Case Report

Primary Hypokalemic Periodic Paralysis: Long-term Management and Complications in a Child

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Hypokalemic periodic paralysis (HPP) is a rare genetically determined neuromuscular disorder caused by mutation in skeletal muscles calcium and sodium channels. It presents with recurrent episodes of flaccid paralysis. A 9-year-old girl presented with recurrent episodic flaccid quadripareis with complete recovery in-between the episodes. Investigations during the acute episode revealed marked hypokalemia with electrocardiogram changes. Next-generation sequencing showed pathogenic missense mutation in CACNA1S gene. She responded well to oral potassium supplementation, acetazolamide, and spironolactone therapy. Muscle weakness in HPP is reversible, and long-term management reduces frequency of paralysis and prevents permanent weakness.

INTRODUCTION

Hypokalemic periodic paralysis (HPP) is a rare neuromuscular disorder characterized by episodic muscle weakness and occasionally life-threatening arrhythmia.¹ The recurrent paralytic episodes are characterized by concomitant hypokalemia (serum potassium <3.5 mmol/L) leading to depolarization-induced loss of excitability.² Heavy exercise, carbohydrate-rich evening meals, pregnancy, and menstruation are important triggers. Disease progression and recurrent episodes may result in permanent disability. Here, we report a case of HPP with recurrent episodes of flaccid weakness and long-term management issues.

CASE REPORT

A 9-year-old girl presented with acute onset neck pain followed by weakness of all limbs for 24 h duration. She had a cheese burger with mayonnaise sauce at dinner and slept well. In the morning she reported inability to move limbs, sit, and turn in the bed with neck pain. She had history of three similar episodes in the past from 7.5 years of age. Each episode usually lasted for 24–36 h, and resolve spontaneously without any residual weakness. Most of these episodes were noted early in the morning and relation to food was not noticed by the parents. There was no history of limb pain, stiffness, or cramps in-between the episodes. There was no history of respiratory difficulty, bowel and bladder involvement, recurrent diarrhea, excessive urination, poor weight gain, or any prolonged drug intake. She was born to non-consanguineous parents, and her family history was unremarkable.

On examination, she had normal higher mental functions, was hypotonic, and quadriparetic with hyporeflexia. Respiratory and diaphragmatic functions were normal. During the acute event, she had hypokalemia (1.6 mEq/L, normal: 3.5–5.5 mEq/L) with...
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electrocardiogram (ECG) changes. Other electrolytes, hemogram, liver function, renal function tests, and pH were normal. Her creatine kinase level was elevated (11298 U/L, normal: 34–171 U/L). She was treated with intravenous potassium chloride infusion with ECG monitoring and her weakness improved.

Secondary causes of HPP were ruled out. Sanger sequencing of CACNA1S and SCN4A revealed a pathogenic heterozygous missense mutation (R1239H) in exon 30 of CACNA1S gene, confirming the diagnosis of HPP.

For recurrent similar episodes, she was advised to avoid the triggers, and adherence to low-sodium, carbohydrate, and potassium-rich diet. She continued to have similar episodes of weakness, and hence maintenance therapy with oral potassium citrate (4 mEq/kg/day) given. Compliance remained an issue with oral potassium powder; she was initiated on oral acetazolamide (8 mg/kg/day). Tolerance to acetazolamide remained poor, with frequent gastritis and gastroenteritis. Spironolactone (75 mg/day) was initiated. She remained compliant to therapy with good response and frequencies of episodes were reduced markedly. She had occasional recurrence during adolescence, with heavy meals. However, she developed androgenic adverse effects leading to reduced compliance to spironolactone. She is maintained on oral acetazolamide now with oral potassium. Currently she is 18 year old, with relatively stable course and no permanent weakness.

**DISCUSSION**

The primary or familial HPP is autosomal dominant skeletal muscle channelopathies with decreased penetrance in females and it is caused by mutation in α subunit of skeletal muscle L-type calcium channel gene CACNA1S or the voltage-gated sodium channel gene SCN4A. Episodic weakness occurs based on the concentration of extracellular potassium ions, which are responsible for membrane excitability. The final pathway is aberrant depolarization that inactivates ion channels leading to muscle fiber inexcitability.

