Hypokalemic Thyrotoxic Periodic Paralysis With Thyrotoxic Psychosis and Hypercapnic Respiratory Failure

Authors

Bushra Abbasi, MD, Zain Sharif, MD and Laurie R. Sprabery, MD

Editor

Fred A. Lopez, MD

Abstract: Thyrotoxic periodic paralysis is a rare and potentially lethal neuromuscular disease that manifests as recurrent episodic muscle weakness associated with hypokalemia and thyrotoxicosis. Paralysis can rarely involve respiratory muscles leading to acute respiratory failure. The disease primarily affects people of Asian descent, but it is being increasingly reported in other ethnic groups. We review the literature and report a case of hypokalemic thyrotoxic periodic paralysis manifesting as thyroid storm with episodic acute respiratory failure requiring recurrent intubation and eventually requiring thyroidectomy for resolution of symptoms.

Key Indexing Terms: Thyrotoxic periodic paralysis; Hypokalemia; Hyperthyroidism; Na K ATPase; Hyperinsulinemia. **[Am J Med Sci 2010;340(2):147–153.]**

Hypokalemic thyrotoxic periodic paralysis (TPP) is an acute reversible metabolic emergency that is characterized by a combination of muscle weakness, hypokalemia, and thyrotoxicosis. It mainly affects males of Asian descent; however, with the admixture of populations, it is being increasingly recognized in the Western countries. Hypokalemia mostly results from profound intracellular shift of potassium. The thyrotoxic symptoms are often subtle and therefore the disease often remains unrecognized during initial evaluation. Prompt potassium supplementation and beta blockers can prevent the poor cardiopulmonary outcome, which along with correction of the thyroid disorder can lead to early recovery of periodic paralysis and prevents recurrence.

CASE REPORT

A 27-year-old Korean man with no medical or surgical history was brought to the hospital with vague complains of anorexia, insomnia, muteness, and disinterest. All of his symptoms had begun since his wife left him and went back to Korea. According to the family, during the past 3 to 4 days, the patient had been behaving unlike his usual self and had been in a labile mood. In the emergency room, he was agitated, screaming loudly and incoherently. He was pulling out intravenous (IV) lines and was throwing things at the nurses. Review of symptoms was positive for a 10-lb weight loss and hallucinations. He did not have any allergies, and his social history was negative for any tobacco, alcohol, or illicit drug use. At the time of presentation, his vital signs were stable except for tachycardia of 140/min. On physical examination, he was agitated and combative. His mucous membranes were dry, and he had a mild thyromegaly. He was alert, awake, oriented to time, place, and person and had slightly increased deep tendon reflexes, with normal motor strength and sensations. Cranial nerves were intact bilaterally. Chest was clear to auscultation, cardiovascular system had a regular rate and rhythm, tachycardic, no murmur, rubs, or gallops. Abdomen was nontender and nondistended, bowel sounds were positive. His initial laboratory workup, including complete blood count, complete metabolic profile, erythrocyte sedimentation rate, C reactive protein, urine drug screen, alcohol, salicylate, and acetaminophen levels, was normal. Computed tomography of the head was negative, and electrocardiography showed sinus tachycardia. Initially, it was thought that he was suffering from some form of depressive psychosis. Overnight, his temperature increased to 104°F. He was tachycardic up to 160 seconds and became extremely combative requiring soft restraint for self-protection. A diagnosis of thyroid storm with thyroid psychosis was made because he had a Burch and Wartofsky[1] Thyroid Storm Criteria score of 75. The patient was transferred to the intensive care unit. Thyroid functions were sent, which revealed a markedly low thyroid-stimulating hormone (TSH) of <0.001 μcIU/mL (0.35–6.0 μcIU/mL), FT4 >5.6 ng/dL (0.9–1.8 ng/dL), and TT3 of 543 ng/dL (75–175 ng/dL). Radioactive iodine uptake demonstrated diffuse increased uptake in the thyroid gland consistent with Graves disease. Antithyroid peroxidase anti-

From the Department of Internal Medicine, University of Tennessee Health Science Center, Memphis, Tennessee.

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Correspondence: Bushra Abbasi, MD, Department of Internal Medicine, University of Tennessee Health Science Center, Memphis, TN (E-mail: bzabbasi@yahoo.com).

TABLE 1. Types of hypokalemic paralysis

HPP = Inc. K+ influx	Non-HPP = Inc. total body deficit
TPP	Bartter/Gitelman syndrome
FPP	RTA
	Primary hyperaldosteronism
	Vomiting/diarrhea/diuretic/liquor

Inc., increased.

bodies were increased to 1623 along with increased thyroid stimulating immunoglobulin/TSH receptor Ab. The patient at this time was started on propranolol, propylthiouracil, and potassium iodide. In the intensive care unit, he remained critical and had multiple episodes of severe persistent hypokalemia with hypercapnic respiratory failure and complete flaccid paralysis requiring recurrent emergent intubations. He remained hyperthyroid and hypokalemic with potassium between 2.2 and 2.8 mEq/L despite aggressive potassium replacement and antithyroid therapy. Because the patient started developing liver dysfunction with propylthiouracil, he was changed to methimazole. He was also continued on high-dose propranolol along with potassium iodide and corticosteroid for Graves disease. Because there was no response to this therapy and patient remained symptomatic, definitive treatment with total thyroidectomy was performed. After surgery, his methimazole and potassium iodide was discontinued and repeat TSH increased to 0.01 and FT4 came down to 1.4. He was successfully extubated, and his potassium improved to normal. He was placed on a maintenance dose of propranolol, corticosteroid, and synthroid. At the time of discharge, his TSH and FT4 had reverted to normal and remained normal on follow-up at posthospital discharge.

