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CLINICAL VIGNETTE

A Unique Presentation of Thyrotoxic Hypokalemic Periodic Paralysis

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Case Report

A 37-year-old Hispanic female, with no significant past medical history, presented with an abrupt onset of lower extremity weakness. Upon awakening at 2:30 am she attempted to get out of bed and found that she could not move her legs. She denied respiratory or swallowing difficulties or weakness in her upper extremities. She presented to the Emergency Department and was noted to have 3/5 strength in her bilateral lower extremities. Patellar reflexes were reported to be 3+ bilaterally. The rest of her physical exam was unremarkable. Laboratory tests were notable for hypokalemia with a potassium level of 2.9 mmol/L (normal 3.5 – 5 mmol/L). The rest of her laboratory studies as well as an electrocardiogram, non-contrast CT scan of the head, chest x-ray, and lumbar spine MRI were unremarkable. After repletion of her potassium, her symptoms resolved, and she was discharged with a diagnosis of hypokalemic periodic paralysis.

The patient was seen in follow-up two weeks later and her symptoms of weakness had resolved. However, she was complaining of persistent numbness in both legs. She had increased her dietary potassium intake, and a potassium level drawn on that day was 4.1 mmol/L. The patient was reassured and given another follow-up in two weeks for another repeat chemistry.

She instead returned one week later complaining of a burning sensation in bilateral legs and a shuffling gait. She had hyperreflexic patellar reflexes (3+) and diminished ankle reflexes (1+). Both lower extremities had intact sensation but were tender to palpation. Her gait was described as a "spastic shuffling gait". A chemistry panel was normal, including a potassium level of 3.8 mmol/L. A thyroid stimulating hormone level was drawn and returned at 0.01 (0.34 - 5.60 IU/mL). She was diagnosed with hyperthyroidism, started on propylthiouracil (PTU) and given a follow up appointment in the Endocrinology Clinic.

One month later in Endocrinology Clinic, the patient's symptoms of weakness and leg pain were improving. Her TSH was of 0.26 (0.34 – 5.60 uIU/mL), and the plan was to continue with PTU with plans for radioactive iodine for definitive treatment.

Discussion

Epidemiology

Hypokalemic periodic paralysis due to thyrotoxicosis is a complication seen frequently in Asian populations. Incidences of periodic paralysis in Chinese and Japanese thyrotoxic patients have been reported as 1.8 and 1.9%, respectively[1] . Sporadic cases have been reported in non-Asian populations, such as Caucasians, Afro-Americans, American Indians, and Hispanics. The incidence in Western countries is unknown but the number of cases reported has increased. In the United States, the incidence has been reported in non-Asian populations to be approximately 0.1-0.2% that of Asian countries[2,3].

Interestingly, even though there is a higher incidence of thyrotoxicosis in women, thyrotoxic periodic paralysis predominantly affects males. Overall, the male to female ratio ranges from 17:1 to 70:1.

Clinical Features

Thyrotoxic periodic paralysis typically presents in the young male, 20-40 years of age. The attacks usually are recurrent episodes of muscle weakness that range from mild weakness to complete flaccid paralysis. They generally first involve the lower limbs, progress to the girdle, then to the upper limbs. The involvement can be asymmetrical. The episodes of weakness can last from a few hours to 72 hours. There is usually complete recovery in between the attacks. Prodromal symptoms of muscle aches, cramps and stiffness of affected muscles may be experienced[1].

The episodes of muscle weakness or paralysis, commonly referred to as "attacks" usually occur a few hours after a large meal or in the early morning hours upon awakening. More than two thirds of

patients present to the emergency room between the hours of 21:00 and 09:00[1]. The attacks can also be precipitated by carbohydrate-rich meals, sweet snacks, alcohol, or strenuous exercise. Attacks usually do not occur during the exercise period itself but are noted shortly after the exercise routine is completed.

Pathogenesis/Biochemical Features

The hallmark hypokalemia that is seen in thyrotoxic periodic paralysis is the result of a rapid and large shift of potassium from the extracellular into the intracellular compartment of muscles. It is important to keep in mind that it is a shift of potassium and not a true loss of potassium when acutely treating patients. The shift in potassium is due to an increased sodium-potassium-adenosine tripohosphate (Na/K-ATPase) pump activity. In hyperthyroid patients, the thyroid hormone increases Na/K-ATPase activity, which results in an intracellular shift of potassium in skeletal muscle, liver, and kidney. In addition to thyroid hormones, catecholamines and insulin have also been found to increase pump activity. This insulin response would explain the association between large, carbohydrate meals, sweet snacks and periodic paralysis. Thyrotoxicosis produces a B-adrenergic response that also increases pump activity. This would explain why B-adrenergic blockers can abort or prevent paralytic attacks. Finally, exercise increases release of potassium and rest promotes an influx of potassium. This is why attacks of paralysis occur after exercise and not during exercise.

Because patients with thyrotoxic periodic paralysis have an increased activation of Na/K-ATPase activity, numerous studies looking at genetic predispositions have been performed. However, no clear association or genetic predisposition has been found.

Treatment

Treatment of periodic paralysis involves immediate supplementation with potassium. However, care should be taken to avoid excessive supplementation as rebound hyperkalemia can occur during recovery once the potassium has shifted back out into the intravascular space. Therefore supplementation should be given at a slow rate (unless there are cardiopulmonary complications). Potassium chloride (KCl) can be given orally, 2 g every 2 hours or intravenously, 10 mEq/h[1]. In addition, potassium supplements should not be given for prophylaxis or in between attacks.

Nonspecific B-adrenergic blockers, such as propranolol, have also been proposed as possible alternative immediate treatment options. Three case studies have shown that β-blockade rapidly reversed paralysis in patients who did not respond to oral potassium replacement. Additional case reports also demonstrated that in two-thirds of cases, propranolol at 40 mg four times a day prevented recurrent paralytic attacks in carbohydrate-induced paralysis. However, given the small number of case reports, more studies are needed to determine the treatment efficacy with propranolol.

Until definitive treatment is obtained, patients should avoid precipitating factors to prevent recurrent attacks. This includes avoiding heavy carbohydrate meals, high salt, alcohol, and undue exertion. In addition, propranolol 20 to 80 mg orally three times a day should be given to prevent recurrent attacks of paralysis. This can be administered in addition to antithyroid drugs or after radioactive iodine when the patient is not yet euthryoid.

Definitive treatment for patients with hyper-thyroidism due to Grave's disease, multinodular goiter, or toxic adenoma would be with radioactive iodine or thyroidectomy to control their underlying thryoid disease that is driving this condition.

Conclusion

Thyrotoxic periodic paralysis is usually seen in Asian males, with one case reported in a Hispanic male[4]. This case is unique in that it occurred in a Hispanic female without significant clinical signs or symptoms suggestive of a hyperthyroid state upon presentation. The diagnosis at initial presentation was delayed like most cases of thyrotoxic periodic paralysis because of the subtleness of the clinical features of thyrotoxicosis. Practitioners should consider obtaining a screening TSH in patients who present with hypokalemic periodic paralysis. This is a curable disorder that resolved when a euthryoid status was achieved.

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