Early-Onset Gitelman Syndrome Presenting with Recurrent Hypokalaemia and Tetany in an Eight-Year-Old Girl: A Case Report

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Abstract:

Gitelman syndrome (GS) is a rare autosomal recessive renal tubular disorder characterised by hypokalaemia, hypomagnesaemia, metabolic alkalosis, and hypocalciuria. It typically manifests during adolescence or adulthood, while paediatric presentations are uncommon and often misdiagnosed. We report the case of an eight-year-old girl presenting with recurrent episodes of severe hypokalaemia and muscle cramps triggered by acute gastroenteritis. Genetic testing identified two heterozygous pathogenic variants in the solute carrier family 12 member 3 (SLC12A3) gene, confirming GS.

Key words: Gitelman Syndrome, Metabolic Alkalosis, Hypokalaemia, Hypomagnesaemia, SLC12A3.

Introduction

Gitelman syndrome (GS) is an autosomal recessive disorder affecting the thiazide-sensitive sodium-chloride cotransporter (NCC) in the distal convoluted tubule of the kidney, with an estimated incidence of one in 40,000 individuals.[1] The lack of function of the NCC increases the amount of sodium in the collecting duct, increasing urinary excretion of potassium and hydrogen, and promoting reabsorption of urinary calcium and excretion of magnesium. This is responsible for the metabolic abnormalities. GS typically presents during adolescence or early adulthood with symptoms ranging from muscle cramps and fatigue to tetany and cardiac arrhythmias. Paediatric presentations, particularly in early childhood, are rare and often challenging to diagnose due to overlapping symptoms with more common conditions such as gastroenteritis or neurological disorders.

We describe an unusual case of GS in an eight-year-old girl presenting with recurrent hypokalaemia and muscle stiffness after illness, emphasising the clinical and diagnostic approach and management considerations.

Case Report

An eight-year-old girl presented to the emergency department with a two-day history of loose stools and vomiting, accompanied by severe abdominal pain and painful stiffness of both hands suggestive of tetany. The child was conscious but restless and hyperventilating. Examination revealed mild dehydration, carpopedal spasm, and periorbital twitching. There was no history of fever, seizures, or trauma.

The family reported a previous hospitalisation one year earlier following a diarrhoeal illness with similar symptoms, during which she was diagnosed with hypokalaemia. Due to her restlessness during that episode with abnormal stiffening of hands, a neurological exam and magnetic resonance imaging (MRI) were done, both of which were normal. There was no significant family history of renal or genetic disorders. The child had a history of easy fatigability, which the parents attributed to dietary issues.

Laboratory investigations on admission revealed a venous blood pH of 7.383 with markedly elevated lactate (11.9 mmol/L), hypokalaemia (3.14 mEq/L),

and hypomagnesaemia (1.4 mg/dL). Serum calcium was normal. Neurological evaluation, including electroencephalography (EEG), was normal. Dehydration was corrected with intravenous fluids, but persistent hypokalaemia (3 mEq/L) and metabolic alkalosis (pH of 7.483) were noted. Urinalysis demonstrated increased potassium excretion and decreased urinary calcium excretion. The child did not have hypertension, and the ultrasonography of the kidneys, ureters, and bladder (USG–KUB) was normal.

The patient's symptoms improved, and she was discharged with a recommendation for paediatric nephrology follow-up. Within two weeks, she presented again with similar complaints precipitated by vomiting. Repeat laboratory investigations confirmed metabolic alkalosis (pH of 7.53), hypokalaemia (2.8 mEq/L), hypomagnesaemia (1.4 mg/dL), and reduced urinary calcium excretion. Given the biochemical profile and clinical presentation, a diagnosis of GS was considered. As the child continued to experience tetany during the hospital stay, intravenous magnesium was administered for 24 hours until serum magnesium levels rose to 2.1 mg/dL and the symptoms resolved.

A paediatric nephrology consultation was obtained, and genetic testing for mutations in the solute carrier family 12 member 3 (SLC12A3) gene was performed. The patient was started on oral magnesium oxide supplementation, which was well tolerated. Magnesium oxide was continued on discharge. Genetic analysis identified two heterozygous pathogenic variants in SLC12A3, confirming autosomal recessive GS.

During subsequent follow-up visits, the child remained asymptomatic on maintenance therapy, with stable electrolytes and no further episodes of spasms or weakness.

Discussion

GS is a rare, heterogeneous disease typically characterised by the presence of hypokalaemia, metabolic alkalosis, hyperreninemic hyperaldosteronism, hypomagnesaemia, and hypocalciuria, although variable clinical presentation and severity can occur.[2] Most patients are diagnosed during adolescence or adulthood, but neonatal presentation and diagnosis may also occur.[3] This phenotypic variability is associated not only with the SLC12A3 mutation identified but also with the presence of other modifier genes, the co-existence of compensatory mechanisms, sex, diet and environmental factors.[4]

A range of symptoms may occur due to the underlying biochemical abnormalities seen in these patients. The most frequent complaints include cramps, muscle weakness, fatigue, and tetany.[5,6] Although thirst and salt cravings are frequent symptoms due to renal salt wasting and subsequent hypovolaemia,[5,6] these complaints were not reported by our patient. The child was also normotensive. Polyuria and nocturia are also frequently reported due to urinary salt and water wasting. Abnormal glucose metabolism is also common in GS.[7]

Though 24-hour urine samples may be more accurate, spot urine samples are usually adequate to evaluate the renal excretion of potassium, magnesium, calcium, sodium and chloride.[8] The classic biochemical hallmarks — hypokalaemia, hypomagnesaemia, metabolic alkalosis, and hypocalciuria — help distinguish GS from other tubulopathies like Bartter syndrome, which typically presents earlier and with hypercalciuria and more severe salt wasting.

Our patient's presentation with recurrent hypokalaemia episodes precipitated by gastroenteritis is typical of paediatric GS, which is often diagnosed during or after dehydration episodes, revealing the underlying defect. It was noted that the patient's symptoms did not correspond to the serum potassium levels, which were initially near normal, indicating a lack of correlation between the two. Initial symptoms such as muscle cramps and carpopedal spasm reflect neuromuscular irritability from electrolyte disturbances. Persistent hypokalaemia despite dehydration correction, coupled with decreased urinary calcium excretion, is highly suggestive of GS, warranting evaluation.

Management focuses on correcting hypokalaemia and hypomagnesaemia to reduce symptoms and prevent complications such as arrhythmias. Oral magnesium supplementation and potassium-sparing agents are mainstays, but clinical response and tolerance vary. Regular monitoring for growth and renal function is essential.

Advances in genetic testing allow early and definitive diagnosis, enhancing patient counselling and tailored therapy. This case reinforces the need for awareness among clinicians about paediatric presentations of GS to avoid misdiagnosis and unnecessary testing, such as neurological imaging or interventions.

Future directions include exploring gene therapy and novel pharmacological agents that improve tubular function, though evidence remains limited. Multidisciplinary care involving nephrologists, paediatricians, and geneticists is optimal.

Conclusion

This case report documents an early childhood presentation of genetically confirmed GS manifesting as recurrent electrolyte abnormalities and neuromuscular symptoms. It highlights the importance of considering inherited tubulopathies in children with refractory hypokalaemia, especially following dehydration. Early recognition and genetic confirmation allow precise diagnosis and effective management, improving clinical outcomes and quality of life. Increased clinical suspicion is vital to preventing complications and unnecessary investigations.

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