



## Thyrotoxic periodic paralysis- A case report

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### Abstract:

**Background:** Thyrotoxic Periodic Paralysis (TPP) is a potentially lethal manifestation of hyperthyroidism, which is characterized by hypokalemia and muscular weakness due to intracellular shift of potassium. It is a rare complication of hyperthyroidism, which, in more than 90% of cases, is found in Asian populations with 10-24% prevalence in hyperthyroid patients. Although Graves' disease represents the most common cause, TPP can appear with hyperthyroidism of any origin. The combination of clinical features of hyperthyroidism with hypokalemia, hypophosphatemia, and normal arterial acid-base balance provides the best indication of TPP. The underlying hyperthyroidism may often be subtle, causing difficulty in early diagnosis.

**Case Report:** We describe a 42-year old male with no co-morbidities, who presented to our hospital with complaints of recurrent episodes of paraparesis. Finally, the patient was diagnosed as a case of thyrotoxic periodic paralysis even though patient had no symptoms of thyrotoxicosis. The patient responded dramatically to the administration of potassium supplements, beta blockers and anti-thyroid drugs.

**Conclusion:** All the patients with hypokalemic periodic paralysis should be investigated for thyrotoxicosis because management of thyrotoxicosis is essential to prevent further attacks of TPP. Absence of clinical features of thyrotoxicosis in TPP is common.

**Key words:** hypokalemia, periodic paralysis, thyrotoxicosis

### Introduction:

Acute muscle hypoasthenia has various causes and is sometimes of multi-factorial origin. If extreme weakness is associated with hypokalemia, the differential diagnosis is of hypokalemic paralysis.<sup>1</sup> The etiology of hypokalemic paralysis can be generally classified into two groups: hypokalemic periodic paralysis due to shift of potassium into the intracellular space without a total potassium deficit, and non-hypokalemic periodic paralysis due to a large potassium deficit via gastrointestinal or renal loss.<sup>2</sup>

Thyrotoxic periodic paralysis (TPP) is a potentially lethal manifestation of hyperthyroidism, which is characterized by hypokalemia and muscular weakness due to intracellular shift of potassium and subsequent hypokalemia.<sup>3</sup> Although Graves' disease represents the most common cause, TPP can appear with

hyperthyroidism of any origin: hyperfunctional multi-nodular goiter, TSH-secreting pituitary adenoma, subacute thyroiditis of de Quervain, Jod-Basedow disease, amiodarone therapy, an overdose of thyroid hormone, thyrotoxicosis factitia, and in one report, a single toxic adenoma.<sup>1</sup> Treatment with low-dose potassium supplements and non-selective beta-blockers should be initiated upon diagnosis, and the serum potassium level should be frequently monitored to prevent rebound hyperkalemia.<sup>2</sup>

The incidence of TPP in Chinese and Japanese thyrotoxic patients has been reported at 1.8% and 1.9%, respectively, whereas in North Americans at 0.1%-0.2%. In the Chinese, TPP occurs in 13% of male and 0.17% of female thyrotoxic patients, in a series published in 1967. The male to female ratio ranges from 17: 1 to 70: 1 despite the fact that hyperthyroidism is more common in females (female-to-

male ratio of 9: 1).<sup>2</sup>

We report the clinical and laboratory findings in a patient with TPP without associated symptoms of thyrotoxicosis.

### Case report:

A 42-year-old man of Asian descent after a heavy meal developed symptoms of bilateral lower limb weakness of sudden onset. He presented to the emergency department approximately within 2 hours of onset of symptoms. He had another similar episode 2 months back, symptoms lasted for almost 3 hours after which they subsided. There was no other associated history of sweating, palpitation, heat intolerance, weight loss, insomnia. No one in the family had history of similar complaints. Physical examination revealed paraparesis (Bilateral Grade 3/5) and bilateral hyporeflexia without thyromegaly or lymphadenopathy. Laboratory investigations revealed hypokalemia (K-2.5 mmol/L), altered thyroid function tests (TSH-0.005 mIU/ml, T3-2.17ng/ml, T4-13.36ug/dl) with normal serum magnesium levels, urinary potassium and acid base balance. ECG showed sinus tachycardia. The ultrasound revealed diffuse enlargement of the thyroid gland and increased vascularization and FNAC was suggestive of colloid goiter. Patient was started on potassium supplements I.V. and oral, along with Propranolol and anti-thyroid drugs (Tablet Carbimazole 10mg 1-1-1). Symptoms improved within the next 6 hours and he regained full power of both limbs the next morning. Serial monitoring of serum potassium showed stable values and patient was discharged after 2 days. The combination of clinical features of hyperthyroidism with hypokalemia, hypophosphatemia, and normal arterial acid-base balance provides the best indication of TPP. However, even when the patient has no clinical signs or symptoms suggestive of hyperthyroidism possibility of TPP should be considered as patients need not have features of

hyperthyroidism always.

