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Case Report

Thyrotoxic Periodic Paralysis in a Hispanic Young Adult Male

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Abstract

Thyrotoxic periodic paralysis is a rare complication of hyperthyroidism, characterized by severe hypokalemia and episodes of skeletal muscle paralysis. Although it is commonly described in adult East Asian men, TPP has been reported in individuals of all ages and ethnic backgrounds. We describe the case of a young adult Hispanic male who presented to a Pediatric Emergency Department with paralysis and was diagnosed with TPP. We will review TPP, focusing on the clinical presentation, pathophysiology and treatment.

ABBREVIATIONS

TPP: Thyrotoxic Periodic Paralysis; **FHPP:** Familial Hypokalemic Periodic Paralysis

INTRODUCTION

Thyrotoxic Periodic Paralysis (TPP) is a rare complication of thyrotoxicosis characterized by hypokalemia and muscle paralysis. It closely resembles familial hypokalemic periodic paralysis (FHPP). TPP is a difficult condition to recognize, with a reported average delay to diagnosis of almost 14 months [1]. When a patient in a pediatric emergency department is found to have hypokalemia, gastrointestinal or urinary losses are the most common etiologies. If acute muscle weakness is present, FHPP is considered. However, as TPP is a rare cause of hypokalemia, it is seldom included in the differential.

TPP is more common in males with a 30:1 male-to-female ratio[1]. Although TPP can occur in individuals of all ages and ethnicities, it is most frequently described in individuals of Asian descent typically between 20 and 40 years of age. The incidence of TPP among Asian patients with hyperthyroidism is 1.8-1.9% as compared to 0.1-0.2% among hyperthyroid patients in the US [2]. TPP is rarely reported in Hispanic individuals, with only case reports found in the literature mostly describing affected males [1,3-7]. Recently a case series of three young Hispanic males was reported, emphasizing the diverse ages and ethnicities now recognized in patients with TPP [8].

We present a case of TPP in a young adult Hispanic male presenting to the pediatric emergency department with acute paralysis. The diagnosis of TPP in this case was atypical, as it was made during the patient's initial presentation of paralysis. The rarity of this disorder, variations in ethnicity and gender, and the lack of inclusion of TPP in the differential diagnosis for acute paralysis or hypokalemia often lead to a delay in diagnosis commonly seen in these patients. The infrequent presentation to pediatric settings has the potential to even further lengthen this delay.

CASE PRESENTATION

A 20 year old Hispanic male presented to the pediatric emergency department with significant muscle weakness. One day prior to presentation, he ate 6 candy bars and later developed severe muscle weakness in his extremities. The next morning, he was found by his mother to be unable to get out of bed and was taken to the pediatric emergency department. The patient had a similar episode three months prior which self-resolved. He did not seek medical attention for his previous episode.

The patient's medical history was significant for an anxiety disorder diagnosed three years prior to presentation. He reported a 40 pound weight loss, intermittent diarrhea, and palpitations. Family history was noncontributory, with no reports of cardiovascular, neurologic, or hormonal disorders, including thyroid disease or episodes of paralysis. Vital signs showed hypertension and tachycardia. Physical exam revealed a large goiter. Neurological exam was significant for 2/5 strength in his proximal muscles, tongue fasciculation's and a fine tremor with normal sensation. Blood work revealed hypokalemia with a potassium level of 2.4 mmol/L. Thyroid function tests showed a suppressed TSH of 0.009 (normal: 0.400-4.60) uU/mL and an elevated free T4 of 7.77 (normal: 0.800-1.70) ng/dL and T3 of 651 (normal: 81.0-199) ng/dL, consistent with hyperthyroidism.

He was diagnosed in the pediatric emergency department with TPP and hyperthyroidism, later confirmed through antibody testing to be due to Graves' disease (thyroid stimulating immunoglobulin 331% (normal: <141%). He was admitted to the Pediatric ICU and given intravenous fluids with potassium.

