Case Report

Early to recognize and Early to recover: A case series on Thyrotoxic periodic paralysis

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ABSTRACT

Thyrotoxic periodic paralysis (TPP) is a rare disease of muscle, presenting with sudden onset weakness of muscles with or without features of hyperthyroidism. The disease most commonly occurs in the Asian population representing about 1.9% of thyrotoxic patients. It involves a predominantly male population with no family history, with or without hypokalemia. Pathophysiology is still not clearly understood. We are describing, a case series of two different patients of TPP presented to our emergency department (ED). One patient presented with classical episodic weakness of both lower limbs specifically during the night times with spontaneous reversal of weakness early in the morning. Another patient presented with complete weakness of both lower limbs for the past 1 day. Both of them had a history of weight loss and intermittent palpitations. They were promptly diagnosed in the ED and successfully treated. We recommend evaluating thyroid function status in the emergency room with the aforementioned clinical features, as early recognition and correction of thyrotoxic state are the definitive treatment helping in a complete reversal of weakness. Potassium supplements, beta-blockers, and antithyroid medications are used in treating acute attacks and preventing recurrence.

Keywords: Familial periodic paralysis, Hyperthyroidism, Hypokalemia, Thyrotoxic periodic paralysis

Thyrotoxic periodic paralysis (TPP) is an uncommon manifestation of hyperthyroidism [1]. The disease is fairly common in Asian populations representing 1.9% of patients with hyperthyroidism but rarely reported in Caucasians and the Western world [2]. TPP is characterized by episodic muscle weakness, often involving lower limbs which may progress to the upper limbs and is associated with or without hypokalemia [3]. The episodes of muscle weakness resolve spontaneously within 24 h, without any residual paralysis.

Here, we present a case series of two cases among adult males. A male patient in the second to fourth decade of life with recurrent attacks of muscle weakness with or without signs of hyperthyroidism should raise the suspicion of TPP. As in most patients presenting with periodic muscle weakness of lower limbs, there were only mild or no signs of hyperthyroidism, TPP often becomes a missed diagnosis [4].

CASE SERIES

Case 1

A 40-year-old gentleman farmer by occupation with no previous medical history presented to our emergency department (ED) with complaints of both lower limb weakness for the past 12 h. He noticed weakness on waking up that morning which started distally in the legs and progressed up to the hip. He had recurrent episodes of muscle weakness of both lower limbs for the past 20 days more during nights which usually recover without any sequelae by the next morning. He remained asymptomatic in between the attacks. In addition to this, there was a history of weight loss of more than 10 kg in the past 3 months along with intermittent palpitations. There were no significant medical history and similar history in the family members. On physical examination, he was a healthy male with a thin build, regular pulses, and normal blood pressure. He was having fine tremors on stretching his hands. Neurologic examination revealed normal higher mental function, intact cranial nerves, with lower limb power grade 2/5 on both sides and upper limb with power 5/5. Both lower limbs had decreased deep tendon reflexes with intact sensations. Cardiovascular, pulmonary, and abdominal examinations were unremarkable.

In the emergency room, to rule out hypokalemia, immediate arterial blood gas analysis (ABG) was done which was suggestive of low normal potassium levels of 3.5mEq/L. An electrocardiogram (ECG) was suggestive of normal sinus rhythm. Evaluation of thyroid function status showed thyroid-stimulating hormone

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(TSH): <0.005 μU/ml (0.27–4.2 μU/ml); $T_{3:}$ 4.12 ng/ml (0.8–2 ng/ml); Total $T_{4:}$ 17.76 μg/dL (5.1–14.1 μg/dL); and Free $T_{4:}$ 5.01ng/ml (0.9-1.7ng/ml). History along with clinical features and the hyperthyroid picture was suggestive of TPP. The neurology team was involved and the patient was started on Propranolol 40 mg/day and Carbimazole 20 mg/day. The patient's lower limb power improved to 5/5 on day 2. He was discharged with normal lower limb power on day 3.

Case 2

A 30-year-old male entrepreneur with no previous medical history presented to our ED with complaints of the lower limb weakness for the past 1 day. He had a history of weight loss of around 8 kg in 1 month which was associated with intermittent palpitations. There was no significant family history of similar illnesses. On physical examination, he was a moderately built healthy male with normal vital signs. Neurologic examination revealed normal higher mental function with intact cranial nerves. He had a power grade of 0/5 on both lower limbs, with decreased deep tendon reflexes bilaterally and with intact sensations. His upper limb power was 5/5 with intact sensations and normal deep tendon reflexes. Cardiovascular, pulmonary, and abdominal examinations were unremarkable. History of lower limb weakness, weight loss, and intermittent palpitations in a healthy male patient with or without hypokalemia prompted us to perform thyroid function tests in the emergency room to rule out TPP.

Immediate ABG was done suggestive of low potassium levels of 1.84mEq/L. ECG was suggestive of prolonged QTc interval and U waves. Evaluation of thyroid function status revealed TSH: <0.005 μU/ml (0.27–4.2 μU/ml); $FT_{3:}$ 10.20 (1.8–5.6pg/ml); and Free $T_{4:}$ 5.69ng/ml (0.9–1.7ng/ml). With history and clinical features along with thyroid function status, the patient was diagnosed to have TPP. The neurology team was involved and started on Propranolol 40 mg/day and Carbimazole 15 mg/day. The patient was discharged on day 4 with normal lower limb power.

