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Thyrotoxic Periodic Paralysis as a Presentation of Thyrotoxicosis: A Case Report

Abstract

Thyrotoxic periodic paralysis (TPP) is a rare but potentially serious complication of hyperthyroidism characterized by muscular weakness and hypokalemia in a patient with thyrotoxicosis. It is predominantly seen in Asian males.The etiology of thyrotoxicosis in most of the cases of TPP is Graves' disease. We present a case of a 19-year-old male who presented in emergency with paraparesis. Investigations revealed hypokalemia and thyrotoxicosis related to toxic nodular goitre. Diagnosis of thyrotoxic periodic paralysis was made and patient was treated with potassium replacement, propranolol and antithyroid treatment.

Introduction

Periodic paralysis is a group of neuromuscular disorders of different etiologies characterized by paroxysmal, short-lasting hypo-reflexic skeletal muscle weakness of limbs without any sensory involvement and loss of consciousness. These disorders can be classified into familial or primary periodic paralysis and secondary periodic paralysis. Primary periodic paralysis is due to single-gene mutations leading to abnormalities of sodium, potassium, calcium and chloride channels on membranes of muscle cells. Hence, they are also called as channelopathies.[1] Secondary periodic paralysis may be due to known causes such as thyrotoxicosis, chronic renal failure, paramyotonia congenita or may be associated with the use of drugs like ACE inhibitors, angiotensin-II-receptor blockers or diuretics. The serum potassium levels are usually altered during attacks in both primary and secondary periodic paralysis which may be low, high or normal. In primary periodic paralysis the potassium levels are normal in between the attacks, whereas it may remain abnormal in secondary periodic paralysis in the inter-ictal period.[2] Primary hpokalemic periodic paralysis has been reported to be the commonest among all types of periodic paralysis. Thyrotoxic periodic paralysis (TPP) is the most common cause of secondary or acquired periodic paralysis.

Case Report

A 19-year-old male patient presented to the medical emergency with history of sudden onset of weakness of both lower limbs. As per the patient's history, he slept at night normally but on waking up in the morning he was not able to stand or walk. There was no history of preceding fever, vomiting, diarrhea, trauma or seizures. He was a nonsmoker and nonalcoholic. On examination, patient was conscious and oriented, his pulse rate was 104 beats/min and BP was 110/70 mmHg and rest of general physical examination was unremarkable. Systemic examination revealed power of 0/5 in all muscle groups in both the lower limbs and 3/5 in all muscle groups in upper limbs. Examination of other systems was normal. Routine investigations were normal except for the presence of severe hypokalemia with a serum potassium of 1.6 meq/L (normal range 3.5–5.0 meq/L), serum phosphorus level of 3.4 mg/dL (normal range 3–4.5 mg/dL) and mild hypomagnesemia with serum magnesium level of 1.5 mg/dL (normal range 1.8–3.0 mg/dL). ECG showed

hypokalemic changes with prolonged PR interval, increased P-wave amplitude and widened QRS complexes. He was managed with intravenous potassium infusion followed by oral potassium supplementation. He had complete recovery from weakness within 12 hours of starting the therapy.

After recovery his history was reviewed in detail which revealed symptoms of weight loss, increased appetite and intermittent palpitations since last 4 months. There was also a history of sudden death in family where his elder brother died 2 years back and his mother was on levothyroxine replacement therapy for primary hypothyroidism since last 5 years. Detailed examination revealed a multinodular goiter which was confirmed on ultrasonography. Thyroid function tests revealed Free T_4 of 55.3 pmol/L (normal range: 10–23 pmol/L), freeT_3 of 11.6 pmol/L (normal range: 2–7 pmol/L) and a TSH level of <0.15mIU/L (normal range: 0.5–4.7 mIU/L). Radioactive iodine uptake scan showed a toxic nodule (increased iodine uptake in the nodule). There was no exophthalmos, sensory or cranial nerve deficits. He was managed with oral potassium supplements and propranolol. The patient showed dramatic improvement of his symptoms. The patient was discharged on tablet Carbimazole 10 mg three times a day, with the dose being monitored based on FT_4 level regularly. His final diagnosis was thyrotoxic periodic paralysis secondary to toxic nodular goiter. His thyroid function tests returned to normal after 6 weeks of antithyroid therapy. Potassium supplements and propranolol were stopped after 2 weeks of discharge and antithyroid therapy was continued. His potassium levels have been maintained within normal limits since then and there has been no further episode of weakness.

Discussion

TPP is a rare syndrome characterized by muscular weakness and paralysis associated with hypokalemia in a predisposed patient with thyrotoxicosis.[3] TPP can occur in any ethnicity but majority of cases are seen in Asian males, in the age group of 20–40 years.[4,5] Although hyperthyroidism is more common in females, TPP is seen more commonly in males with a male-to-female ratio of 20:1 or higher.[6] The incidence of TPP is approximately 2% in patients with thyrotoxicosis of any cause.[7] In an Indian study on 30 cases of hypokalemic periodic paralysis, thyrotoxicosis was found in 16.7% of all cases.[8] Although TPP is most commonly seen in Graves' disease, it can occur with thyrotoxicosis of any cause and it is not related to severity or duration of thyrotoxicosis.[7] The etiology of thyrotoxicosis in our case was toxic nodular goitre.

