WHAT IS YOUR DIAGNOSIS?

Hyperthyroidism, Myalgia, Rapidly Progressing Paralysis

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A 26-year-old Hispanic woman presented to the emergency department (ED) with myalgia and weakness. The work-up revealed profound hyperthyroidism, with a TSH < 0.01 mIU/mL (normal, 0.4-4.2 mIU/L), potassium 2.4 mEq/L (normal, 3.7-5.2 mEq/L), hypophosphatemia, and low urinary potassium. There were no prior symptoms, and family history was negative for endocrinopathies. She was admitted and started on methimazole (10 mg bid) for thyroid suppression and given propranolol (10 mg bid) for anticipated hyperadrenergic adverse effects. The remainder of her hospital stay was uneventful, and she was discharged six days after admission. Soon after, an outpatient thyroid scan ordered by her primary care provider confirmed that the patient had Graves disease.

Eight months later, the patient returned to the ED with myalgia and rapidly progressing paralysis from the neck down; she was immediately intubated. Her potassium level was 1.2 mEq/L. An ECG revealed conduction abnormalities consistent with hypokalemia.

THE DIAGNOSIS

Based on the patient's paralysis, hyperthyroidism, and hypokalemia, she was diagnosed with thyrotoxic hypokalemic periodic paralysis (THPP). This rare endocrinopathy causes electrolyte disturbances that can result in paralysis and lethal tachyarrhythmias.[1-6]

Patients with THPP typically have a history of myalgia, cramping, and stiffness followed by weakness or paralysis that tends to develop rapidly, most commonly in the late evening or early morning (see Table on page 24).[1-9] Proximal muscles are predominantly affected symmetrically, and the attacks usually resolve over a period of hours to several days. Ocular, bulbar, and respiratory muscles are usually spared, but these can be affected by the hypokalemia.[1]

DISCUSSION

Traditionally, THPP has been seen primarily in Asia, with an incidence as high as 2%.[1-6] The incidence in the United States is lower

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TABLE
Signs and symptoms of thyrotoxic hypokalemic periodic paralysis

History and physical exam
Minimal symptoms of hyperthyroidism
Mild tachycardia
Hypertension
Myalgia
Weakness and/or paralysis
Serum abnormalities
Low TSH
Increased T3 and T4
Hypokalemia
Hypophosphatemia
Hypercalciuria
Hypophosphaturia
Low potassium excretion
Normal acid-base status
Mild metabolic acidosis
Electrocardiographic abnormalities
Increased P-wave amplitude
Decreased T-wave amplitude
Prolonged PR interval
Widened QRS complex
U waves
Arrhythmias

(0.1%-0.2%), and THPP occurs primarily in Asian, African, Hispanic, and Native American populations.[1,4,6]

Although thyrotoxicosis is more common in women, THPP has a predilection for men (20:1).[1,3-6] THPP occurs in patients with hyperthyroidism, most commonly from Graves disease,[1,6] who are exposed to certain precipitating factors, such as exercise, carbohydrate loading, high-salt diet, excessive alcohol consumption, trauma, cold exposure, infection, menstruation, or emotional stress.[1,6] THPP can also occur in people taking medications such as corticosteroids, β_2-adrenergic bronchodilators, epinephrine, acetazolamide, insulin, NSAIDs, thyroxine, amiodarone, and tiratricol.[1,5,6] THPP is more common in the summer.[1]

A genetic basis for THPP. A Kir2.6 mutation results in a thyroid hormone-sensitive channelopathy involving the sodium-potassium-adenosine triphosphate (Na+,K+-ATPase) pump, which appears to be responsible for THPP.[1-6,8,9] This mutation should not be confused with the pathogenesis of familial periodic paralysis (FPP)—a hereditary disorder resulting in abnormalities in calcium, sodium, and potassium channels on skeletal muscle cells that leads to multiple electrolyte derangements and paralysis identical to that observed in THPP.[1]

Hypokalemia may be exacerbated by catecholamine-induced potassium shifts.[1,4,6] This is from the increased β_2-adrenergic stimulation from the concurrent hyperadrenergic state caused by the underlying hyperthyroidism.[1,4,6] Hyperinsulinemia from sympathetic stimulation of the insulin-releasing pancreatic beta cells also exacerbates hypokalemia.[1,4,6]

Focus treatment on correcting electrolytes

Initial evaluation of a patient suspected of having THPP should include a complete blood count, TSH measurement, serum and urine electrolyte tests, and an ECG. Further work-up, including ultrasound and scan of the thyroid upon confirmation of thyrotoxicosis and hypokalemia, may be required. Physical examination may reveal thyromegaly. Exophthalmos and other hyperthyroidism symptoms often are absent.[1]

Diagnosis confirmed? Treat the hypokalemia first. Acute management of THPP centers on electrolyte correction. Total body stores of potassium in patients with THPP are usually normal, so the clinician must use care to avoid excessive potassium administration.[1-5] Rebound hyperkalemia can occur in patients who receive > 90 mEq/L of potassium chloride within 24 hours.[1]

Definitive therapy may include antithyroid medication, radioactive iodine ablation (RIA), and/or thyroidectomy.[1-5] All have the common goal of controlling the hyperthyroidism and preventing recurrent paralysis, which occurs in 62.2% of patients within the first three months following diagnosis.[3] If antithyroid medications fail, then RIA is the next choice.[1] Beta-blockers work by decreasing the Na+,K+-ATPase activity from the underlying hyperadrenergic state.[1] Administration of acetazolamide—which

is the primary treatment modality for FPP and idiopathic periodic paralysis—can precipitate THPP attacks and is contraindicated.[1,5]

If medical management is unsuccessful or the patient develops compression symptoms, then thyroidectomy should be considered.[3] If the patient chooses thyroidectomy, medical optimization with antithyroid medications is indicated to mitigate the risks of anesthesia. When the thyroidectomy is performed by an experienced thyroid surgeon, the long-term results are excellent.

Case patient. Once this patient's hypokalemia was corrected, she was successfully extubated. Despite appropriate medical therapy, her hyperthyroidism was poorly controlled. The endocrinologist believed that RIA was suboptimal for three reasons: 1) it might result in incomplete ablation, 2) it required a long treatment period to be effective, and 3) its prolonged course of treatment extended the time interval that the patient would be at risk for recurrent paralysis.

A surgeon was consulted for definitive treatment with thyroidectomy. The patient's medications were changed to propylthiouracil (150 mg every 8 h) and propranolol (10 mg bid) until a euthyroid state was achieved and she could tolerate a general anesthetic without precipitating a thyroid storm. Two months later, she underwent total thyroidectomy without complication. Her postoperative course was normal.

THE TAKEAWAY

Thyrotoxic hypokalemic periodic paralysis is rare. Patients typically present with myalgia, cramping, and stiffness that progress to paralysis. Prompt electrolyte repletion is paramount for successful outcomes.[1-5] Control of hyperthyroidism is the long-term goal.[1-5] Definitive therapy can be achieved medically or surgically. Total thyroidectomy is a reasonable treatment option for medically refractory hyperthyroidism or when RIA is contraindicated. Long-term prognosis is excellent. **CR**

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