### Discussion:

Thyrotoxic periodic paralysis (TPP) usually affects young Asian males in the age group of 20-40 years. A typical TPP attack is characterized by transient episodes of muscular weakness usually involving the lower limbs. High carbohydrate load is by far the most common precipitating factor for an attack of TPP in Indian population; high salt intake, trauma, strenuous exercise, exposure to cold and alcohol intake are some of other precipitating factors. Some drugs like diuretics, estrogens and laxatives may also precipitate the attack. A seasonal variation is observed with more frequent attacks occurring in summer months especially in tropical and subtropical climate regions. The seasonal variation may be due to increased outdoor activity and consumption of sweet drinks like sugarcane juice in summer.<sup>3</sup>

Neurological examination done at the time of attack usually demonstrates muscle weakness typically affecting the proximal muscles of the lower limbs and is usually symmetric.<sup>4</sup> Decreased muscle tone is the most common clinical finding. Deep tendon reflexes are markedly diminished.<sup>4</sup> Sometimes areflexia may also be present. Some patients experience recurrent episodes of weakness in between the episodes; patient usually has complete recovery.<sup>3</sup> Differential diagnosis of TPP includes familial hypokalemic periodic paralysis, Guillain-Barré syndrome and other causes of proximal myopathy (**Table I**).<sup>5</sup>

Various factors are involved in pathogenesis of TPP including genetic, environmental and acquired factors.<sup>4</sup> The genetic factors could include a defect in one of the ion channels involved in excitation-contraction coupling ( $\text{Ca}^{2+}$ ,  $\text{Na}^{+}$ , and  $\text{K}^{+}$ ) or a defect in one of the

**Table I: Differential diagnosis of Thyrotoxic periodic paralysis**

	<b>Thyrotoxic hypokalemic periodic paralysis (TPP)</b>	<b>Familial hypokalemic periodic paralysis (FPP)</b>	<b>Guillain-Barré syndrome</b>	<b>Proximal myopathy</b>
<b>Age of onset (years)</b>	20-45 (95%)	Before 16 (80%)	All	All
<b>Male to female ratio</b>	30:1	3:1	1.5:1	More common among men
<b>Family history of paralysis</b>	No	Yes	No	No
<b>Deep tendon reflexes</b>	Usually absent or depressed	Usually absent or depressed	Absent or depressed	Normal and often hyperactive
<b>Clinical course</b>	Remission when euthyroidism is reached	Chronic myopathy	Recovery; residual deficit in up to 20%; death in some patients	Weakness of proximal muscles that remits when euthyroidism is reached
<b>Duration of muscle symptoms</b>	30 min-6h	≥ 24h	Progressive over days to 4 weeks	Throughout thyrotoxic state
<b>Potassium level during the muscle symptoms (mmol/L)</b>	1.5-3.0	2.8-3.5	Normal	Normal
<b>Genetic inheritance</b>	Mutation in KCNJ18 gene in up to 33% of patients	Mutation in CACNIAS gene (80%) and SCN4A gene (15%)	None	None

channel's regulatory subunits ( $\beta$ ,  $\delta$ , or SUR).

Alterations in one of these genes would be responsible for the generation of non-functional ion channels, which would define the TPP as an endocrine channelopathy. The environmental factors include the excessive consumption of carbohydrate-rich foods, alcohol, or resting after intense exercise. Thyrotoxicosis would be the limiting factor and essential for the paralysis crisis.<sup>4</sup>

A traditional pathogenesis of TPP is associated with  $\text{Na}^+$ - $\text{K}^+$  ATPase activity. An increased  $\text{Na}^+$ - $\text{K}^+$  ATPase activity directly induced by thyroid hormone and indirectly induced by hyper-adrenergic

activity, hyperinsulinemia, and androgen is mostly involved.