The patient was also started on methimazole and propranolol for his hyperthyroidism. His potassium was monitored closely and normalized after 12 hours of treatment. His muscular weakness improved significantly as his hypokalemia resolved. He was discharged home on methimazole and propranolol and his thyroid function improved gradually over the next several weeks. He received radioiodine ablation for definitive therapy six months after his initial presentation. Paralysis did not recur.

DISCUSSION

The clinical presentation of TPP is characterized by recurrent, transient episodes of muscle weakness. Proximal muscles of the lower limbs are often affected first. Episodes of paralysis can last up to 72 hours. Rarely, respiratory muscles can be involved. Impairment of bowel or bladder function or sensory involvement has not been reported.

Paralytic episodes can occur regardless of degree of hyperthyroidism, and severity of paralysis is unrelated to the degree of hyperthyroidism. In fact, paralysis is often the initial presenting sign of hyperthyroidism that leads patients to seek medical attention, as in the case of our patient. TPP is most commonly described in individuals with Graves disease, however it has been reported in all causes of hyperthyroidism, including lymphocytic thyroiditis, toxic nodular goiter, solitary toxic thyroid adenoma, iodine-induced thyrotoxicosis, excessive thyroxine use, and thyrotropin-secreting pituitary adenomas [5].

TPP has a multifactorial etiology, involving genetic predisposition, thyrotoxicosis, and environmental factors. The hallmark feature is hypokalemia, often with a potassium level of <3.0 mmol/L. Although the pathogenesis of TPP is not completely understood, it is thought to be caused by the combination of an overly active sodium-potassium adenosine triphosphatase (Na/ K^+ ATPase) in the setting of decreased activity of the inward rectifying potassium channel (Kir) resulting in a massive intracellular shift of potassium and hypokalemia (Figure 1).

In normal muscle cells, potassium is pumped intracellularly by the Na/ K^+ ATPase while the efflux of potassium is facilitated by the Kir channel. If Na/ K^+ ATPase is overactive, excess potassium is transported intracellularly, leading to hypokalemia. Multiple hormones can increase the activity of Na/ K^+ ATPase including thyroid hormones, insulin, catecholamines, and testosterone. Testosterone increases activity of the Na/ K^+ ATPase, explaining the male predominance of TPP. In addition, patients often report a high carbohydrate meal or snack prior to paralysis, as the increased insulin levels triggered by the excess carbohydrates induces paralysis by increasing Na/ K^+ ATPase pump activity [9]. In our case, the large intake of candy caused a rapid increase in our patient's insulin levels, which likely precipitated his paralytic episode.

Normally, high intracellular potassium is corrected by a corresponding increase in potassium efflux through the Kir channel. However, when the Kir channel is mutated or during conditions of elevated insulin or catecholamines, extracellular flow of potassium is inhibited. This diminished potassium efflux contributes significantly to the increase in intracellular potassium. It has been postulated that both over activation of Na/ K^+ ATPase pump and a lack of compensated outward potassium flow through the Kir channel must be present to cause TPP [9].

