [4]. Although BS and GS share several phenotypic characteristics, GS can be distinguished by having hypomagnesemia and hypocalciuria. Hypomagnesemia occurs due to the presence of an inactivating mutation in the gene SLC12A3, on chromosome 16, which codes for the thiazide-sensitive sodium-chloride cotransporter and the magnesium transporter on the apical membrane of the distal convoluted tubule (DCT). GS is a benign tubulopathy that either has no symptoms or may manifest as mild weakness, weariness, salt seeking, thirst, nocturia, muscle weakness, paralysis, paresthesias, and the symptoms related to neuromuscular excitability, such as tetany and infrequent seizures [5].

Access this article online	
Received - 12 May 2023 Initial Review - 27 May 2023 Accepted - 26 Jun 2023	Quick Response code
DOI: 10.32677/ijcr.v9i6.4043	

CASE REPORT

A 55-year-old male with recurrent hypokalemia was admitted to the general medicine department with complaints of muscle weakness, dizziness, low blood pressure of 108/72 mmHg (systolic blood pressure was always below 110 mmHg with positive anamnesis), polyuria, and nocturia. His medical history was not significant, and he had a negative family history. He denied using any drugs other than vitamin supplements intake. When the patient was being treated in a hospital for community-acquired pneumonia at the age of 53, this illness was first discovered. Although, for the last 6 months, he has been taking oral magnesium and potassium supplements inconsistently.

During the physical examination, he showed normal hydration, skin and mucosa coloration, a blood pressure of 108/68 mmHg, and a regular pulse frequency of 80 beats/min. The cardiopulmonary assessment was normal, with no evidence of peripheral edema. The remaining physical checkup was normal. A metabolic alkalosis was presented during the gas analysis (pH 7.435; HCO3 33.1 mmol/L; pCO_2 38 mmHg). In biochemical analysis, the report confirmed hypokalemia (2.42 mmol/L), hypomagnesemia (0.35 mmol/L), and hypochloremia (89 mmol/L). Urea (58 mg/dL), Serum creatinine (2.8 gm/dL), serum sodium level (123.4 mmol/L), and remainder ionogram were normal. Further investigation found raised plasma-active renin (2719 fmol/L/s), normal aldosteronemia (16.7 ng/mL in orthostatic; NR 4–31), hypocalciuria (0.73 mmol/L; NR 2.5–7.5), and a greater amount of urine excretion of sodium

Correspondence to: Subhankar Das, Tirupatinagar C-64, Jagatpura, Jaipur - 302017, Rajasthan, India. E-mail: subhankar20015das@gmail.com

(126.5 mmol/L; NR 20–110) and chloride (166 mmol/L; 55–125). The estimated glomerular filtrate rate was 120 mL/min/1.73 m^2, and the potassium transtubular gradient was 11.6. Other tests such as renal ultrasonography and renal and adrenal CT indicate normal kidney function (Table 1). A correlation between hypokalemia, hypomagnesemia, metabolic alkalosis, hypocalciuria, and low blood pressure led to the diagnosis of GS.

The patient took medication according to the prescribed manner, which includes magnesium aspartate 1230 mg once a day (OD), Tolvaptan tablet 15 mg OD, potassium chloride capsule 600 mg twice daily (BD), and started taking magnesium aspartate or potassium aspartate 250/250 mg orally four times per day (qid) from admission time. During counseling, the patient was advised to keep up a high-sodium and high-potassium diet by nutritionists. 20 days later, the patient's serum potassium and magnesium levels were 2.9 mmol/L and 0.52 mmol/L, respectively. The patient recovered slowly with the proper care of the healthcare team.

DISCUSSION

A frequent clinical issue with potentially fatal symptoms is chronic hypokalemia, long-term symptomatic hypotension, hypomagnesemia, and metabolic alkalosis. Our patient is affected by these conditions. The two main diagnoses in this situation (vomiting and diuretic abuse) were ruled out by measuring high urinary chloride excretion and having no history of using diuretics, respectively. The genetic syndromes of Gitelman and Bartter were the only remaining differential diagnoses. Due to its more severe phenotype, earlier start, frequent rise in urinary calcium excretion, and normal or modest hypomagnesemia, Bartter syndrome is considered implausible. On the basis of laboratory test reports, a final diagnosis of GS was made.

GS is an autosomal recessive renal tubulopathy that occurs due to the presence of an inactivating mutation in the gene SLC12A3. Since sodium-chloride cotransporter is sensitive to thiazides and found in the epithelial cells of renal DCT, it is encoded by the gene in the vast majority of instances [6]. Its distinguishing characteristics are secondary hyperaldosteronism, hypomagnesemia, and hypocalciuria, which cause hypokalemia and metabolic alkalosis. Hypomagnesemia can inhibit parathyroid hormone secretion [7].