DISCUSSION

TPP is a rare presentation of hyperthyroidism [1]. The attacks are episodic, predominantly involving lower limbs more than the upper limbs with predominant involvement of proximal muscles. Sensory functions are preserved [5]. Weakness usually resolves within 24 h and the recovery of muscles is in the reverse order of paralysis, without any neurologic sequelae.

Comparable to our cases, Barahona *et al*. reported a case of a healthy male who is in his fourth decade and presented with episodic muscle weakness predominantly in the lower limbs for 2–3 months. Initial episodes were treated as hypokalemic periodic paralysis but later, found to have hyperthyroidism with symptoms of thyrotoxicosis. He was diagnosed as a case of TPP and treated with anti-thyroid medications with no further episodes of weakness on follow-up [4]. This reinforces evaluating thyroid function status in a young male presenting with the lower limb weakness to the emergency.

The biochemical abnormality observed during attacks is hypokalemia with normal total body potassium stores, as the abnormality is due to an intracellular shift of potassium rather than a loss. Other biochemical abnormalities seen are hypophosphatemia and hypomagnesemia [6]. Factors provoking the attacks of TPP are excess carbohydrate intake, strenuous physical activity, and catecholamine surge (as recurrent episodes are seen early in the morning) [7].

The pathophysiology behind TPP is not clearly understood, although the association between hypokalemia and paralysis may be attributable [1]. The potassium ion in the body is controlled mainly by two channels, the Na-K ATPase pump and inward rectifying potassium channels (Kir). Both these channels work together to control serum potassium levels. In these, the Na-K ATPase pump pumps potassium into the cells (influx), whereas Kir channels control potassium efflux from the cells [8]. Thyroid hormone levels alter the function of the Na-K ATPase activity at the plasma membrane (T4 more than T3) resulting in increased intracellular transport of potassium in hyperthyroidism (Fig. 1) [9,10]. Insulin also potentiates the activity of the Na-K ATPase pump, resulting in periodic paralysis with excess carbohydrate intake. Likewise, hyperthyroidism increases tissue responsiveness to beta-adrenergic stimulation, which is linked to enhanced Na-K ATPase activity [5]. In addition to catecholamine surge during the early morning, another feature contributing to periodic paralysis is potassium influx into skeletal muscles at night followed by exercise-induced potassium efflux during day time [11].

Diagnosis is mainly clinical when paralysis occurs with signs and symptoms of hyperthyroidism. The presentation is identical to familial periodic paralysis (FPP). FPP can be differentiated from TPP with positive family history and without hyperthyroidism, as both of them are predominantly seen in males. In addition, FPP is associated with a mutation in ionic channel genes such as CACNA1S, SCN4A, and KCNE3 [4]. Hypokalemic periodic paralysis is also seen in other metabolic disorders such as primary aldosteronism, Bartter or Gitelmann's syndrome, and renal tubular acidosis [12]. In TPP and FPP, hypokalemia and paralysis are due to intracellular shifts of potassium rather than an excessive renal excretion seen in metabolic disorders [13].

Management of TPP is focused on the treatment of acute attacks as well as definitive treatment. Acute episodes can be managed with potassium supplements by intravenous infusions in the setting of hypokalemia. It carries the risk of rebound

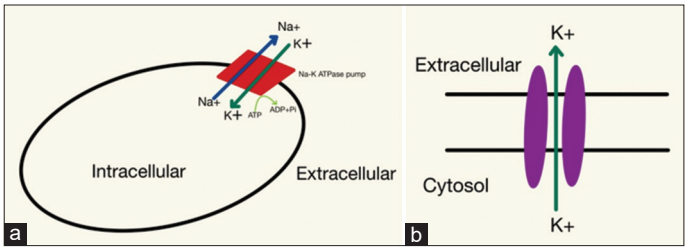

Figure 1: (a) Na-K ATPase pump depicting influx of potassium into the cell [9]; (b) Kir channel [10].

hyperkalemia during extracellular potassium shifts [14], as patients with TPP do not have an actual deficiency of potassium. Definitive treatment includes correction of hyperthyroid state and avoiding precipitating factors such as excess physical exertion, excess carbohydrate intake, and emotional stress. Beta-blockers are used to treat thyrotoxic state and to improve periodic paralysis by blocking the effect of catecholamines on ion channels [15]. Antithyroid medications such as methimazole, carbimazole, or propylthiouracil are used to decrease thyroid hormone production.

CONCLUSION

TPP is an acute painless weakness of muscles affecting the lower limbs predominantly. Commonly seen in Asian population with male predominance associated with features of hyperthyroidism. The absence of features of hyperthyroidism or previous similar episodes does not exclude the diagnosis. Early recognition and prompt treatment with beta-blockers and potassium supplements resulted in a complete reversal of weakness in the patients. Hence, it is important to consider evaluating thyroid function in male patients presenting to emergency room with acute painless muscle weakness with or without hypokalemia.

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