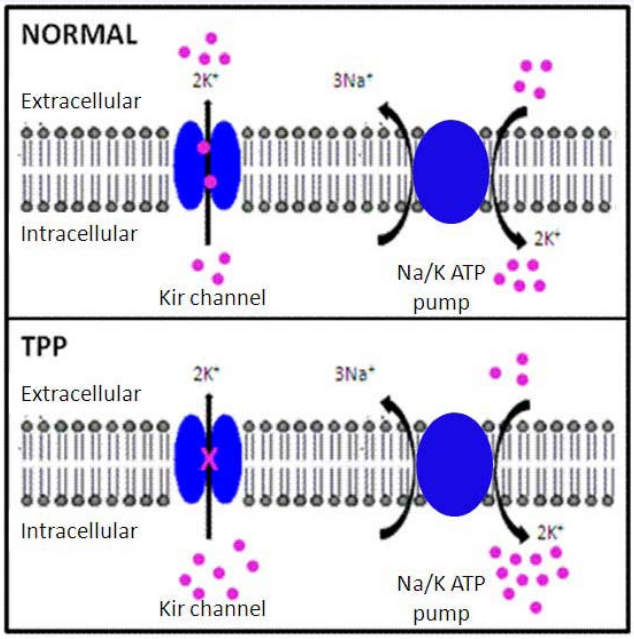

Figure 1 Pathophysiology of TPP in a skeletal muscle cell. In normal muscle cells, K^+ diffuses to the extracellular space through the Kir channel. K^+ is also pumped intracellularly by the Na/ K^+ ATPase pump. In TPP, the Na/ K^+ ATPase pump is overactive due to hormonal changes. In conjunction with a mutated K^+ channel which decreases extracellular flow of K^+, there is a massive intracellular shift of K^+ leading to hypokalemia.

Genetics are believed to be a contributing factor to the etiology of TPP. One study found a mutation in the KCNJ18 gene encoding the Kir2.6 channel in up to 33% of individuals with TPP [10]. However in many TPP patients no genetic mutations have been uncovered.

In addition to hypokalemia, patients often present with hypophosphatemia, hypomagnesemia, and low urine potassium excretion with a normal acid-base balance. Thyroid function studies are consistent with hyperthyroidism, with a suppressed TSH and elevated T4 and/or T3 as in our patient. Electrocardiographic changes can occur in TPP, including tachycardia, increased QRS voltage, and first-degree atrioventricular block.

Patients with TPP are often misdiagnosed initially with FHPP. However, TPP can be distinguished from FHPP by a careful history, including family history, and physical exam (Table 1). Medical providers should look specifically for signs and symptoms of hyperthyroidism including tachycardia, hypertension, exopthalmos, goiter, fine tremor, tongue fasciculation's, irregular menses, and weight loss. Our patient's large goiter alerted the medical team to consider TPP at presentation in the emergency department, which facilitated prompt diagnosis and treatment.

Initial treatment of TPP involves potassium supplementation, propranolol, and anti-thyroid drugs. Although paralysis is self-limited and overall body potassium is not depleted, studies have shown improved recovery time with potassium replacement [11]. Potassium supplementation can be given either PO or IV.

Table 1: Comparison of TPP versus FHPP.*

	TPP	FHPP
Most common age of onset	20-40 years	Before 16 years
Most frequent ethnicity	East Asian	Caucasian
Male to female ratio	30:1	3:1
Family history of paralysis	Rare	Frequent
Family history of thyroid disease	Frequent	Rare
Clinical features of hyperthyroidism	Yes	No
Potassium level during paralysis	1.5-3.0 mmol/L	2.8-3.5 mmol/L

* Adapted from Maciel et al. [1].

If IV supplementation is used, careful monitoring is required to avoid rebound hyperkalemia. In our case, IV potassium was started after the patient was found to be hypokalemic, but prior to the documentation of hyperthyroidism by serum thyroid function tests. Propranolol is often used in conjunction with anti-thyroid medications to ameliorate the effects of hyperthyroidism by decreasing peripheral conversion of T4 to T3. As a β-adrenergic antagonist, propranolol lowers heart rate and systolic blood pressure, inhibits the catecholamine effect and improves hypokalemia. Anti-thyroid medications are given until definitive therapy can be accomplished via surgery or RAI. Normalization of thyroid levels via anti-thyroid drugs is often the initial therapy but due to the high likelihood of recurrence with even slight elevations in thyroid hormone levels, definitive treatment of hyperthyroidism is often recommended.

In conclusion, TPP is a rare but serious complication of hyperthyroidism, which can occur in individuals of all ages and ethnicities. To allow for prompt treatment, TPP should be considered in all individuals who present acutely with hyperthyroidism, muscle weakness and hypokalemia. Ongoing research into TPP continues to deepen our understanding of pathophysiology of this unique disorder.

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