

# Hypokalemic Periodic Paralysis: An Unexpected Finding of Hypothyroidism

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## Abstract

Hypokalemic periodic paralysis (HPP) is a rare syndrome of muscular weakness and paralysis associated with hypokalemia and usually with hyperthyroidism. Even more rare is its association with hypothyroidism. This serious subtype of periodic paralysis can result in arrhythmias, respiratory failure and death. The severity of the attacks varies from mild pain and weakness to total paralysis. The attacks spontaneously abate and the patient recovers within 3-36 hours. Cognitive and sensory functions remain intact, deep tendon reflexes may be normal, diminished, or absent and thyroid gland enlargement may be difficult to appreciate. Episodes of Hypokalemic Periodic Paralysis (HPP) may be triggered by consuming a high carbohydrate meal or a period of rest after extreme physical activity, as well as menses, emotional stress, trauma, alcohol, infection and certain medications. We report a case of hypokalemic periodic paralysis in an African-American with Graves' disease presenting to the Emergency Department (ED) after ingesting a high carbohydrate meal and who was found to be in a hypothyroid state. The paralysis in this patient was so transient the staff actually questioned the validity of his complaints! We will review pathogenesis, clinical features, diagnosis, and treatment. Additionally, we will offer some practical points for maintaining a high clinical suspicion.

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## Case report

A 43-year-old African American man presented to the ED with a chief complaint of paralysis of his lower extremities. Upon arrival to the hospital, he experienced a complete lower extremity weakness that prevented him from getting out of his vehicle. Passers-by called for assistance and he was placed on a stretcher by hospital personnel. Shortly after being triaged to a room he stood up and was walking around the ED looking for a phone! The staff was quite surprised and began questioning the validity of the patient's complaints! History revealed a 6 months history of "feeling shaky"

accompanied by diaphoresis, fatigue, diffuse muscle aches, a 20 pound weight loss, heat intolerance, and marked by intermittent profound bilateral proximal lower extremity weakness. Four months prior to his ED visit, he was seen for these symptoms by his primary care physician. Significant findings then revealed a potassium of 2.8 mEq/L, and a thyroid scan consistent with a diffuse goiter. He was diagnosed with Graves' disease and given outpatient methimazole 5 mg TID, which resolved his symptoms. He discontinued the medication after 1 month and subsequently noted a gradual return of symptoms with paroxysms of lower extremity weakness and paralysis. However, symptoms were periodic and brief and thus, he never sought medical attention or resumed medication. Additionally, he admitted to a brief episode of sudden, brief dysphagia three months prior to presentation. On the day of presentation he ate a large portion of freshly baked ginger cake and within 30 minutes experienced a complete and sudden onset of bilateral lower extremity paralysis that resolved spontaneously and prompted his visit to the ED.

He had a past medical history of hypertension, and Graves' disease and a past surgical history of right orchiopexy for torsion and a right inguinal hernia repair. His medications included methimazole 5 mg TID, and metoprolol 50 mg BID. The social history was unremarkable for smoking, alcohol, or drugs of abuse and the patient lived with his wife. The family history was unremarkable for any autoimmune disorders, thyroid disease, or neurological/muscular diseases. A review of systems was otherwise noncontributory.

Physical examination revealed a well-developed African American male with a blood pressure at 158/85 mmHg, pulse rate of 105/min, respiratory rate of 16/min, oxygen saturation of 99% on room air, and an oral temperature of 36.5°C. On head and neck exam there was evidence of proptosis without lid lag or retraction, and mild diffuse injection of conjunctiva. There were no tongue fasciculations. The thyroid gland was normal in size by palpation, and without bruits or nodules. Chest exam revealed good air movement bilaterally without adventitious sounds. Heart sounds were normal without gallops, murmurs or rubs. Abdominal exam was unre-

markable. Neurologically, the patient was awake, alert, oriented and mentating normally. Cranial nerve exam was unrevealing, and reflexes were all symmetrical and normal (2+) with an absent plantar flexor reflex bilaterally. Extremities showed no visible atrophy, fasciculations, spasticity, tremors, or hypertrophy. There were symmetrical bilateral proximal muscle weaknesses (4/5) at the hip flexors, extensors, abductors, adductors, and gluteals. Tenderness was elicited in the lower limb girdles on palpation. Normal anal sphincter tone. There were no rashes and no evidence of ticks. The remainder of the physical examination was unremarkable.

An electrocardiogram (ECG) was obtained and revealed a regular sinus tachycardia, and no evidence of severe hypokalemia (flat T's, U waves, ST depression, prolonged QT).

Electrolyte analysis (obtained just before paralysis had resolved) was notable for a potassium level of 3.0 mEq/L (normal 3.5-5.3 mEq/L). The remainder of the electrolytes and the serum levels of urea nitrogen, creatinine, and glucose were within normal limits. The complete blood count was notable for mild normocytic anemia. His thyroid stimulating hormone level (TSH) was markedly elevated at 45 ng/dL (normal range 0.45-4.5 ng/dL) indicating that he was in a hypothyroid state.

Given the elevated TSH, hypokalemia and paroxysmal muscle weakness, a diagnosis of hypothyroid hypokalemic periodic paralysis was made. The patient's treatment in the ED consisted of 40 mEq of potassium chloride replacement via oral route. He was observed in the ED for 7 hours with complete resolution of his episodic weakness and endocrinology was consulted.

