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Thyrotoxic Periodic Paralysis: A Case Report and Discussion of Clinical and Imaging Features

Thyrotoxic Periodic Paralysis: A Case Report and Discussion of Clinical and Imaging Features

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ABSTRACT

Thyrotoxic Periodic Paralysis (TPP) is a rare manifestation of thyrotoxicosis, resulting in periodic episodes of acute onset muscle weakness in the setting of hypokalemia. The thyrotoxic form of Hypokalemic Periodic Paralysis (HPP) is less studied than the more well-known familial form due to fewer reported cases and smaller prevalence. This case study presents a 30-year-old African American male with multiple episodes of acute lower extremity muscle weakness, tachycardia, and a history of heat intolerance. Abnormal findings on thyroid ultrasound coupled with increased thyroid related immunoglobulins led to a diagnosis of TPP related to exacerbation of newly-found Graves' disease. The case study will further discuss the importance of imaging in assessing the etiology of TPP with review of relevant literature.

Keywords: thyrotoxic periodic paralysis, thyrotoxicosis, hypokalemia, hypokalemic periodic paralysis, Graves' disease

INTRODUCTION

Thyrotoxic Periodic Paralysis (TPP) is a rare manifestation of thyrotoxicosis. It is one of the lesser common subsets of hypokalemic periodic paralysis (HPP), the more common subset being Familial Hypokalemic Periodic Paralysis (FHPP). HPP can be extremely dangerous for patients to develop, since episodes may potentially lead to fatal muscle weakness via involvement of respiratory muscles, or life-threatening cardiac arrhythmias in the setting of hypokalemia[1]. The prevalence of TPP in North America is stated to be 0.1-0.2%[2]. Majority of the cases are found in the Asian population, and are extremely rare in the African American patients. Thus, there is significant value in studying individual cases of TPP in the African American population, as there is sparse data on such a rare occurrence of an

already rare disease.

1. Potassium 1.6 (L) (3 5-5 0 mmol/L)
2. Phosphate 0.6 (L) (2 7-4 6 mg/d)
3. Magnesium 1.5 (L) (1 6-2 6 mg/dL)
4. TSH <0.01 (L) (0 27-4 20 u[IU]/mL)
5. Free T4 3.3 (H) (0 8-1 8 ng/dL)
6. Free T3 8.9 (H) (2 0-4 4 pg/mL)

THYROID STIMULATING IMMUNOGLOBULIN 409 (H (<140% [BASELINE]

Due to abnormalities of the thyroid panel, thyroid ultrasound was requested. A diffusely heterogeneous and enlarged thyroid gland was visualized on grayscale ultrasound, with markedly increased vascularity on color Doppler assessment.

DISCUSSION

Clinical Presentation:

TPP is a rare condition presenting with periodic episodes of muscle weakness in the setting of hypokalemia and hyperthyroidism. The muscle weakness usually starts in the lower extremities and the laboratory values show elevated free triiodothyronine or thyroxine levels. TPP can also present with nonspecific cramping, muscle pain, stiffness, and decreased deep tendon reflexes, with intermittent resolution of symptoms[3] . Concurrent symptoms of hyperthyroidism, such as palpitations, weight loss, tremor, and heat intolerance, may also be present[4] . Episodes may be precipitated by meals with high carbohydrates, alcohol, trauma, and stress[3,5] . Our patient's presentation aligns with the typical presentation of TPP described above, demonstrating periodic episodes of weakness (acute myopathy) in the lower extremities, signs of hyperthyroidism, and elevated free T3 and T4, all within the setting of hypokalemia. Ultrasound imaging confirmed clinical findings of hyperthyroidism via thyroid storm, noting enlarged heterogeneous thyroid gland with diffusely increased vascularity on color Doppler assessment. Graves' disease workup confirmed autoimmune activity behind hyperthyroidism.

Demographics:

TPP typically presents in Asian males around the 2nd to 5th decades and has a prevalence of 10% in Asian countries. The prevalence of TPP is about 0.1-0.2% in non-Asian populations[5,6] . In Japanese people, the

DRw8 subtype of the HLA gene complex increases their risk of developing periodic paralysis[7] . However, the same subtype found in the Caucasian population increases their risk for Graves' disease, but not necessarily periodic paralysis[8] . TPP seems to be primarily studied in Asian populations, but not so much in the Caucasian or African American patients[9] . The first couple cases of an African American patient presenting with TPP in literature were published in 1961 and 1984, the latter of which did not possess the above HLA subtype[10,11] . A report in 1994 describes that 4 cases have been reported within a 13 year period at the researchers' institution, implying that cases of TPP in the African American population may be underreported[12] . Since then, more cases of TPP in the African American population have been described, reporting similarly to the clinical presentation of TPP described above[13–18] , with an additional case being reported from native Africa as well[19] .

