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CASE REPORT

Thyrotoxic periodic paralysis: A treatable cause of weakness

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Thyrotoxic periodic paralysis (TPP) is a rare disorder seen predominantly in adolescent Asian males. We report a patient who presented with sudden onset of progressive body weakness, associated with palpitations, and tremor. Biochemical investigations showed hypokalaemia, elevated free thyroxin (FT4) and suppressed thyroid-stimulating hormone (TSH) consistent with TPP. He was started on oral carbimazole, hypokalaemia was treated, and the body weakness resolved. It is important for clinicians to consider the diagnosis of TPP, in patients presenting with acute onset of weakness, as TPP is a treatable cause of paralysis, and delayed recognition could potentially lead to unnecessary interventions and even death

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INTRODUCTION

Thyrotoxic periodic paralysis is a rare disorder, which requires a high index of suspicion in patients who present with sudden onset of proximal muscle weakness of the limbs. Hypokalaemia in TPP results from an intracellular shift of potassium induced by the thyroid hormone sensitization of Na^+/K^+–ATPase pump of the skeletal muscles, and was first identified by Rosenfeld in 1902.[1] This disorder has been reported in different Asian countries. The presence of different HLA antigen subtypes such as DRw8, A2, Bw22, Aw19, B17, B5, and Bw46 has been observed in the Asian population making it more susceptible to TPP.[2]

Genetic mutations in the control of Na+, K+, adenosine triphosphatase (ATPase) activity, which controls the exchange of intracellular potassium with extracellular sodium within the same HLA antigen subtype has been described for the occurrence in different ethnic groups in the epidemiology of TPP.[3]

TPP is characterized by hypokalemia (< 3.0 mmol/L) with hyperthyroidism. Unrecognized TPP has been associated with complications such as arrhythmia and respiratory failure with fatal outcome.[3] Early diagnosis and prompt treatment could save life as it is a treatable-disorder.

CASE REPORT

A 29-year-old male presented to the Emergency Department complaining of progressive body weakness for 2 days. During initial presentation, he was still able to ambulate, however on admission, he was unable to move, walk and stand up. The weakness was sudden onset, and symmetrical, starting in the lower limb. He had palpitations and tremors of both hands as well. However, there was no history of excessive sweating, irritability, heat intolerance or weight loss, and no changes in skin and hair. On further questioning, he had similar episodes of body weakness that self-resolved over the past 2 months.

There was no history of trauma, fever, vomiting, loose stool and seizures. Patient also denied shortness of breath, abdominal pain, and other neurological symptoms. There was no history of alcohol intake and recent drug ingestion. There was no significant past illness and family history.

On examination, his blood pressure was 114/72 mm Hg, pulse rate was 90/min and respiratory rate 16/minute. Neck examination revealed diffuse thyroid enlargement, which was non tender, smooth and firm. There was no sign of ophthalmopathy. Neurological examination showed increased tone in the lower limb, 3/5 power on right side and 2/5 on the left side with normal reflexes. Power, tone and reflexes were normal for both upper limbs. There were no sensory deficits and the cranial nerves were intact. Systemic examination was normal. Electrocardiography showed prolonged QT interval.

In the Emergency department, his potassium level was 1.8 mmol/L. Intravenous (IV) potassium was started at 10 mEq/ hour and the potassium rose to 2.0 mmol/L. He was admitted to the medical ward for further treatment. His clinical presentation and laboratory abnormalities were consistent with TPP (Table 1). He was started on potassium chloride suspension 15ml TDS, Slow potassium tablets 1.2g TDS and Carbimazole 15 mg once daily. He was discharged on the fourth day with a potassium level of 3.8 mmol/L, and complete resolution of symptoms. He was advised for continued follow up and compliance to treatment.

