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Research Article

THYROTOXIC PERIODIC PARALYSIS: A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

Thyrotoxic periodic paralysis is a rare disorder but it should always be considered in patients with acute paralysis and severe hypokalaemia. Although the diagnosis is a challenge to clinicians, periodic paralysis must be differentiated from other causes of weakness and paralysis so that proper treatment can be initiated as soon as possible. We are presenting a 46 year old male patient with history of Graves's disease who presented with sudden onset muscle paralysis. Patient was on propranolol and carbimazole medication regularly and showed both tachycardia and hypertension. Neurological examination revealed flaccid paralysis of all extremities which involved the proximal and distal muscles. Sensation was intact but deep tendon reflexes were slightly diminished, ECG showed prolongation of PR interval and flattening of T wave. Haematological investigations showed marked hypokalaemia, low thyroid stimulating hormone level along with elevated triiodothyronine and thyroxine level. Iodine-123 thyroid scan demonstrated an asymmetric enlargement of left lobe thyroid gland with significantly increase in uptake at 2 and 24 hrs. The patient's condition improved dramatically after intravenous potassium supplementation. So he was diagnosed to be suffering from thyrotoxic periodic paralysis. It is a rare condition in non-Asians and diagnosis at initial presentation is often delayed because of the subtleness of the clinical features of thyrotoxicosis and similarities of the paralysis with other more common conditions. Early diagnosis prevents serious cardiopulmonary complications. Thyrotoxic periodic paralysis is a curable disorder that resolves when euthyroid status is achieved.

CASES

A 46 year old male patient with history of Graves's disease for past 1 year (on propranolol and carbimazole medication regularly) presented in emergency room with sudden onset muscle paralysis. Patient was absolutely well three days back before this presentation. Suddenly at evening he was unable to move his upper and lower extremities. The weakness was bilateral and involved both the proximal muscle of shoulder and hips as well as distal extremities. He had no respiratory and swallowing difficulty and was able to move his facial and neck muscles. There were no pains or paresthesia. Prior to this episode the patient was healthy and denied any recent history of diarrhoea, chest pain, shortness of breath, weight change. He also denied use of alcohol or other drugs or significant change in diet or activity level but he suddenly stopped his medication for Graves's disease 10 days prior to this incident. There was no other family history of similar episodes and no other significant illness. Bladder or bowel involvement was not there. On physical examination, the patient's heart rate was 140/minute; blood pressure was 180/86 mmHg. His built was normal, skin was cool and dry, oral mucosa was moist. No jugular venous distension, goiter or

lymphadenopathy was appreciated. Cardiac examination revealed tachycardia with regular rhythm and no murmur. Examination of lung and abdomen was unremarkable. There was no deformity or edema of the extremities and distal pulses was presents and was equal bilaterally. Neurological examination revealed flaccid paralysis of all extremities which involved the proximal and distal muscles. Sensation was intact but deep tendon reflexes were slightly diminished. Cranial nerve function was intact.

Routine chemistry, liver enzymes and complete blood count were normal except for a potassium level of 1.6(normal 3.5-5 mmol/L). ECG revealed prolongation of PR interval and flattening of T wave. Six hours after initiation of intravenous potassium replacement (total dose given 80 mmol) patient's neurologic symptoms had completely resolved. However his blood pressure remains elevated but ECG revealed normal sinus rhythm and rate.

Follow up studies were performed to determine the etiology of hypokalaemia. Urine sodium and potassium and serum aldosterone and renin levels were measured to rule out adrenal involvement and were found to be normal. Thyroid stimulating hormone(TSH), triiodothyronine(T3) and thyroxine(T4) levels were obtained and revealed a markedly abnormal TSH of 0.05 U/ml with elevated levels of T3 (260 ng/dl) and T4 (20.2 µg/dl). Iodine-123 thyroid scan subsequently demonstrated an asymmetric enlargement of left lobe thyroid gland with significantly increase in uptake at 2 and 24 hrs. Patient was a diagnosed case of Graves's disease on carbimazole for control of underlying hyperthyroidism and propranolol for control of blood pressure and tachycardia. Patient was discharged home with an advice to continue antihyperthyroid drug and bete blocker and to follow up with an endocrinologist.

DISCUSSION

Thyrotoxic periodic paralysis (TPP) is one of the causes of hypokalaemic paralysis (HP). HP is a condition characterized by muscle weakness associated with changes in potassium levels. This hypokalaemia can occur either due to transient shifts of potassium intracellularly (hypokaelemic periodic paralysis or HPP) or reduction in absolute potassium levels in body (non hypokalemic periodic paralysis).