Reduced  $\text{K}^+$  channel efflux in TPP: The enhanced  $\text{Na}^+$ - $\text{K}^+$  ATPase activity causes initial hypokalemia, and the reduced outward  $\text{K}^+$  current caused by hypokalemia, loss of function mutation, or hormone (adrenalin or insulin) -mediated inhibition on  $\text{K}^+$  channels can potentially inhibits total  $\text{K}^+$  efflux, leading to the trapping of  $\text{K}^+$  in the cell; a vicious cycle of hypokalemia-induced paradoxical depolarization and an inactivation of  $\text{Na}^+$  channel with muscle inexcitability and paralysis can result.<sup>6</sup>

The diagnosis of TPP is mainly based on biochemical parameters. Hypokalemia is the hallmark of TPP. This hypokalemia is

due to rapid shift of potassium into the cells from the extracellular space. Hypokalemia is not necessarily due to net loss potassium from the body. Sometime hypokalemia may be profound with serum potassium levels  $<3.0$  meq/L. Severe hypokalemia may be associated with life threatening ventricular arrhythmias.

Hypokalemia in TPP may also be associated with hypophosphatemia and hypomagnesemia. Both hypophosphatemia and hypomagnesemia are due to intracellular shift. TPP is also associated with increase in serum creatinine phosphokinase. The creatinine phosphokinase is of muscle origin.

ECG findings which are typical of hypokalemia includes increased amplitude of P waves, widening of QRS complexes, prolonged PR interval and appearance of U waves.

Electromyogram (EMG) performed during weakness at the time of acute attack reveals typical myopathic pattern. The amplitude of compound muscle action potential is markedly reduced. Nerve conduction studies are normal.<sup>3</sup>

The treatment of TPP has two main objectives: Immediate correction of hypokalemia and prevention of recurrent attacks. As patients with TPP have marked hypokalemia, immediate potassium replacement is warranted to prevent the life threatening arrhythmias. Depending on the general condition of the patient, potassium supplementation is given either orally or intravenously.<sup>2</sup> One prospective study compared treatment with intravenous potassium chloride to normal saline infusion and found a shorter recovery time with use of potassium (6.3 v/s. 13.5 hours).<sup>3</sup>

Immediate potassium supplementation is absolutely essential to prevent cardiopulmonary complications. Potassium chloride can be given intravenously or orally or both. The dose may vary between 50 and 200 mmol. The only caution with overzealous and excessive potassium replacement is the fear of developing

rebound hyperkalemia. Potassium supplementation should be done at a slow rate.

Potassium supplementation has no role in prevention of further paralytic attacks and therefore should not be prescribed to patients in between attacks. In a retrospective case series, patients who received intravenous potassium recovered more quickly than those who received oral supplementation.<sup>2</sup>

Non-selective beta blockers like propranolol can be given at the time of acute attacks and also to prevent recurrence. Propranolol can be given both orally and intravenously. Propranolol acts by decreasing the activity of Na/K-ATPase. It can be given in a dose of 20 -80 mg every eight hourly. Acetazolamide, which has been reported to decrease the frequency of paralytic attacks in FHPP, should never be given to patients with TPP as it may actually worsen the attack.<sup>2</sup>

Although glucocorticoids have been used to treat hyperthyroidism, they may also produce detrimental effects, including the development of TPP. A literature review revealed at least 2 cases of TPP induced by methylprednisolone and 2 cases caused by a single dose of prednisone.<sup>7</sup>

Prevention of recurrent attacks is by avoidance of precipitating factors such as

1. High carbohydrate diet
2. High salt intake
3. Stress: -Infection, Surgery, emotional stress
4. Hypothermia/cold
5. Undue exertion
6. Drugs: Diuretics, Acetazolamide, Estrogens, Corticosteroids

TPP does not occur once the patient has achieved euthyroid status, so adequate and definitive control of hyperthyroidism is the mainstay of treatment to prevent subsequent attacks.<sup>8</sup>

A Medline based review of TPP over 40 years, which analysed 281 primary articles and 168 references found that the features of hyperthyroidism are often subtle in patients with thyrotoxic periodic paralysis.

The review also notes that the recurrent episodes of paralysis remit with definitive control of hyperthyroidism.<sup>9</sup>

### Conclusion:

From the present case report, we conclude that all the patients with hypokalemic periodic paralysis should be investigated for thyrotoxicosis because absence of clinical features of thyrotoxicosis and subclinical hyperthyroidism in TPP is common. Management of thyrotoxicosis prevents attacks of thyrotoxic periodic paralysis.

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