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SHORT COMMUNICATION

A diagnosis to consider in paralysis aggravated by excessive carbohydrate intake: Hypokalemic periodic paralysis associated with *CACNA1S* in a pediatric patient

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ABSTRACT

A nine-year-old female was admitted to the pediatric emergency room with weakness in all four extremities, preventing her from standing or walking. The patient reported that symptoms began after consuming a high amount of carbohydrates. Laboratory analyses indicated a potassium concentration of 2.4 mmol/L. After potassium replacement, the patient's symptoms returned to baseline levels. A genetic study revealed a heterozygous mutation in the CACNA1S gene. Hypokalemic periodic paralysis is an uncommon channelopathy marked by intermittent muscle weakness, frequently induced by elevated carbohydrate consumption. Although environmental factors such as carbohydrate loading can exacerbate symptoms, genetic analysis plays a crucial role in confirming the diagnosis. This instance underscored the necessity of identifying food triggers in individuals with CACNA1S mutations and incorporating hypokalemic periodic paralysis into the differential diagnosis of acute muscle weakness in young patients.

Keywords: *CACNA1S*, channelopathy, hypokalemic periodic paralysis.

Hypokalemic periodic paralysis (HPP) is an uncommon neuromuscular condition marked by painless muscular weakening, often exacerbated by factors such as diet and exercise. It is an autosomal dominant skeletal muscle channelopathy with an estimated prevalence of 1 to 1.5 per 100,000 individuals.[1] Hypokalemic periodic paralysis is most commonly associated with mutations in the calcium channel gene *CACNA1S* and can present with varying phenotypes.[2] The majority of patients experience episodes of periodic paralysis lasting from several hours to days, typically manifesting during adolescence, while some individuals present with proximal muscle weakness without overt episodes of paralysis. Long-term follow-up studies on HPP remain limited, leaving gaps in our understanding of its natural history. Understanding the fundamental mechanisms of HPP necessitates an analysis of insulin's role in electrolyte homeostasis. Elevated glucose concentrations prompt insulin release from pancreatic beta cells, which activates GLUT4 (glucose transporter type 4) in skeletal muscle, thus enhancing glucose absorption. Insulin promotes sodium influx into cells by activating sodium-hydrogen antiporters in the cell membrane, which then activates Na^+/K^+-ATPase (sodium-potassium adenosine triphosphatase) activity.[3] This activation leads to potassium flux via active transport in high-energy metabolic states. Periodic paralysis has also been linked to conditions beyond potassium imbalances, such

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as thyrotoxicosis.[4] These disorders are frequently diagnosed based on clinical presentation prior to validation through genetic testing. This case report underscored HPP aggravated by elevated carbohydrate consumption.

CASE REPORT

A nine-year-old female was admitted to the pediatric emergency room with acute onset of weakness in all four extremities and trunk muscles, accompanied by inability to walk that had started the previous night. The patient reported no preceding vigorous physical activity, and the symptoms began after ingestion of a high-carbohydrate meal. Two months earlier, the patient had experienced a similar episode, during which the serum potassium level was 2.3 mmol/L, and complete recovery was observed within 6 h. Between attacks, the patient was completely asymptomatic.

The patient was the second child of a nonconsanguineous couple, with no family history of similar symptoms or neurological disorders. On admission, vital signs were stable, and the patient was fully conscious and oriented. Neurological examination revealed severe generalized muscle weakness with Medical Research Council Grade 1/5 strength in both upper and lower extremities and diminished deep tendon reflexes. No muscle atrophy, paresis, or percussion myotonia was detected.

An initial 12-lead electrocardiogram demonstrated a U-wave deflection following the T-wave and a prolonged QTc interval of 500 msec (Figure 1). Laboratory tests showed a potassium of 2.4 mEq/L, thyroid-stimulating hormone of 1.41 uIU/mL, creatine kinase of 313 U/L, and a normal complete blood count. The patient was admitted to the pediatric ward and received 40 mEq of oral potassium. Within hours, the potassium level normalized to 4.9 mEq/L, and by the following morning, the symptoms had completely resolved. The repeated potassium level was 4.0 mEq/L. Contrast-enhanced cranial and spinal magnetic resonance imaging and nerve conduction studies were normal.

The patient subsequently received an additional 40 mEq of oral potassium, accompanied by a suggestion for primary care follow-up and ongoing oral potassium supplementation after discharge. Genetic analysis was performed to investigate possible etiologies of hypokalemia, and a heterozygous *CACNA1S* mutation was identified.

Weakness attacks may frequently be induced by exhaustion, high carbohydrate and sodium intake, alcohol use, cold exposure, stress, excitement, panic, corticosteroid administration, and anesthetic interventions. The patient was advised to avoid these typical triggers. She further obtained nutritional and psychological counseling, along with lifestyle change advice to prevent flare-ups. The patient did not undergo treatment with acetazolamide or potassium-sparing diuretics. At present, flare-ups are mitigated through lifestyle adjustments, nutritional counseling, and clinical assessments, with potassium levels remaining normal between episodes. Written informed consent for the publication of this case report was obtained from the patient's parents.

