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Case Report

A 6-year-old Female With Frequent Vomiting and Carpopedal Spasm

Seyedeh Fatemeh Marzani[1*]

1. Department of Pediatric Nephrology , School of Medicine, Hakim Children's Hospital, Tehran University of Medical Sciences,Tehran, Iran.

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Corresponding Author:
Seyedeh Fatemeh Marzani
Address: Department of Pediatric Nephrology, Hakim Children's Hospital, School of Medicine, Tehran University of Medical Sciences,Tehran, Iran.
E-mail: dr.f.marzani69@gmail.com

ABSTRACT

Background and Aim: Gitelman syndrome (GS) is a rare tubulopathy with an autosomal recessive inheritance pattern. Mutations in the thiazide-sensitive Na-Cl transporter gene lead to hypokalemia, metabolic alkalosis, and hypomagnesemia.

Case Presentation: In this case report, we introduced a 6-year-old female who presented with urinary tract infection symptoms and frequent vomiting. She suffered from carpopedal spasm when blood sampling was done. At presentation, she had acute respiratory alkalosis with complete metabolic compensation, mild hypokalemia, and hypomagnesemia. After discharge, further studies, including genetic testing, were conducted, which identified an *SCL12A3* mutation—a homozygous pathogenic variant—that confirmed the diagnosis of Gitelman syndrome. Oral supplementation of potassium and magnesium was initiated for treatment.

Conclusion: The diagnosis of GS can be easily missed. Clinical Suspicion is the first step toward confirming a diagnosis.

Keywords: Gitelman syndrome (GS), Metabolic, Alkalosis, Hypokalemia, Hypomagnesemia, Hypocalciuria, *SLC12A3*, Mutation

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Introduction

The prevalence of Gitelman syndrome (GC) is approximately 1 in 40,000, with a higher occurrence noted in Asia. Patients with GC are often asymptomatic or exhibit mild symptoms, including weakness, fatigue, cravings for salt, increased thirst, nocturia, constipation, or muscle cramps. The typical biochemical abnormalities observed in the blood include hypokalemic metabolic alkalosis, hypomagnesemia, and hypocalciuria [1].

SLC12A3 is located on chromosome *16q13*. It consists of 26 exons and encodes the thiazide-sensitive channel NaCl cotransporter (NCC). To date, more than 350 mutations have been identified in patients with GS [2]. We introduced a case of a 6-year-old female with symptomatic hypokalemia diagnosed as having GS [1].

Case Presentation

A 6-year-old female, accompanied by her mother, presented to the emergency department with coryzal symptoms and frequent vomiting that had started 3-4 days prior. At the time of blood sampling, she suddenly experienced carpopedal spasms, which gradually disappeared after intravenous calcium and magnesium injection. She had a history of abdominal pain, constipation, morning nausea, fatigue, and weakness for the past 2.5 years. Additionally, her mother reported nocturnal enuresis following the initiation of oral calcium and magnesium supplementation.

None of the patient's family members reported experiencing similar symptoms. She did not take any medications except for polyethylene glycol for 2 months. During physical examination, she appeared ill and moderately dehydrated, but her blood pressure was normal. Laboratory investigations at the beginning of the presentation are summarized in Table 1.

At presentation, she continued to exhibit a hypokalemic state, with urinary potassium (UK) levels at 12 mmol/L; after correction of hypokalemia and potassium depletion, UK increased to 80 mmol/L. Interestingly, we observed mild hypomagnesemia (1.4 mg/dl) and hypocalciuria, with a urinary calcium/creatinine ratio (Uca/cr) of 0.03, as well as respiratory alkalosis. The patient had normal serum calcium levels (10.1 mg/dL) but low parathyroid hormone levels; additionally, insufficient levels of 25-hydroxycholecalciferol were found. Urinalysis was normal. Echocardiography and renal sonography showed no impairments. An ECG revealed a prolonged corrected QT interval (QT_c=0.46), and she was advised to correct the electrolyte abnormalities.

Because of conflicting data at the time of presentation, she was discharged with potassium and magnesium chloride supplementation without a definite diagnosis, and whole-exome sequencing (WES) was requested. A pathogenic variant was identified in homozygosity in the splicing region of exon 6 of the *SLC12A3* gene (c. 1180+1 G>T), confirming the diagnosis.

Discussion

Hypokalemia is a prevalent electrolyte impairment in hospitalized children. The differential diagnosis of hypokalemia is extensive, making the identification of its etiology challenging. Common causes of hypokalemia include insufficient potassium intake and excessive potassium loss in the gastrointestinal tract and kidneys. Potassium redistribution can result in hypokalemia without an overall deficiency in total body potassium.