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### Discussion

Thyrotoxic hypokalemic periodic paralysis (THPP) is a rare syndrome of muscular weakness and paralysis associated with hypokalemia and hyperthyroidism.<sup>1</sup> This serious subtype of periodic paralysis can result in arrhythmias, respiratory failure and death.<sup>2-4</sup> The incidence is 0.1% amongst hyperthyroid North American white men<sup>5</sup> and 13% of hyperthyroid Chinese men,<sup>6</sup> and 4% of hyperthyroid Japanese men.<sup>7</sup> This condition is very rare African-American men, only a few case reports have published.<sup>5,8,9</sup> Additionally, its association with hypothyroidism is extremely rare.<sup>10-12</sup>

We identified only 2 published reports of hypothyroid hypokalemic periodic paralysis.<sup>12,13</sup> Interestingly, there was an association with paralysis and the ingestion of a high carbohydrate meal.<sup>13</sup>

The clinical signs of hypo or hyperthyroidism are not always apparent and it is imperative to include this entity in the dif-

ferential diagnosis of acute weakness in the emergency department. More interestingly, is the fact that the paralysis was precipitated by a high carbohydrate meal.

The history, physical examination, and laboratory findings in this case were consistent with the diagnosis of hyperthyroid HPP. Our patient was male, in his 40s, had clinical findings of hyperthyroidism, and confirmed diagnosis of Graves' disease, symptoms resolved within 6-7 hrs, more severe attacks occurred with high carbohydrate meals (donut, ginger cake), and distant attacks had ceased with hyperthyroid treatments. The potassium was not severely low in our patient and this was reflected in a basically normal ECG. Since rebound hyperkalemia can occur in 40% patients, whether or not the potassium level was lower at the time of the initial paralysis in our patient can not be ruled out.<sup>14</sup> In one report, a patient presented with normal levels of potassium.<sup>15</sup>

Previous case reports highlight marked hypokalemia in their cases of hyperthyroid HPP, yet our patient had a potassium levels of 2.8 mEq/L and 3.0 mEq/L, with a normal ECG. In addition, our patient did not reveal a palpable thyroid nodule/goiter. This case demonstrates the wide range of clinical and laboratory findings that can be exhibited by HPP, especially in the form associated with thyroid disease.

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### Pathophysiology

Although the pathophysiology of HPP has not been completely elucidated, researchers surmise that there is an intracellular shift of potassium leading to progressive depolarization of the resting membrane potential. The sarcolemma become inexcitable and patients experience paralysis.<sup>5</sup> Additionally, insulin, carbohydrate, and androgen administration can activate the sodium-potassium ATPase pump (Na-K ATPase)<sup>16,17</sup> so that precipitating factors such as insulin or high carbohydrate diets serve as triggers for paralytic attacks. In hyperthyroid HPP patients have a significantly higher Na-K ATPase activity than in those without the disease<sup>18</sup> resulting in intracellular shifting of potassium. Patients experience hypokalemia and a decrease in the ability of muscle cells to depolarize and contract when stimulated.<sup>2</sup> Since the hypokalemia is not a depletion of total body potassium, but rather a shift in potassium extracellularly, the symptoms of weakness or paralysis resolve over a period of 3-36 hours.

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### Treatment

The initial treatment of HPP is potassium replacement. This not only helps with recovery of paralytic attacks, but more importantly, also prevents cardiac arrhythmia. Care must be taken as the hypokalemia is only an intracellular shift of potassium and iatrogenic hyperkalemia can ensue if potassium is

replaced too aggressively. For this reason, some physicians have proposed the use of IV potassium only in severely hypokalemic, unstable patients, or patients who can not tolerate replacement by mouth.

Milder cases of paralysis probably resolves spontaneously, but the main goal of therapy is to establish a euthyroid state. In patients with mild attacks of HPP which resolve on their own or with oral supplementation therapy, and subsequently have

no recurrences in the ED for more than 6 hours, discharge with close primary care and endocrinology follow-up for thyroid function studies, and long-term therapy is appropriate. Admission is recommended in cases of ongoing HPP crises, severe hypokalemia, arrhythmias or any sign of instability. Keep in mind high carbohydrate meals as a precipitant and advise the patient accordingly.

### Differential Diagnosis of acute weakness in the Emergency Department

Landry Guillain-Barré syndrome  
Myasthenia gravis  
Lyme disease/ Tick Paralysis  
Polymyositis  
Rhabdomyolysis  
Porphyria  
Diphtheria  
Pollomyelitis  
Botulism  
Metals (Arsenic, Thallium)  
Organophosphate poisoning  
Tetrodotoxin (puffer fish)  
Paralytic shellfish toxin  
Spinal cord compression  
Myopathies  
Neuropathies  
Electrolyte abnormalities  
(e.g. hypophosphatemia, hypermagnesemia)  
Psychiatric disorders  
Spinal and neuromuscular diseases  
Dyskalemic periodic paralysis  
(THPP, familial or nonfamilial periodic paralysis)  
Andersen's syndrome<sup>1\*</sup>  
Brody's disease<sup>2\*</sup>  
Rippling muscle disease<sup>3\*</sup>  
Schwartz-Jampel syndrome<sup>4\*</sup>  
Stiff-person syndrome<sup>5\*</sup>

\*1\* Andersen's syndrome (a triad of potassium-sensitive periodic paralysis, ventricular dysrhythmias, and dysmorphic features)

\*2\* Brody's disease (a myopathy characterized by impaired muscle relaxation, caused by a deficiency of Calcium-ATP in sarcoplasmic reticulum)

\*3\* Rippling muscle disease (an inherited, poorly defined myopathy, marked by muscle stiffness, weakness, and an unusual sensitivity to stretch, manifested by rippling waves of muscle contraction)

\*4\* Schwartz-Jampel syndrome (an inherited condition manifested by a combination of muscle stiffness and mild, largely nonprogressive muscle weakness, joint contractures, generalized myotonia, skeletal anomalies, and facial), and

\*5\* Stiff-person syndrome (a rare central nervous system disorder characterized by progressive rigidity and painful spasms of the axial and limb muscles).

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