Precipitating factors of TPP include high carbohydrate diet, rest after strenuous exercise, cold exposure, infection, alcohol and emotional stress. Weakness in majority of cases develop at night or early morning.[4] There is also a seasonal predilection for patients of TPP to develop the crisis in warmer months.[4,7] TPP most commonly presents in third to fourth decade of life as rapid onset, transient, symmetrical muscular weakness associated with hypokalemia. The lower limbs are predominantly affected but it can involve all four limbs. Proximal muscle groups are more severely affected than the distal muscle groups in the limbs.[9,10] The paralysis is reversible with correction of hypokalemic and hyperthyroid state; however, the condition is potentially life-threatening as severe hypokalemia can result into arrhythmia and respiratory failure may ensue due to bulbar and diaphragmatic weakness.

The pathogenesis of periodic paralysis in TPP is not clear yet. Transcellular distribution of potassium is maintained by the Na+/K+– ATPase activity in the cell membrane, and it is mainly influenced by the action of insulin and beta-adrenergic catecholamines.[11] Hypokalemia in TPP is thought to result from an intracellular shift of potassium and not total body depletion. It has been shown that the Na^+/K^+ ATPase activity in platelets and muscles is significantly higher in patients with TPP.[12] Hyperthyroidism results in a hyper-adrenergic state, which may lead to the activation of the Na^+/K^+ ATPase pump which results in increased cellular uptake of potassium.[5,11] Thyroid hormones especially T_3 may also directly stimulate Na^+/K^+ ATPase activity and increase the number and sensitivity of beta receptors.[11,13] Cases of TPP associated with normal K level have also been seen, which indicates the role of some factors other than hypokalemia. Treatment of these patients with beta blockers and antithyroid drugs without potassium replacement prevents further attacks in TPP indicating the involvement of thyroid hormones in the pathogenesis of TPP.[10,14,15] Patients with TPP have also been found to have hyperinsulinemia during episodes of paralysis and increased basal insulin levels in between the attacks, which may be secondary to the hyper-adrenergic state related to hyperthyroidism.[16] This may explain the attacks occurring after high-carbohydrate meals. However, weakness in TPP cannot be fully explained by these mechanisms as TPP occurs only in minority of patients with hyperthyroidism. Thus, additional factors, like genetic predisposition are presumed to contribute and may also explain the racial difference in prevalence of this condition. Few genetic mutations in the K channel gene ($KCNE_3$) and several gene polymorphisms have been reported in literature.[3] A new gene KCNJ18 has

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been identified which is located on 17p11.1-2 encodes an inwardly rectifying potassium channel (Kir2.6). Kir2.6 mutations have been found in 33% of patients with TPP and are thought to be leading to hypokalemia by interfering with assembly of K channel.[17] The diurnal variation in potassium movement where there is nocturnal potassium influx into skeletal muscle would explain the tendency for thyrotoxic periodic paralysis to occur at night.[18]

Hypokalemia is the most common electrolyte abnormality seen during an acute crisis. Besides hypokalemia, hypophosphatemia and hypomagnesemia are also known to occur in association with thyrotoxic periodic paralysis. The correction of hypophosphatemia without phosphate administration supports the possibility of intracellular shift of phosphate. The most common arrhythmias in TPP are sinus tachycardia, atrial flutter, atrial fibrillation, extrasystoles and paroxysmal supraventricular tachycardia. Electrocardiographic findings are supportive of a diagnosis of TPP rather than sporadic or familial periodic paralysis are sinus tachycardia, elevated QRS voltage and first-degree AV block (sensitivity 97%, specificity 65%). In addition to ST-segment depression, T-wave flattening or inversion and the presence of U waves are typical of hypokalemia.[19]

The management of TPP includes treatment of acute attack as well as treatment of the underlying condition to prevent future attacks. The paralytic symptoms and signs improve as potassium returns from intracellular space back into the extracellular space.[6] Rapid administration of oral or intravenous potassium chloride can abort an attack and prevent cardiovascular and respiratory complications.[5] A lower dose of potassium is the treatment of choice for facilitating recovery and reducing rebound hyperkalemia due to release of potassium and phosphate from the cells on recovery.[3] Rebound hyperkalemia occurred in approximately 40% of patients with TPP, especially if they received >90 mmol of potassium chloride within the first 24 hours. Additionally, propranolol, a nonselective blocker, which prevents the intracellular shift of potassium and phosphate by blunting the hyperadrenergic stimulation of Na^+/K^+ ATPase, should be given as an adjunct for the remission of the acute crisis and prevention of recurrences till euthyroid state is established.[20] The definitive therapy forTPP includes treatment of hyperthyroidism with antithyroid medications, surgical thyroidectomy, or radioiodine therapy.[21]

TPP is a serious complication of thyrotoxicosis. It is the commonest secondary cause of hypokalemic periodic paralysis. This diagnosis must be considered in all cases presenting with hypokalemic periodic paralysis as it responds well to treatment and early diagnosis can prevent potentially lethal complications of thyrotoxicosis.

Conflict of Interest: None

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