In a hypokalemic patient with renal loss, the next step is to assess venous blood gas. In patients with metabolic alkalosis, excessive urinary chloride loss, and low or normal blood pressure, Bartter syndrome and GS are suspected. GC is a rare and heterogeneous condition characterized by a wide range of clinical presentations and severity, which can be influenced by various *SLC12A3* mutations, as well as other modifier genes, compensatory mechanisms, sex, and dietary factors.

Common manifestations include muscle weakness [3], carpopedal spasms, or tetanic episodes triggered by hypomagnesemia. Blood pressure may be reduced or remain normal. A prolonged QT interval has been reported in approximately 50% of patients. Other frequent symptoms include palpitations, fatigue, paresthesia, and numbness; our patient has experienced fatigue and paresthesia for the past 2.5 years [4]. Besides these symptoms, there are rare presentations, such as seizures, pseudotumor cerebri, ventricular tachycardia, blurred vision, rhabdomyolysis, and sclerochoroidal calcifications [1]. There is a noted association between autoimmune thyroid disease and GS, although thyroid function tests in our patient were normal [5].

Mild symptoms may be overlooked by patients, and the wide variety of signs can confuse healthcare providers, leading to delayed or incorrect diagnoses. Paying attention to all symptoms, no matter how minor, is crucial for accurate diagnosis. The use of newer diagnostic methods, such as genetic testing, can aid in the detection of the

Table 1. Laboratory results

Parameters	Values	Normal Range
BUN (mg/dl)	18	7-18
Creatinine (mg/dl)	0.5	0.44-0.65
Sodium (mmol/l)	140	134-143
Potassium (mmol/l)	3	3.3-4.6
Calcium (mg/dl)	10.1	8.8-10.8
Phosphorus (mg/dl)	4.2	3.3-5.6
Magnesium (mg/dl)	1.4	1.5-2.3
Chloride (meq/l)	92	102-112
PH	7.56	7.35-7.45
$PaCO_2$ (mmHg)	21.9	35-45
HCO_3(mmol/l)	19.8	22-26
BE (mmol/l)	-0.9	(-2)-(+2)
PTH (pg/ml)	5.2	11-67
TSH (IU/ml)	1.5	0.5-4.5
FT4 (ng/dl)	1.7	0.7-2
Urin (PH)	7	5.5-7
Urine specific gravit (Max osmolality/L)	1.016	1308–1324
Urine protein (mg/m²/day)	Negative	<100
Urine potassium (mmol/l)	80	-
Urine Calcium (mg/dl)	1	<4 mg/kg/24 h
Urine Creatinin (mg/dl)	33	6–8 years; Female 12.4–26.6 mg/kg/day
25 Hydroxy Vitamin D (ng/ml)	21	Insufficient: 20-30

disease. Biallelic inactivating mutations in the *SLC12A3* gene cause GS. Over 350 mutations in *SLC12A3* have been identified in these patients. In the study by Vargas-Poussou et al. [2] which genetically analyzed 448 GS patients, 79 cases were homozygous (25%), and 236 were compound heterozygous (74.9%). These mutations included 64% missense, 14% frameshift, and 2% in-frame small deletions or insertions, 14% splice site changes, and 6% nonsense changes. Generally, these mutations were found in heterozygous compound cases, except for c.1180+1G>T, which is more prevalent in the Gypsy population [2]. Gypsies in Iran reside in several cities, including Lorestan, from which our patient originated.

Conclusion

The diagnosis of GS can be easily missed. Clinical suspicion, raised by the identification of biochemical changes and symptoms, is the first step toward confirming a precise diagnosis, which should be corroborated by genetic testing.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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References

[1] Emma F, Goldstein SL, Bagga A, Bates CM, Shroff R. Pediatric nephrology. Berlin: Springer Nature; 2022. [Link]

[2] Vargas-Poussou R, Dahan K, Kahila D, Venisse A, Riveira-Munoz E, Debaix H, et al. Spectrum of mutations in Gitelman syndrome. J Am Soc Nephrol. 2011; 22(4):693-703. [DOI:10.1681/ASN.2010090907]

[3] Palmer BF, Clegg DJ. Physiology and pathophysiology of potassium homeostasis: Core curriculum 2019. Am J Kidney Dis. 2019; 74(5):682-95. [DOI:10.1053/j.ajkd.2019.03.427] [PMID]

[4] Cruz DN, Shaer AJ, Bia MJ, Lifton RP, Simon DB. Gitelman's syndrome revisited: An evaluation of symptoms and health-related quality of life. Kidney Int. 2001; 59(2):710-7. [DOI:10.1046/j.1523-1755.2001.059002710.x]

[5] Zhou H, Liang X, Qing Y, Meng B, Zhou J, Huang S, et al. Complicated Gitelman syndrome and autoimmune thyroid disease: A case report with a new homozygous mutation in the SLC12A3 gene and literature review. BMc Endocr Disord. 2018; 18(1):82. [DOI:10.1186/s12902-018-0298-3]