Table 1: The biochemical parameters of the patient during initial presentation

Parameter	Value	Normal range
Serum potassium, mmol/L	2.42	3.6–5.4
Serum magnesium, mmol/L	0.35	0.7–1.0
Serum sodium level, mmol/L	123.4	135–145
Blood urea, mg/dL	58	10–50
Blood calcium level mmol/L	0.73	2.5–7.5
Serum creatinine, g/dL	2.8	0.6–1.6
Plasma renin activity, fmol/L/s	2719	100–1.500
Serum chloride, mmol/L	89	96–108
Urine sodium, mmol/L	126.5	20–110
Urine chloride, mmol/L	166	55–125

The clinical signs are similar to those using thiazide diuretics for a long time [8]. Clinical signs and biochemical abnormalities, such as hypomagnesemia, hypokalemia, metabolic alkalosis, and hypocalciuria, are used to make the diagnosis of GS. This type of patient responds to thiazide with a blunted natriuretic response but responds quickly to furosemide, indicating that the abnormality is at the level of the distal tubule. Analysis of the GS gene's DNA for mutations may help to confirm the diagnosis [9] According to global consensus suggestions, blood potassium and magnesium levels should be maintained at or above 3.0 mmol/L and >0.6 mmol/L, respectively, in GS patients [10,11]. Most asymptomatic patients do not receive treatment, and they only sometimes have ambulatory monitoring. Renal insufficiency can progress, but it is incredibly uncommon [12].

CONCLUSION

This case report features a patient who has the usual GS symptoms of hypomagnesemia, persistent hypokalemia, and metabolic alkalosis. Inconsistently, the patient was taking oral magnesium and potassium supplements over the course of 6 months. A frequent rise in urinary sodium and chloride excretion and normal or mild hypomagnesemia are considered implausible. When thiazide diuretics are used for a prolonged period of time, the clinical symptoms are the same. During patient counseling, nutritionists provided a diet chart to patients to avoid recurrent electrolyte imbalance. After 20 days, his serum potassium and magnesium levels were 2.9 mmol/L and 0.52 mmol/L, respectively. We strengthened ion supplementation, and the patient gradually achieved a full recovery.

ACKNOWLEDGMENT

The patient's confidentiality was maintained. The Institutional Ethics Committee (IEC) of Institute for Medical Sciences and Research Centre, Jaipur National University, does not require IEC approval for this present case. All patient data and records were de-identified and anonymously collected before analysis.

REFERENCES

1. Riveira-Munoz E, Chang Q, Godefroid N, Hoenderop JG, Bindels RJ, Dahan K, *et al*. Transcriptional and functional analyses of SLC12A3 mutations: New clues for the pathogenesis of Gitelman syndrome. J Am Soc Nephrol 2007;18:1271-83.
2. Kondo A, Nagano C, Ishiko S, Omori T, Aoto Y, Rossanti R, *et al*. Examination of the predicted prevalence of Gitelman syndrome by ethnicity based on genome databases. Sci Rep 2021;11:16099.
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;59:710-7.
4. Bettinelli A, Bianchetti MG, Girardin E, Caringella A, Cecconi M, Appiani AC, *et al*. Use of calcium excretion values to distinguish two forms of primary renal tubular hypokalemic alkalosis: Bartter and Gitelman syndromes. J Pediatr 1992;120:38-43.
5. Blanchard A, Bockenhauer D, Bolignano D, Calo LA, Cosyns E, Devuyst O, *et al*. Gitelman syndrome: Consensus and guidance from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney

Int 2017;91:24-33.
6. Simon DB, Nelson-Williams C, Bia MJ, Ellison D, Karet FE, Molina AM, *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.
7. Pantanetti P, Arnaldi G, Balercia G, Mantero F, Giacchetti G. Severe hypomagnesaemia-induced hypocalcaemia in a patient with Gitelman's syndrome. Clin Endocrinol (Oxf) 2002;56:413-8.
8. Jeck N, Schlingmann KP, Reinalter SC, Kömhoff M, Peters M, Waldegger S, *et al*. Salt handling in the distal nephron: Lessons learned from inherited human disorders. Am J Physiol Regul Integr Comp Physiol 2005;288:R782-95.
9. Knoers NV, Starremans PG, Monnens LA. Hypokalemic tubular disorders. In: Oxford Textbook in Clinical Nephrology. Vol. 3. India: University Press; 2005. p. 995-1004.
10. Gitelman Syndrome Collaborative Study Group. Expert consensus for the diagnosis and treatment of patients with Gitelman syndrome. Zhonghua Nei Ke Za Zhi 2017;56:712-6.
11. Knoers NV. Gitelman syndrome. Adv Chronic Kidney Dis 2006;13:148-54.
12. Bonfante L, Davis PA, Spinello M, Antonello A, D'Angelo A, Semplicini A, *et al*. Chronic renal failure, end-stage renal disease, and peritoneal dialysis in Gitelman's syndrome. Am J Kidney Dis 2001;38:165-8.

Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Das S, Kumari S, Kumari S, Kataria Y, Sahanawaz M. Intensive care management of Gitelman syndrome: A rare case. Indian J Case Reports. 2023;9(6):185-187.