DISCUSSION

Hyperthyroidism refers to a disorder of accelerated synthesis and secretion of thyroid hormones from the thyroid gland. Thyrotoxicosis is a hypermetabolic clinical syndrome resulting from any cause of excessive serum thyroid hormone concentration. The thyroid storm is an extreme manifestation of thyrotoxicosis involving a severe systemic dysfunction of the thermoregulatory, central nervous, cardiovascular, and gastrointestinal systems. TPP is a rare thyroid disorder associated with thyrotoxicosis, which manifests as repeated episodes of hypokalemia and acute muscle weakness lasting hours to days.

TYPES

TPP is a well-established phenomenon.[2] In general, hypokalemic paralysis can be divided into 2 main groups: hypokalemic periodic paralysis (HPP) and the non-HPP. The HPP occurs due to an acute and massive shift of potassium into the cells, whereas the non-HPP occurs due to a large total body deficit.[3] According to cause, the HPP can be further grouped into the TPP and the familial periodic paralysis. Similarly, the non-HPP can be grouped into Bartter syndrome/Gitelman syndrome, renal tubular acidosis, primary hyperaldosteronism and secondary to excessive vomiting, diarrhea, diuretic or liqorice use (Table 1).[4–6]

EPIDEMIOLOGY

TPP is most widely known and studied in the Asian population, including Chinese, Japanese, Vietnamese, Filipino, and Koreans. Its incidence is 10-fold higher in this population compared with the whites.[4,7] Sporadic cases have been reported in the non-Asian populations, including the whites, Afro-Americans, and Hispanic.[8]

TABLE 2. Epidemiology

Asians: Chinese, Japanese, Vietnamese, and Korean
Male > female, 17:1 to 70:1
80% between 20 and 39 yr

Despite the higher incidence of thyroid disease in women, this entity is far more common in men with a preponderance ratio of 17:1 to 70:1.[7,9,10] Approximately 80% of patients are between the ages of 20 to 39 years (Table 2).[4,9]

CLINICAL PRESENTATION

TPP is a rare neurologic manifestation of thyrotoxicosis. The neurologic manifestations of thyrotoxicosis are limited and rare. In many cases, they present in conjunction with the systemic features of the disease but may be the presenting symptoms in some patients.

The neurologic manifestations of thyrotoxicosis are as follows:

1. Cognitive impairment and seizures: cognitive impairment with behavioral and personality changes are common in hyperthyroidism. It is usually subacute but may progress to degenerative dementia over a protracted course.[11] A more fulminant course is seen when it presents as part of the spectrum of thyroid storm progressing from agitated delirium to somnolence and ultimate coma.[12] In elderly patients, the only manifestation maybe a less activated presentation with depression and lethargy called apathetic thyrotoxicosis.[13] Seizures occur as part of the encephalopathy of acute thyrotoxicosis with nonspecific electroencephalography findings of diffuse, slow, bitemporal sharp waves and polyspike slow wave discharges.
2. Movement disorders—*tremors*: tremors are common in thyrotoxicosis. Approximately 76% of all patients presenting with a new diagnosis of hyperthyroidism had tremors.[14] It is primarily seen on movement or action and resembles an exaggerated physiologic tremor. It is treated with betablockers, which suggests its origin secondary to the hyperadrenergic state of thyrotoxicosis.[14] *Chorea*: chorea is a rare complication of hyperthyroidism, occurring in only 2% of the patients.[15] It may be unilateral, bilateral, or multifocal but mostly involves the extremities and spares the trunk. It is thought to occur secondary to a direct effect of thyrotoxicosis on the central nervous system but may also be induced by hyperthyroidism from increased sensitivity of dopamine receptors. It improves or resolves with correction of thyroid hormones.[15,16]
3. Stroke: ischemic stroke is a rare complication of hyperthyroidism except in cases of cardiogenic embolism in patients with hyperthyroid-induced atrial fibrillation (AF). AF occurs in 10% to 15% of hyperthyroidism patients; however, thyrotoxicosis causes <1% of AF cases.[17] Some studies suggest that stroke in the setting of thyrotoxic AF is more frequent than in nonthyrotoxic AF.[18–20]
4. Cerebral venous sinus thrombosis (CVT): CVT is a rare thrombotic cerebrovascular disorder with high morbidity and mortality. The mechanism of CVT association with