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RESEARCH ARTICLE
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GITELMAN SYNDROME PRESENTING AS HYPOKALEMIC PERIODIC PARALYSIS

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ABSTRACT:
Gitelman syndrome (GS) is a very rare inherited disorder characterized by renal tubular dysfunction, primarily affecting the kidneys' ability to reabsorb electrolytes. There is a mutation in the gene SLC12A3 in the distal convoluted tubule of the nephron that causes this disease. Symptoms include weakness, fatigue, tingling, and muscle spasms. Diagnosis is often incidental during lab tests or when symptoms appear. Treatment focuses on correcting electrolyte imbalances with magnesium and potassium supplements, aldosterone antagonists like spironolactone, and NSAIDs for symptom management. In the presented case, a 26-year-old female was diagnosed with Gitelman syndrome after presenting with tingling and spasms. The treatment included spironolactone, vitamin D3, febuxostat, indomethacin, and a potassium supplement. Regular follow-up is essential to prevent further complications.

Keywords: - *Gitelman Syndrome, Rennin angiotensin-aldosterone system, Tubulopathies, Sodium chloride co-transporter.*

INTRODUCTION

GS is an autosomal recessive disorder known for causing salt loss through the kidneys. It is marked by renal potassium loss, leading to hypokalemia, metabolic alkalosis, low calcium levels in urine (hypocalciuria), low magnesium levels in the blood (hypomagnesemia), and increased levels of renin and aldosterone (hyperreninemic hyperaldosteronism). This condition is also called familial hypokalemia-hypomagnesemia. [1,2]

In Asia, GS may be more prevalent than in other parts of the world. It is one of the most common inherited tubulopathies, affecting 1 to 10 people per 40,000, and prevalence varies from 1 to 10 cases per 40,000 people.[3] There is a mutation in the SLC12A3 gene that encodes the thiazide-sensitive sodium-chloride cotransporter (NCC) that causes GS. A vital role of the NCC is to reabsorb sodium and chloride ions from urine back into the bloodstream so that electrolytes are maintained within the body.[4] Sodium chloride wasting and the resulting activation of the renin-angiotensin-aldosterone system (RAAS) account for the clinical presentation of this rare tubulopathy.[5] A definitive diagnosis of Gitelman syndrome is confirmed by identifying mutations in the NCCT gene through direct sequencing, though this test is not always accessible at all institutions.[6] We present a case of severe hypokalemia and paralysis. Several types of skeletal muscle ion channels are involved in hypokalemic periodic paralysis. Calcium channels are most commonly involved, while sodium channels are less frequently affected. The patient usually presents with generalized or focal flaccid paralysis associated with hypokalemia, which generally resolves spontaneously within a few hours. Various laboratory tests were performed to identify the underlying cause of this diagnosis.

CASE PRESENTATION:

A 26-year-old woman presented to the ED with two days of progressive weakness in her lower limbs, following muscle cramps. The weakness extended to her upper limbs but was not accompanied by sensory, cranial nerve, or bladder/bowel involvement. She had a history of recurrent episodes of weakness and hypokalemia over the past three years, responding well to potassium supplementation. The patient reported no history of vomiting, diuretic use, or intake of alcohol or laxatives. There was no sign of muscle atrophy, asymmetry, or fasciculations, and diagnostic tests excluded myasthenia gravis. Furthermore, there were no symptoms related to thyroid or autoimmune disorders.

On examination, the patient's vital signs were normal, with intact higher mental functions. She had 0/5 muscle power in both limbs, absent reflexes, and no sensory or cranial nerve involvement. ECG showed ST-T flattening. Arterial blood gas analysis revealed hypokalemia (K 2.7) with metabolic alkalosis, suggestive of hypokalemic periodic paralysis. Lab results confirmed hypokalemic metabolic alkalosis, secondary hyperaldosteronism, hypomagnesemia, and hypocalciuria, indicating renal potassium wasting.

The patient was treated with IV potassium chloride and magnesium replacement. Muscle strength improved as potassium levels normalized. Spironolactone (50 mg bid) was added, and her power improved to 4-5/5 in all limbs. At discharge, the patient was prescribed potassium supplements, spironolactone, and a potassium-rich diet, and advised on regular follow-ups.

Table-1: Investigations

Test	VALUE	TEST	VALUE
S. Potassium (3.5-5)	2.7mEq/L	PCO2(35-45)	37mmHg
S. Sodium (135-145)	138mEq/L	HCO3-(22-26)	36MMOL/L
S. Calcium (9-10.2)	10mEq/L	24hrs urinary Na (60-220)	332mEq
S. Magnesium (1.5-2)	1.4mEq/L	24hrs urinary K (<15)	32.5mmil/L
S. Osmolality (285-295)	294mOsm/kg	24hhrs urinary Cl- (60-220)	290mEq
TSH (0.3-5)	4.67IU/mL	24hrs urinary ca+(50-400)	18.8mg/day
Plasma Aldosterone (<15)	30ng/dL	Urine Osmolality (500- 850)	320 Osm/kg

DISCUSSION:

