*CASE REPORT*

# Thyrotoxic Periodic Paralysis

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## Abstract:

Periodic paralysis (PP) is a muscle disease in the family of diseases called channelopathies, manifested by episodes of painless muscle weakness. PP is classified as hypokalemic or hyperkalemic according to level of potassium ($K^+$ ). Most cases of PP are hereditary, but acquired cases of hypokalemic PP have been described in association with hyperthyroidism. We report a case of 48 years old female who presented to ER with one day history of sudden onset of bilateral lower limbs weakness. She gave history of transient episode of bilateral leg weakness one week earlier, recovered spontaneously. She is known case of DM for eight years but has no family history of muscle disorders. Her examination at time of presentation, showed – in addition to the lower limbs weakness-clinical features of thyrotoxicosis. According to her clinical presentation, laboratory findings and the evident data of known association of hypokalemic periodic paralysis (PP) and thyrotoxicosis, the patient was diagnosed as hyperthyroidism with hypokalemic periodic paralysis. The patient responded very well to emergency management of hypokalemia as well as the treatment of thytotoxicosis. Thyrotoxic periodic paralysis (TPP) is a rare but potentially serious complication of thyrotoxicosis resulting in temporary but severe muscle weakness, Prompt recognition of the problem allows for proper short- and long-term management of this condition.

## Introduction:

Thyrotoxic periodic paralysis (TPP) is one of the causes of hypokalemic paralysis (HP). HP is a condition characterized by muscle weakness associated with changes in potassium levels which can occur either due to transient shifts hypokalemic periodic paralysis (HPP) or reduction in absolute potassium levels (non-hypokaelmic periodic paralysis) [(1)]. The underlying cause of hyperthyroidism in the majority of TPP patients is Graves' disease. However, TPP can also be associated with thyroiditis (either spontaneous or induced by interferon therapy), toxic nodular goitre, toxic adenoma, thyroid-stimulating hormone (TSH)-secreting pituitary tumor, and even over dosage of thyroid hormone. [(1)] TPP is usually the early presentation of the underlying thyroid disease. TPP can also be a presenting feature of relapse of the disease. Paralysis only occurs when the patient is 3 thyrotoxic and not when euthyroid. [(2)] Thyrotoxic periodic paralysis (TPP) affects mainly Asian populations, in particular Chinese and Japanese, although isolated cases have also been reported in other ethnic groups such as white, Hispanic, African-American, and American Indian populations. [(1)] Here we report a case of Sudanese female presented with thyrotoxic periodic paralysis.

## Case report:

48 years old female, presented with one day history of sudden onset of bilateral lower limbs weakness to emergency room. The Bulbar, sensory, and bladder functions were unimpaired. No fever, headache or trauma. A transient episode of bilateral leg weakness had occurred one week earlier. She had history of fatigue palpitation and weight loss for three months. She was known to have type 2 DM for the last eight years and was treated with diet and Metformin 500 mg TID. Her diabetes was controlled without any micro or macrovasculor complication, She is married and a mother of two sons. No family history of muscle disorders and she denied using diuretics, laxatives, or recreational drugs.

On Examination; on presentation patient was looking unwell, her body mass index was 24Kg/m2, she was afebrile and her pulse rate was 116 beats/min, blood pressure of 130/70 mm Hg. Respiratory and abdominal examinations were normal. She showed grade 3 symmetrical global limb weakness with normal tone,

reflexes, 4 sensation, and cranial nerve function. She had no muscle tenderness, wasting, or fasciculation. Laboratory investigations showed Random Blood Suger 120mg/dl, Hb A1c 7.0%, sodium 137 mmol/L, potassium 2.4mmol/L, urea 24 mg/dl, creatinine 1.2mg/dl, calcium 9mg/d, ECG: showed sinus tachycardia.

Progress: At 1 PM she was seen at the consultant round and she was noted to have bilateral exophthalmos ,but no goiter was observed ,so thyroid functions test (TFT) were requested. The patient was started on iv potassium chloride for correction of her hypokalemea . Six hours later she recovered from her lower limbs weakness and her serum K was then 3. mmol/L . TFT result received two days later, revealed : Free thyroxin 60pmol/L (N 9-25), Thyroid stimulating hormone < 0.005 mIU/L (N 0.35-5.5) . She was started on carbimazole as 30 mg/day, discharged home and followed after one month at outpatient department (OPD), clear final diagnosis as Thyrotoxic Grave's disease with hypokalemic Periodic Paralysis was given in her discharge card. Two weeks later she presented to ER with a similar presentation and responded to IV KCl therapy as before.

OPD follow up; Patient became Euthyroid in two months time , however after two months from the initial presentation she developed a diffuse soft goiter. Patient was maintained at present on Carbimazole 10mg per/day.

## Discussion:

Thyrotoxic PP is a sporadic form of hypokalemic PP that may occur in association with hyperthyroidism.