DISCUSSION

Hypokalemic periodic paralysis is a rare but potentially debilitating condition that can present with episodic muscle weakness, often triggered by

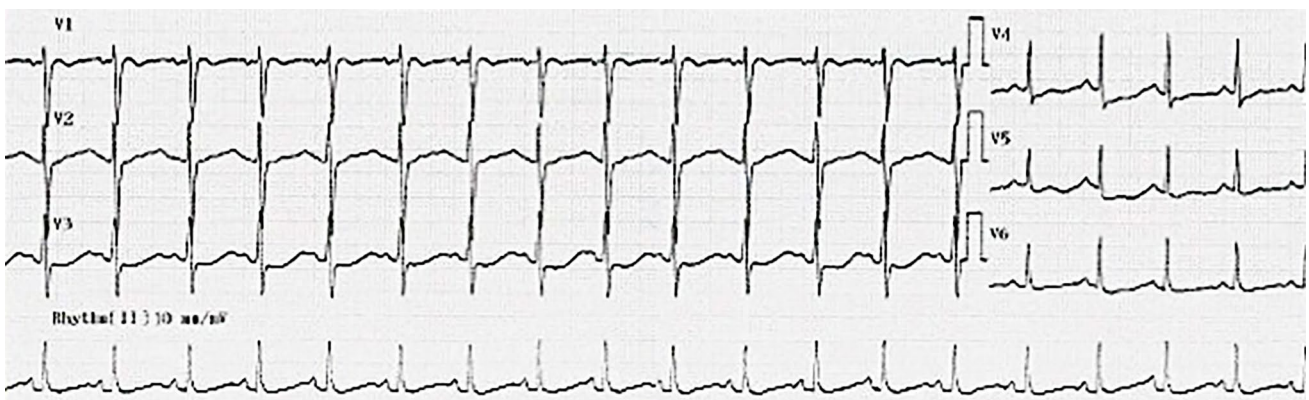

Figure 1. Electrocardiogram in the patient with a serum potassium level of 2.4 mEq/L.

environmental factors such as diet, physical activity, and stress. This case highlighted an unusual yet important trigger, excessive carbohydrate intake, which lead to the acute exacerbation of symptoms in a pediatric patient. While HPP has well-established associations with mutations in the *CACNA1S* gene, the dietary component, particularly carbohydrate loading, warrants attention as a modifiable factor in symptom management.[5] Furthermore, corticosteroid-induced HPP episodes were reported in the literature, highlighting the need for careful consideration of medication history when evaluating patients with acute muscle weakness.[6] The pathophysiology of HPP involves dysregulation of ion channels, particularly calcium channels, which leads to impaired muscle cell membrane stability and potassium imbalance. As in our case, the *CACNA1S* mutation impairs calcium ion flux, contributing to depolarization and triggering the episodes of weakness characteristic of the disease. Notably, carbohydrate-rich meals are known to exacerbate HPP by triggering insulin secretion, which then activates ion transporters and causes a shift in extracellular potassium, resulting in hypokalemia.[7] This mechanism was evident in our patient, whose symptoms were closely associated with the consumption of a high-carbohydrate meal. Similar findings have been reported in thyrotoxic periodic paralysis, where excessive carbohydrate intake serves as a common trigger, further supporting the role of insulin-mediated potassium shifts in these paralytic episodes.[8]

This case is particularly instructive as it underscores the critical importance of genetic testing in confirming the diagnosis of HPP. Although clinical presentation and laboratory findings, such as hypokalemia, can guide diagnosis, genetic analysis remains the gold standard for definitive confirmation.

Furthermore, the absence of a family history of similar symptoms or neurological disorders in this patient suggests the possibility of a de novo mutation, as reported in some cases of HPP.[9] Although the patient's symptoms improved with potassium supplementation, it is essential to emphasize that long-term management of HPP involves more than just acute treatment. Lifestyle modifications, including dietary changes and stress management, are key to reducing the frequency and severity of episodes. In this case, the patient was instructed to avoid high-carbohydrate meals, one of the most potent triggers for her symptoms. Additionally, the importance of regularly monitoring and tracking potassium levels to prevent further attacks cannot be emphasized enough.

In addition to the direct management of HPP, the psychological and emotional support provided to pediatric patients is crucial. Chronic conditions such as HPP, particularly in younger individuals, can impact mental well-being, and addressing this aspect is essential in promoting quality of life. This case also highlighted the need for further research into the natural history and long-term outcomes of HPP, particularly in pediatric populations, as few longitudinal studies currently exist.

In conclusion, this case underscored the necessity for physicians to include HPP in the differential diagnosis of young patients exhibiting unexplained muscle weakness, particularly when dietary triggers such as excessive carbohydrate consumption are present. Prompt genetic analysis and lifestyle modifications can significantly enhance patient outcomes, necessitating additional research to comprehend the long-term therapy of this unusual and intricate ailment.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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