

Case Report: Thyrotoxic Periodic Paralysis

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INTRODUCTION

Thyrotoxic Periodic Paralysis (TPP) presents as a triad of acute attacks of muscle weakness, hypokalemia, and thyrotoxicosis. TPP was first described in East Asian countries, specifically Japan and China, where it was found to occur at an overall incidence of 2% and preferentially affected males.^{1,2} TPP also develops in other ethnicities, however, and given the growing ethnic heterogeneity of global society, it is becoming increasingly important for all physicians to be familiar with the diagnosis and management of TPP. The following case represents a typical presentation of TPP and serves as a valuable resource for informing our differential diagnoses and approach to similar cases in the future.

CASE PRESENTATION

Mr. X is a 52-year old Japanese man with a history of Graves' Disease that had been treated with methimazole. After several years of euthyroidism, the methimazole was tapered down and discontinued altogether 3 months prior to presentation. One month prior to presentation, Mr. X obtained surveillance thyroid stimulating hormone (TSH) testing, which revealed an exceedingly low level of $< 0.02\mu\text{U}/\text{mL}$. Review of systems revealed increased appetite and oral intake without a change in weight during the preceding 2 weeks, but Mr. X was otherwise asymptomatic, felt well, and had not followed up with his endocrinologist. On the night of presentation, when attempting to climb out of bed, Mr. X noted sudden onset of bilateral painless proximal lower extremity weakness characterized by an inability to walk or even raise his legs.

Vitals were significant for blood pressure of 151/82. He was well-appearing, alert, and in no distress. Examination revealed mild exophthalmos, but no lid lag. His thyroid was normal in size and without nodularity or tenderness. Hip flexion and knee extension were notable for 1/5 strength bilaterally, whereas foot dorsiflexion and plantar flexion had 5/5 strength bilaterally. Patellar reflexes were hyporeflexive bilaterally. Achilles tendon reflexes were normal. Upper extremities had normal strength and reflexes bilaterally. His exam was otherwise unremarkable.

Laboratory testing was significant for low TSH of $< 0.02\mu\text{U}/\text{mL}$, low potassium (K^+) of $2.3\text{mEq}/\text{L}$, and slightly elevated creatinine phosphokinase (CPK) of $256\text{U}/\text{L}$.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for bilateral symmetric lower extremity weakness is broad, but can be narrowed by history, examination, and laboratory findings. It is important to consider inflammatory myopathies such as polymyositis and inclusion-body myositis; neuromuscular disorders such as myasthenia gravis, Lambert-Eaton Syndrome, and Guillain-Barre Syndrome; and spinal cord pathologies such as cord compression and transverse myelitis. Additionally, Familial Periodic Paralysis, which is linked to autosomal dominant mutations of voltage-gated calcium channels, presents in a similar manner as TPP and may also be associated with hypokalemia and thyrotoxicosis.¹ Features that narrowed the differential diagnosis for Mr. X's weakness included the absence of muscle atrophy, pain, sensory deficits, bowel or bladder dysfunction, and other systemic symptomatology. The acuity of onset, bilateral and symmetric nature, and sparing of distal extremities were consistent with TPP. Further, Mr. X's underlying Graves' Disease, notable lack of relevant family history, and his relatively older age, gender, and ethnicity supported a diagnosis of TPP. The low TSH and profound hypokalemia confirmed the diagnosis of TPP.

OUTCOME AND FOLLOW UP

Mr. X remained hospitalized for three days without complications. He was treated with intravenous (IV) potassium chloride, oral methimazole 10mg once daily, and physical therapy. His strength recovered rapidly with normalization of his serum K^+ levels, and he was independently ambulatory at the time of discharge. He was discharged on oral methimazole 10mg once daily with endocrine follow-up.

DISCUSSION

TPP is characterized by the acute onset of muscle weakness and hypokalemia in the setting of thyrotoxicosis.^{1,2,4,5,7} It is predominantly associated with Graves' Disease.¹ While there can be variability in the severity of weakness (mild weakness to complete paralysis), limb involvement, and degree of hypokalemia, this case describes a typical presentation. As in Mr. X's case, attacks of paralysis classically manifest at night. History may reveal strenuous exercise, high emotional stress, or a carbohydrate-rich meal during the preceding day.^{1,4}

Attacks may last minutes to days and occur with unpredictable frequency, although the aforementioned risk factors and persistent thyrotoxicosis are likely associated with increased frequency.¹ While the upper extremities may be affected, the most frequently observed presentation is of bilateral painless, non-atrophic, proximal lower extremity weakness with intact sensation, exactly as occurred for Mr. X. Deep-tendon reflexes are usually diminished or absent, but may be normal or even hyperreflexive, regardless of the severity of paralysis.^{4,5} Laboratory assessment reveals severe hypokalemia (average 2.1-2.4 mEq/L) and a suppressed TSH.^{1,2,4,5,7} Additional findings may include a mildly elevated CPK (in 67% of cases), hypomagnesemia, and hypophosphatemia, although these are not necessary for the diagnosis.⁴

The pathophysiology of TPP is believed to be a heightened sensitivity of beta-adrenergic receptors and increased sodium-potassium adenosine triphosphatase (Na⁺-K⁺ ATPase) channel activity, leading to massive intracellular shifts of K⁺ in the setting of an underlying thyrotoxic hyperadrenergic state.^{1,2,4} Recent studies also suggest an additional K⁺ channel mutation causing decreased cellular efflux of K⁺, leading to intracellular retention of K⁺ during provoked events.¹ These mechanisms account for TPP's predilection for individuals with recent adrenergic or insulin surges, often related to exercise, stress, or carbohydrate-rich meals.

The treatment of TPP is three-fold and involves K⁺ repletion, nonselective beta-blockers, and thionamides.¹ Although there are no official guidelines for treatment, experts agree that K⁺ repletion (preferentially by IV route) should be performed gradually with concurrent checking of frequent basic metabolic panels. Rebound hyperkalemia is a common occurrence, particularly in patients who require greater amounts of K⁺ supplementation to correct their deficiency.^{1,7} Muscle weakness improves with normalization of K⁺ levels, and is unrelated to the persistence or degree of thyrotoxicosis.^{1,2} A nonselective beta-blocker such as propranolol should be considered (IV and PO are both reportedly efficacious, but no guidelines exist for dose or frequency), particularly in profound hypokalemia. Propranolol inhibits sensitized beta-adrenergic receptors and prevents further intracellular influx of K⁺, thus aiding in the normalization of extracellular K⁺ levels.^{1,5} Propranolol was not used for Mr. X because his K⁺ normalized rapidly and he was otherwise minimally symptomatic. Finally, as Graves' Disease is the most common thyroid disorder associated with TPP, methimazole should be initiated, typically at a dose of 10-30mg daily.⁷ Ultimately, patients should pursue definitive treatment of their thyroid disease, such as radioiodine ablation or thyroidectomy, as there is increased risk of recurrent TPP in those who have suffered a prior attack and in those with persistently

uncontrolled thyroid disease.^{5,6} While prophylactic K⁺ is not recommended or effective for the prevention of TPP, propranolol is associated with a mild preventive benefit and may be prescribed for patients with a history of TPP.¹

KEY POINTS

Historically a disease of East Asia, TPP should be suspected in any individual presenting with acute-onset muscle weakness and severe hypokalemia, particularly in the setting of thyrotoxicosis. Treatment with K⁺ repletion and propranolol is effective, but clinicians should monitor for rebound hyperkalemia. Given the risk of recurrent attacks, patients with TPP should be referred for definitive treatment of their thyroid disease.

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