Differential Diagnoses:

FHPP and Myasthenic Syndromes constitute other potential muscular disorders that must be ruled out. FHPP is an autosomal dominant genetic disorder characteristic of mutations in ion channels of the skeletal muscle sarcolemma (such as the alpha1 subunit of the dihydropyridine-sensitive calcium channel and sodium channel SCN4A)[20] . FHPP age of onset is typically around the first two decades and frequency of attacks diminishes with age, meaning FHPP is likely to present at a younger age than TPP[21] . Myasthenic Syndromes, such as myasthenia gravis and Lambert Eaton myasthenic syndrome, are autoimmune disorders that affect the neuromuscular junction causing progressive muscle weakness in various muscle groups such as proximal limbs[22] . Myasthenia gravis is becoming increasingly common in the elderly, men being more likely to be diagnosed after the age of 50, and Lambert Eaton myasthenic syndrome usually presents over 40 years of age[22,23] . Both of these myasthenic syndromes tend to present later in life than TPP.

Pathophysiology:

The pathophysiology behind TPP still remains unclear. The Na+/K+-ATPase pump is responsible for maintaining the transmembrane difference of potassium in cells. Both insulin and beta-adrenergic catecholamines are known to activate the function of the Na+/K+-ATPase pump[24] . Hyperthyroidism causes an increase in beta-adrenergic activity, which may activate the pump, driving potassium into cells and causing hypokalemia in the blood[25] . Thyroid hormones may also have direct activity on Na+/K+-ATPase pumps, which may increase activity and function of these pumps[26] . Having meals high in carbohydrates may also precipitate episodes of TPP due to an increase in insulin which activates Na+/K+-ATPase pumps[27] .

Imaging Features:

Ultrasound is the primary imaging modality used in assessing the thyroid. In a retrospective study with

patients diagnosed with TPP, the most common finding on ultrasound consisted of an enlarged thyroid gland, as demonstrated in our patient. This study consisted of 13 patients that had undergone sonographic imaging. Another sonographic finding in the majority of the patients was hyperechoic regions and decreased echogenicity of the thyroid. In the group of patients with decreased echogenicity, the patients' thyroids were either diffusely hypoechoic or had multiple areas of hypoechogenicity. The imaging features closely resemble Graves' disease, which the majority of the patients were already diagnosed with[28] . The thyroid will also be hyperemic on Doppler ultrasound[29] , as was seen in our presented case. The imaging appearance of TPP can vary depending on if there is an underlying hyperthyroid disease. For example, in a recent case study, a male patient with no relevant past medical history was diagnosed with TPP. A thyroid ultrasound of this patient showed multiple bilateral thyroid nodules[30] . TPP can be seen in various etiologies of hyperthyroidism, which can make its sonographic appearance quite variable at times.

Treatment:

Treatment in the setting of an acute attack includes general supportive care, potassium repletion, and nonselective beta blockade in the case of tachycardia or palpitations[3] . The patient should be monitored for rebound hyperkalemia after resolution of an acute attack. Treatment regimen should also work towards achieving a euthyroid state with options including antithyroid medications, radioactive iodine, or thyroidectomy in a patient with Graves' disease[3] . Definitive treatment of hyperthyroidism is noted to result in complete resolution of paralysis[13]. In the present case, the patient is prescribed propranolol and methimazole for prevention of further hyperthyroid attacks. The patient is currently doing well and follows up with endocrinology in the outpatient setting for management of his Graves' disease.

CONCLUSION

TPP is a rare manifestation of thyrotoxicosis that can be diagnosed through investigation of history of present illness, physical examination, laboratory values, and imaging. A history of multiple episodes of muscle weakness and concurrent tachycardia under a setting of hypokalemia and hyperthyroidism should raise a healthcare provider's index of suspicion for TPP. The use of grayscale ultrasound with color doppler can further confirm the etiology behind the hyperthyroidism, which may further support the diagnosis of TPP. Repletion of low potassium is shown to resolve an acute episode of TPP, and prevention of further hyperthyroid attacks via pharmacotherapy (such as propranolol and methimazole), radioactive iodine, or thyroidectomy can result in prevention of future episodes of paralysis secondary to TPP.