GS, also known as familial hypokalemic hypomagnesemia, is primarily categorized by hypokalemia, which is the most common presenting feature. Due to its rarity, GS is often overlooked in the initial differential diagnosis of conditions like weakness and paralysis. The

condition poses significant risks if left undiagnosed, as persistent hypokalemia can lead to serious complications, including cardiac arrest, ventricular arrhythmias, and paralysis.[7]

In the case presented by **Gandhi et al. [8]** a 17-year-old female was diagnosed with GS based on her clinical symptoms, including perioral numbness, carpal spasms, and quadriparesis, as well as laboratory findings of hypokalemia and low serum magnesium. Following intravenous treatment with potassium chloride and magnesium sulfate, the patient began to recover and was subsequently discharged. This case is consistent with other reports in the literature, such as a case described by **Saiki et al. [9],** where a 27-year-old male with a history of intermittent limb weakness was diagnosed with GS after presenting with hypokalemic periodic paralysis. Despite typical biochemical abnormalities, including hypokalemia, hypomagnesemia, and hypocalciuria, no mutations in the thiazide-sensitive NaCl cotransporter gene were identified.

Gulwe VS et al. [10] presented a case presentation on 22-year-old male who was presented to the emergency department with cramps in the lower limbs and tetany in both upper limbs. During his hospital stay, he exhibited persistent hypokalemia, hypocalcemia, and hypomagnesemia. Following a detailed clinical and laboratory evaluation, he was diagnosed with Gitelman's syndrome. He was discharged on oral potassium and calcium supplements, along with potassium-sparing diuretics.

Similarly, **Sinaga et al. [11]** reported an 18-year-old male with severe hypokalemia and periodic paralysis, diagnosed with Gitelman's syndromethrough a thiazide and furosemide challenge test. His treatment included magnesium and potassium supplements, along with a potassium-sparing diuretic, underscoring that GS, while rare, can present in adulthood and should be considered in patients with hypokalemia due to the risk of severe complications.

Management of Gitelman's syndrome involves correcting electrolyte imbalances, as symptomatic hypokalemia requires potassium replacement, often alongside magnesium supplementation. Potassium-sparing diuretics, such as spironolactone or amiloride, may also be beneficial for blood pressure control, as highlighted by **Balasubramani et al**. **[12]** However, management of Gitelman's syndrome is typically simple, involving gradual correction of electrolyte abnormalities, the genetic nature of the disease means recurrence of life-threatening episodes is possible. Therefore, regular exercise and a nutritious diet are recommended to help prevent future episodes.

CONCLUSION:

Gitelman syndrome is a rare cause of hypokalemic metabolic alkalosis, characterized by low magnesium levels, low calcium in the urine, and normal blood pressure. However, it can be diagnosed based on its typical clinical presentation and characteristic biochemical findings. Patients with Gitelman syndrome are advised to follow a diet rich in sodium and potassium. Overall, the long-term prognosis for Gitelman syndrome is excellent.

REFERENCES:

1. Gunde R, Jayashankar CA, Bhat N, Bhat V, Kodapala S. Gitelman Syndrome Manifesting with Acute Hypokalemic Paralysis: A Case Report. Cureus. 2023; 15(9).
2. Parmar MS, Muppidi V, Bashir K. Gitelman Syndrome. [Updated 2024 Apr 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459304/
3. Hiba S, Shazaan N, Abdullah FN, Mehdi KM, Rizvi SW. Gitelman Syndrome and Hypertension: A Case Report. Cureus. 2023; 15(9).
4. De Silva N, Pathmanathan S, Sumanatilleke M, et al. A novel mutation of SLC12A3 gene causing Gitelman syndrome. SAGE Open Med Case Rep. 2022; 10:2050313X221102294.
5. Nakhoul F, Nakhoul N, Dorman E, Berger L, Skorecki K, Magen D. Gitelman's syndrome: a pathophysiological and clinical update. Endocrine. 2012; 41(1):53-57.
6. Grillone T, Menniti M, Bombardiere F, et al. New *SLC12A3* disease causative mutation of Gitelman's syndrome. *World J Nephrol*. 2016; 5(6):551-555.
7. National Organization for Rare Disorder. Gitelman Syndrome:https://rarediseases.org/rare-diseases/gitelman-syndrome/Last updated: 10/9/2024

8. Gandhi K, Prasad D, Malhotra V, Agrawal D. Gitelman's syndrome presenting with hypocalcemic tetany and hypokalemic periodic paralysis. *Saudi J Kidney Dis Transpl*. 2016;27(5):1026-1028.
9. Saiki S, Yoshioka A, Saiki M, Yamaya Y, Hirose G. *Rinsho Shinkeigaku*. 2002; 42(4):317-319.
10. Sinaga F, Naibah R, & Sibuea W. Gitelman Syndrome: An Important Cause of Severe Hypokalemia and Periodic Paralysis. World Journal of Nephrology and Urology, 2016; 5(2):40-47.
11. Balasubramani LN, Iyer S. Gitelman Syndrome: A Cause for Recurrent Hypokalaemia with Tetany. J Clin of Diagn Res.2020; 14(4):OD04-OD05.
12. Gulwe VS, Ukadgaonkar A, Bhutada SS, Dahiya N. Rare presentation of Gitelman's syndrome. Int J Curr Med Appl Sci. 2015; 9(1):36-8.