The diagnosis of HPP can be made by diagnostics criteria proposed by Sansone et al. [Table 1]. Thyrotoxic periodic paralysis is indistinguishable from HPP and assessment of thyroid profile is mandatory. During an acute attack, patients have hypokalemia (<3.5 mEq/L) with or without ECG changes, elevated creatine kinase, reduced, or rarely absent compound motor action potential on nerve conduction studies. Needle electromyography usually shows reduced insertional activity, polyphasic motor unit potentials, positive sharp waves, and fibrillation potentials. Serum potassium concentration is normal in-between the attacks. During an acute episode, T2-weighted fat saturation magnetic resonance sequences show muscle edema, which is more common in calf muscles as compared to upper limb muscles.

Treatment strategy starts from patient education and lifestyle changes to decrease the triggers and minimizing attack frequency and severity. Small frequent meals (to avoid high carbohydrate load), low-sodium diet, and avoidance of hyperosmolar (dehydration, hyperglycemia) states decrease the number of attacks. If the potassium level during an acute episode is unknown, mild exercise at the onset can shorten the severity and duration of an acute episode.

Pharmacological therapy is used to abort an acute attack and for preventive measure. For an acute attack, oral potassium (20–30 mEq/L, every 15–20 min) is sufficient. Carbonic anhydrase inhibitors (CAIs) particularly acetazolamide (5–10 mg/kg/day) and dichlorphenamide (50–200 mg/day) are used for preventive therapy. CAI stimulates urinary bicarbonate excretion, promotes systemic acidosis, enhances opening of calcium sensitive potassium channels, and reduces intracellular sodium.

### Table 1: Consensus diagnostic criteria of hypokalemic periodic paralysis

|   |                                                                 |
|---|------------------------------------------------------------------|
| 1 | ≥2 attacks of muscle weakness associated with serum potassium <3.5 mEq/L. OR |
| 2 | One attack of muscle weakness in the patient and one attack of weakness in one relative with associated serum potassium <3.5 mEq/L. OR |
| 3 | ≥3 of the following features:                                  |
|   | Onset in the first or second decade                            |
|   | Duration of attack (muscle weakness involving ≥1 limbs) longer than 2 h |
|   | The presence of triggers (previous carbohydrate rich meal, symptom onset during rest after exercise, stress) |
|   | Improvement in symptoms with potassium intake                 |
|   | A family history of the condition or genetically confirmed skeletal calcium or sodium channel mutation |
|   | Positive long exercise test                                    |
| 4 | Exclusion of other causes of hypokalemia (drugs, toxins, celiac disease, renal, adrenal and thyroid dysfunction). |
concentration. This decreases the muscle fibers damage and reduces the frequency and duration of further attacks.[6,7] Acetazolamide and other CAI are more effective in patients with CACNA1S as compared with SCN4A mutation.[8,9] Dichlorphenamide may be used in those patients who do not respond to acetazolamide. Common adverse reactions associated with CAI are dysguesia, paresthesia, easy fatigability, muscle cramps, renal stones, and reversible mild cognitive disturbance.[8]

Chronic potassium supplementation and potassium sparing diuretics (spironolactone [25–100 mg/day], triamterene [50–150 mg/day], and eplerenone [50–100 mg/day]) are other treatment options in HPP.[8] Spironolactone and other potassium sparing diuretics are alternative to CAI in patients who have partial response or develop intolerable side effects. Our patient responded well with spironolactone and was symptom free for 3 years; however, she developed androgenic side effects during adolescence that leads to discontinuation of drug. The common side effects of spironolactone are hyperkalemia, gynecomastia, hirsutism, acne, hyponatremia, and renal failure.[10]

Long-term outcome of the patients with HPP is good; however, these patients are sensitive to general anesthesia and may develop muscle paralysis and respiratory weakness. Proximal myopathy, malignant hyperthermia, and life-threatening cardiac arrhythmias are other potential complications.[7]

**Conclusion**

There are no consensus statements for the treatment and acetazolamide has been the therapy of choice since five decades. Spironolactone is an important alternative of CAIs; however, androgenic side effects limit its use.

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**Conflicts of interest**

There are no conflicts of interest.

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