In contrast to other forms of thyroid disease which are more common in women, thyrotoxic PP is much more frequently seen in males. Patients are usually between 20 and 40 years of age, similar to the age distribution for thyrotoxicosis. [(1)]

The mechanism by which hyperthyroidism can produce hypokalemic PP is not well understood Thyroid hormone increases tissue responsiveness to beta-adrenergic stimulation, which, along with thyroid hormone, increases sodium-potassium ATPase activity on the skeletal muscle membrane. This tends to drive potassium into cells, perhaps leading to hyperpolarization of the muscle membrane and relative inexcusability of the muscle fibers. Thyrotoxic patients with PP have been found to have higher sodium pump activity than those without

paralytic episodes. In this way, excess thyroid hormone may predispose to paralytic episodes by increasing the susceptibility to the hypokalemic action of epinephrine or insulin. Insulin resistance with compensatory hyperinsulinemia is suspected to have a role in the pathogenesis of thyrotoxic PP [(3)]. It is of interest to note that Na+,K+-ATPase activity is possibly increased by androgens and inhibited by oestrogens, and this may explain the male predilection for TPP [(4)]. TPP resembles familial hypokalaemic periodic paralysis, which is a channelopathy. A hypothesis surrounding this similarity recently led to the discovery of mutations of an inwardly rectifying potassium (Kir) channel Kir2.6. It is expressed in skeletal muscle and is transcriptionally regulated by thyroid hormone. The gene KCNJ18 was discovered to code for this Kir2.6 channel which promotes a greater influx of potassium into the cells. Kir2.6 mutations were discovered to be present in 25–33% of unrelated TPP patients in a recent study [(5)].

As with all the periodic paralyses, attacks of weakness occur suddenly with generalized weakness and preserved consciousness. Are characterized by transient recurrent episodes of muscle weakness involving proximal more than the distal muscles, with an initial involvement of the lower limbs and subsequently the truncal muscles, and finally all four limbs. The degree of weakness varies from mild weakness to total flaccid paralysis and hyporeflexia. Some patients may experience prodromal symptoms of aches, cramps, or stiffness in the affected muscles. Weakness usually affects skeletal muscles only. However, total paralysis of respiratory, bulbar, and ocular muscles has been reported in severe cases [(6)]. Cognitive and sensory functions remain normal. Recovery is usually complete, but the duration of paralysis can vary from a few hours in a mild attack to 36–72hour in a severe attack. Intervals of weeks to months are common, but some patients experience several attacks per week. The presentation of TPP may be confused with Guillain–Barré syndrome, acute spinal cord compression, myelitis, myasthenic crisis, botulism and hysteria. [(1)] Most commonly, the inciting event is either rest after strenuous physical activity, stress, or a high-carbohydrate load. [(7)] Other events reported to induce attacks in thyrotoxic PP include cold exposure, infection, alcohol intake, pulse corticosteroid therapy, and menses. In many instances, no obvious precipitant is identified. Although attacks of weakness may occur at any time of the day, a high frequency of attacks at night or early in the morning has been reported in thyrotoxic PP. A seasonal variation has also been suggested, with more frequent attacks in summer months diagnosis of TPP is

based on clinical and biochemical evidence of hyperthyroidism and hypokalemia in a patient with a history of recurrent episodes of proximal muscle weakness, affecting mainly the lower limbs, without a family history of this disorder. [8] Laboratory features; the degree of hypokalemia during an attack is variable; 2.1 mmol/L to 1.5 mmol/L. usually, the severity of weakness corresponds to the degree of hypokalemia. Patients with thyrotoxic PP, by definition, have attacks in the hyperthyroid state. Supporting laboratory findings include elevation of serum thyroxine (T4) and low thyrotropin levels (TSH). Patients with elevated T3 and normal T4 levels have been reported.

Other common laboratory findings include mild hypophosphatemia and hypomagnesemia. These findings may help distinguish thyrotoxic PP from familial hypokalemic PP. In one study, a urine calcium to phosphate ratio of higher than 1.7 was a sensitive and specific test to distinguishing thyrotoxic PP from familial hypokalemic PP. Creatine kinase may be normal but has been reported to be mildly elevated in two-thirds of patients, and rhabdomyolysis has been reported . Electrocardiogram changes are common in an attack of thyrotoxic PP, these include those findings consistent with hypokalemia: ST depression, sinus tachycardia, U waves, abnormal PR interval, higher QRS voltage, and first degree AV block. The latter ECG findings are more common in patients with thyrotoxic PP as compared to patients with familial hypokalemic PP. Severe arrhythmias (e.g, second degree atrioventricular block, ventricular fibrillation, and ventricular tachycardia) are not common but are described.[9,10] The results of electromyography, provocative testing, and muscle biopsy are similar to those seen in familial hypokalemic PP, but these tests are often unnecessary . Acute treatment; should include, potassium supplementation may lead to improvement of weakness.[11] As in our case and a retrospective case series, patients who received intravenous potassium recovered more quickly than those who received oral supplementation. There may be a delayed response of a few hours following potassium administration. Required doses of potassium supplementation are variable and range from 10 to 200mEq. Rebound hyperkalemia appears to be a prominent problem in thyrotoxic PP. Correction of hypomagnesemia if present is also recommended. Replacement of potassium may be insufficient to resolve an attack, propranolol has been reported to reverse weakness and hypokalemia in patients with thyrotoxic PP that is unresponsive to potassium administration. These patients received doses of 1mg of intravenous propranolol every 10 minutes

up to a maximum dose of 3mg. High dose oral propranolol (3-4 mg/kg) alone has been reported to rapidly abort the paralysis. [12]

## Conclusion:

In summary, episodes of periodic paralysis usually precede the diagnosis of thyroid dysfunction and do not recur once euthyroidism is achieved. Therefore, it is necessary that an early diagnosis of TPP is made to administer definitive treatment and prevent morbidity and mortality, mainly due to fatal arrhythmias. The presence of acute paralysis, especially with hypokalemia, should prompt the clinician to consider TPP as a cause and evaluate thyroid function.

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