TPP occurs in the settings of hyperthyroidism. It is the most common form of hypokalaemic periodic paralysis and seen primarily in Asian males. The major feature distinguishing TPP from other periodic paralysis is the association of paralytic episodes with hyperthyroid state. Paralytic episodes can be induced in these patients by administrating insulin and glucose, but only when they are hyperthyroid. Euthyroid patients are typically free from spontaneous and induced attacks. The underlying mechanism is not known but it is thought to be different from that of familial hypokalaemic paralysis (FHP). Genetic abnormalities are felt to be responsible for FHP, but such have not been identified in patients with TPP. Acute paralytic episodes are treated with potassium replacement, prophylactic potassium or acetazolamide administration is not likely to benefit these patients since potassium level is normal between episodes and may result in dangerous hyperkalaemia. Beta blocking agents may prevent attacks but definitive treatment is correction of underlying thyrotoxicosis.

The mechanisms for acute muscle weakness in thyrotoxic periodic paralysis are that thyroid hormones can increase Na^+/K^+-ATPase activity in skeletal muscle, liver, and kidney to induce an influx of potassium into the intracellular space. Among the various Na^+/K^+-ATPase subunits the $alfa_1$, $alfa_2$, $beta_1$, $beta_2$ and $beta_4$ subunits are expressed in skeletal muscles and thyroid hormones has been shown to increase Na^+/K^+-ATPase activity in skeletal muscles. The enhanced beta adrenergic response in thyrotoxicosis

further increases Na^+/K^+-ATPase activity and may explain why nonselective beta adrenergic blockers can abort or prevent paralytic attacks. In addition to an increased adrenergic response, patients with TPP have an exaggerated insulin response during oral glucose challenge, compared with thyrotoxic patients without TPP. Insulin-response sequences are present in the upstream region of the Na^+/K^+-ATPase genes and insulin has been shown to stimutate Na^+/K^+-ATPase activity. Hence insulin can play a permissive role for the potassium shift in patients with TPP. The hyperinsulinemic response may explain the association of TPP with carbohydrate rich meals and sweet snacks. Exercise releases potassium from the skeletal muscles and rest promotes influx of potassium. This explains why paralytic attacks occur only during recovery from exercise and stoppage of exercise can abort an attack.

Diagnosis of TPP is based on clinical and biochemical evidence of hyperthyroidism and hypokalaemia in patients with history of recurrent episodes of proximal muscle weakness, affecting mainly the lower limbs without family history of this disorder. The severity of attacks varies from mild weakness to quadriplegia or total paralysis. Bulbar, respiratory and ocular muscles are rarely affected. In majority of patients deep tendon reflexes are markedly diminished or absent. Cognitive and sensory functions remain intact. Onset of paralytic attacks usually coincides with onset of hyperparathyroidism, although symptoms if present are mild. As this patient stopped taking all his drugs (carbimazole, propranolol) for last 10 days, hyperthyroidism state recurred and that lead to hypokalaemia. Some ECG features that can suggest a diagnosis of TPP is triad of sinus tachycardia attributable to the hyperadrenergic state, prolonged QT-U interval attributable to hypokalaemia and prolonged PR interval. A spot urine test for electrolytes and potassium excretion can be very useful. Normal acid base status and low urinary potassium levels are characteristics of hypokalaemia in TPP. Transient hypophosphataemia and hypomagnesemia is also documented alongside elevated creatinine phosphokinase. Some authors also suggested increased urinary calcium/phosphate ratio due to increased urinary calcium excretion as associated with thyrotoxicosis and hypophosphataemia for TPP may be rarely found.

As for treatment, during periodic paralysis and marked hypokalaemia immediate supplementation with potassium chloride (KCl) is warranted to prevent unwanted cardiopulmonary complications. KCl can be given in oral or intravenous form. Dose of KCl required varies between 40 and 200 mmol. Recovery time is shorter in those given IV KCl infusion than those given saline infusion alone. Excessive potassium replacement may result in rebound hyperkalaemia during recovery of paralysis when potassium is shifted back into the intra vascular compartment. Use of potassium supplements is not useful for prophylaxis against further paralytic attacks and should not be given in patient between attacks. Oral or IV propranolol, a nonspecific beta adrenergic blocker had also been proposed as an alternative treatment to ameliorate the paralysis without rebound hyperkalaemia. Three case reports have been reported that IV propranolol rapidly reversed the paralysis in patients with TPP who failed to respond to potassium replacement. Similarly high dose oral propranolol (3-4 mg/kg orally) alone has been reported to rapidly abort paralysis. Because TPP does not recur once the patient is euthyroid, adequate control of hyperthyroidism is the mainstay of therapy. The cause for the hyperthyroidism should be identified. Definitive treatment with radioactive iodine or thyroidectomy should be given to patients with hyperthyroidism due to Graves's disease, multi nodular goiter or toxic adenoma. Patient should avoid precipitating factors including heavy carbohydrate intake, alcohol ingestion, and undue exertion until thyrotoxicosis is under control. Acetazolamide and thyroxine, which have been reported to reduce the frequency of paralytic attacks in

FHPP and other forms of hypokalaemic periodic paralysis, may worsen the attacks in TPP and should be avoided.

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