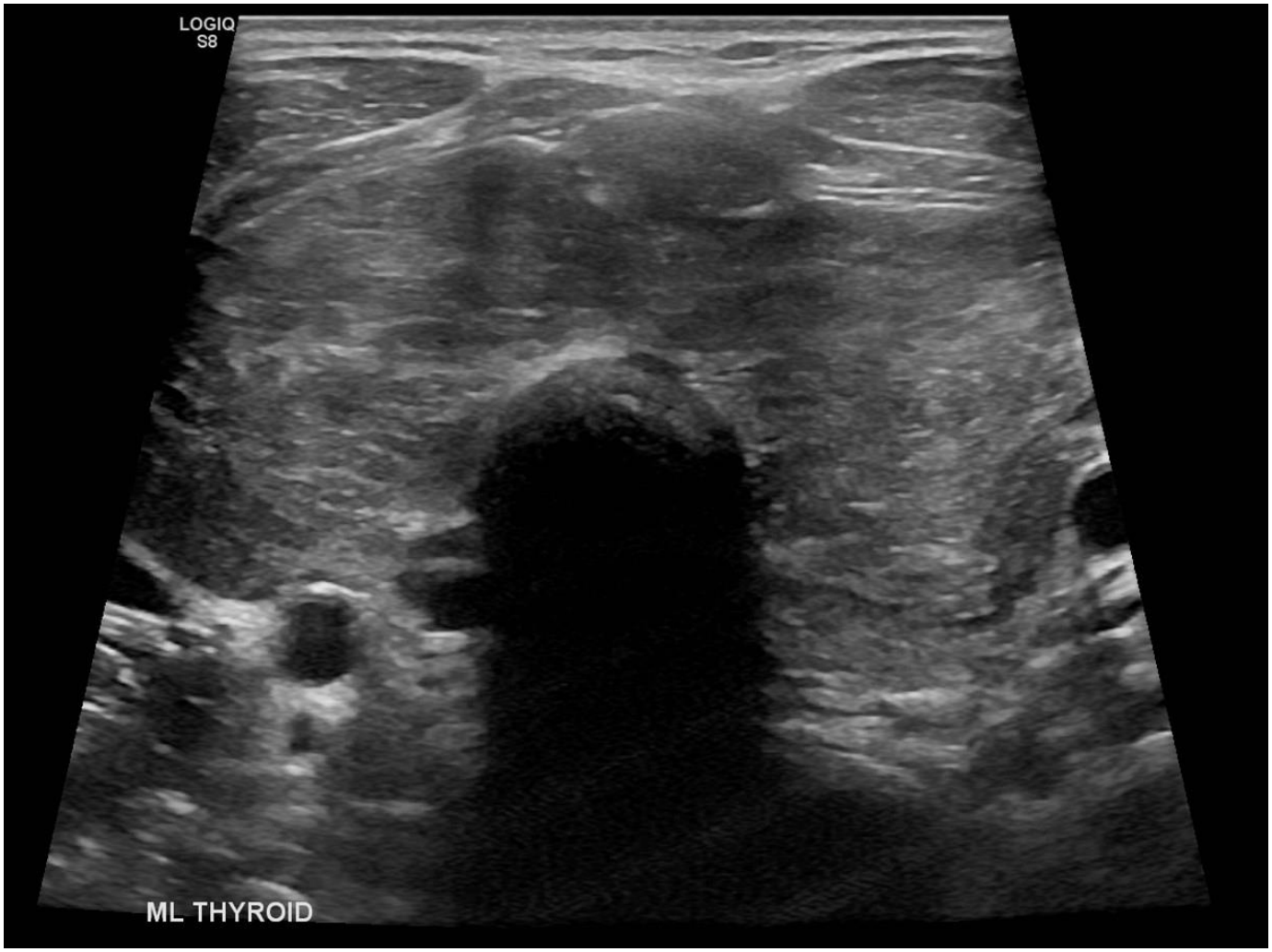

Figure 1 Transverse grayscale image of the thyroid gland at the level of the isthmus demonstrates diffuse enlargement and parenchymal heterogeneity of the entire gland, with overall increased echogenicity.

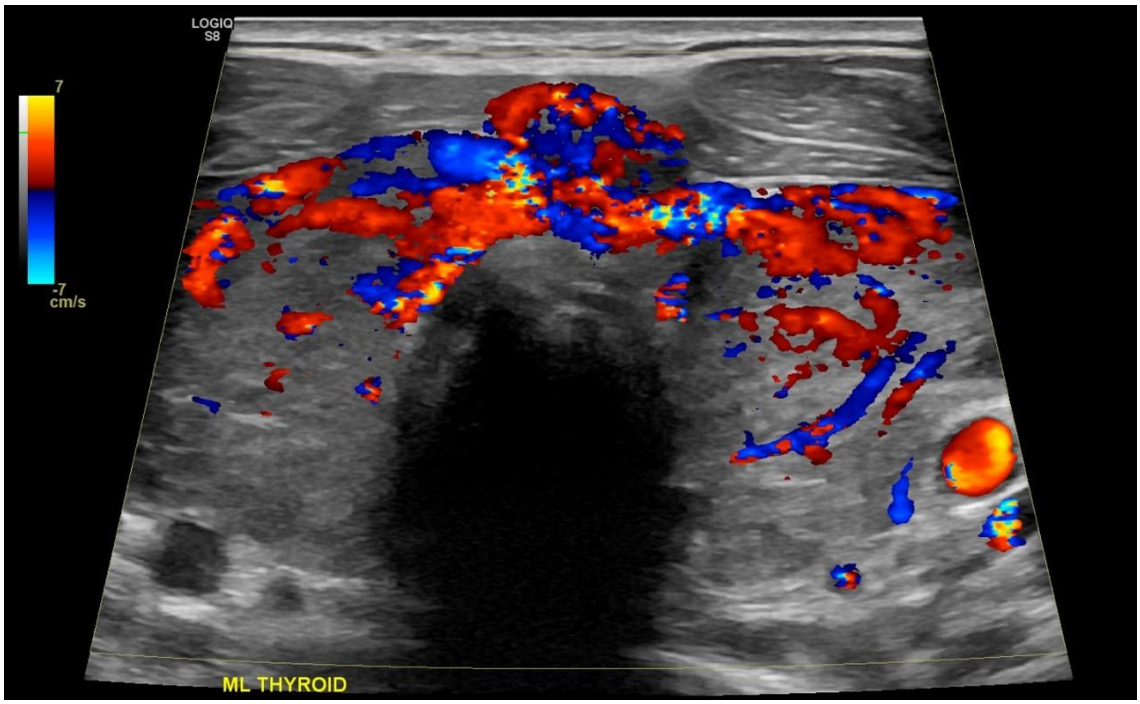

Figure 2

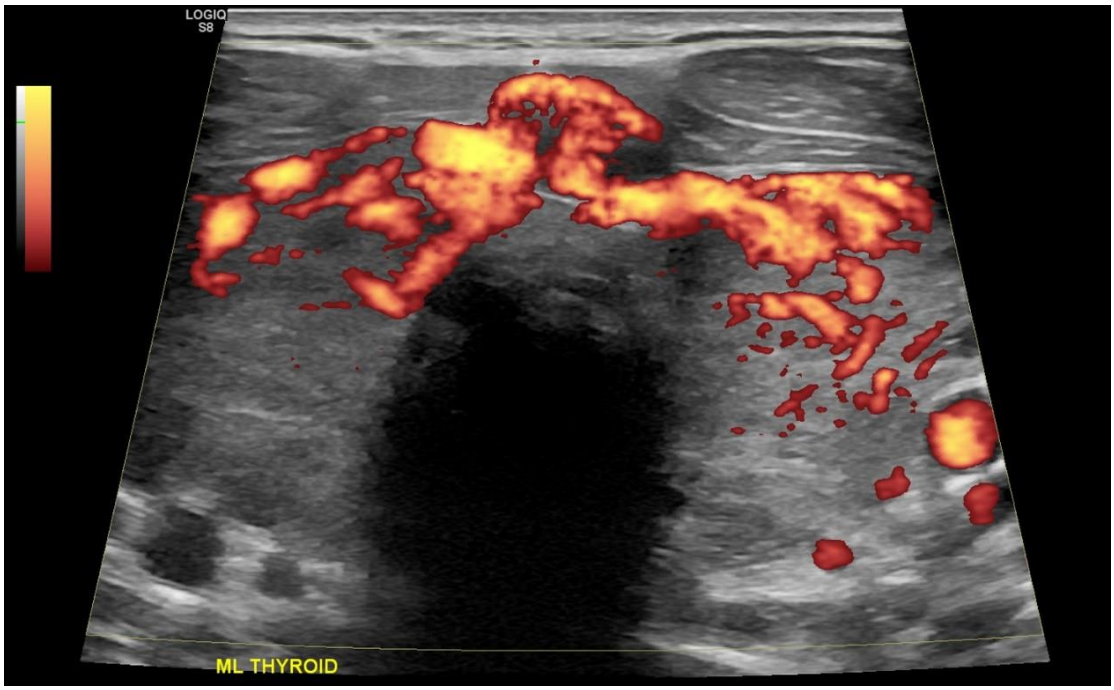

Figure 3 Transverse color (A) and power (B) doppler images of the thyroid gland at the level of the isthmus demonstrate diffusely increased vascularity.

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