Table 1 Laboratory investigation results

Variables	At presentation	Reference range
Potassium	1.8	3.5-5.0 mmol/L
Magnesium	0.79	0.77 – 1.03 mmol/L
Phosphate	0.96	0.81-1.58 mmol/L
Urine Spot Potassium	5.9	12- 62 mmol/L
Thyroid Stimulating Hormone (TSH)	<0.005	0.4 – 4.0 mIU/L
Free Thyroxine (FT4)	20.4	7.8 – 14 pmol/L

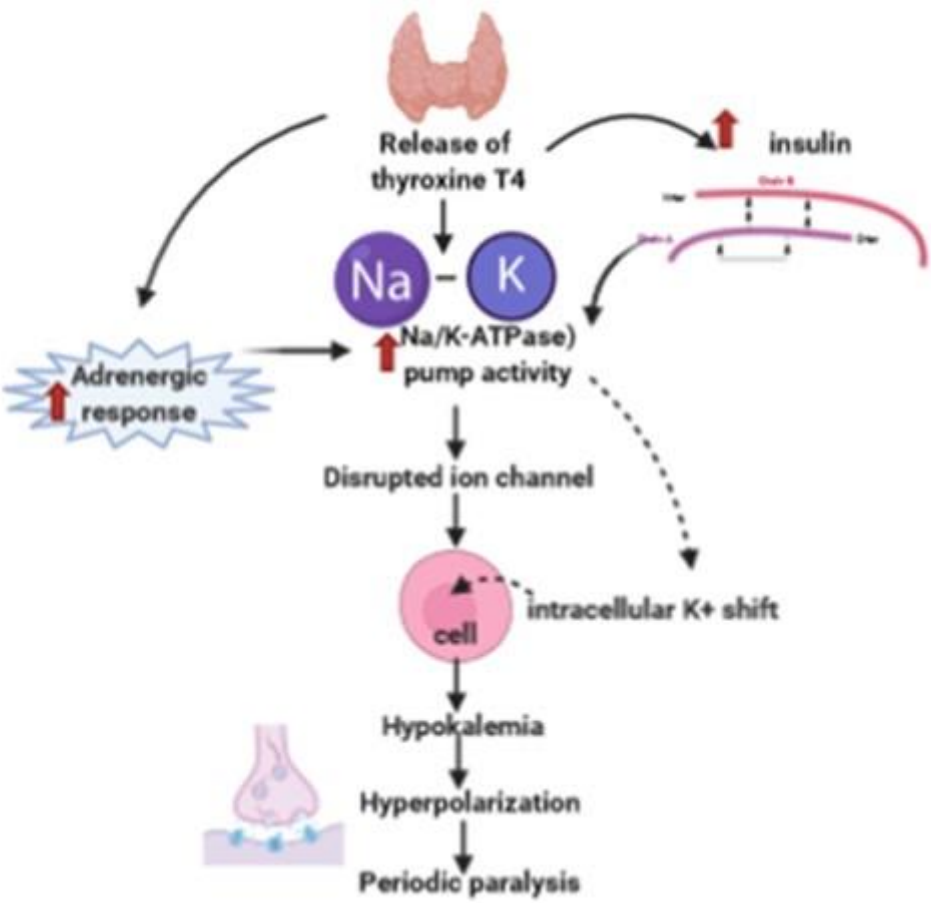
DISCUSSION

Thyrotoxic periodic paralysis is an unusual complication of hyperthyroidism. It is more prevalent in Asian men, in the second and fourth decades of life, although it can be observed in adolescents and children.[4] TPP is observed in hyperthyroidism mostly due to Graves' disease, nevertheless, other conditions like amiodarone-induced thyrotoxicosis, levothyroxine intoxication and thyrotropin (TSH) producing pituitary adenoma, toxic adenoma, thyroiditis and toxic multinodular goitre.[5]

The severity of the episodes may differ from weakness to complete paralysis, generally involving proximal muscles of the limbs. The duration may vary from a few hours to three days.[1] However, the severity of the paralysis does not directly correlate with the degree of hyperthyroidism.[6] The sensory system, higher mental functions and cranial nerves are spared. Patients can manifest with cardiac arrhythmias and thyrotoxic crisis in the worst scenario.[7]

Numerous hypotheses have been made to explain TPP, but the pathogenesis remains uncertain. The proposed mechanism for TPP was that thyroid hormone stimulates and augments the K^+-Na^+ ATPase action on the cellular membrane, causing an intracellular shift of potassium. The disruption of these cellular transport mechanisms involving the K^+-Na^+ ATPase pump causes irregularities in muscle contractibility and paralysis.[1] In thyrotoxicosis, the enhanced beta-adrenergic response further increases K^+-Na^+ ATPase activity. Hyperinsulinemia has been shown to stimulate K^+-Na^+ ATPase activity in an acute attack of TPP.[8](Figure 1).

Figure 1 Mechanism of paralysis in TPP



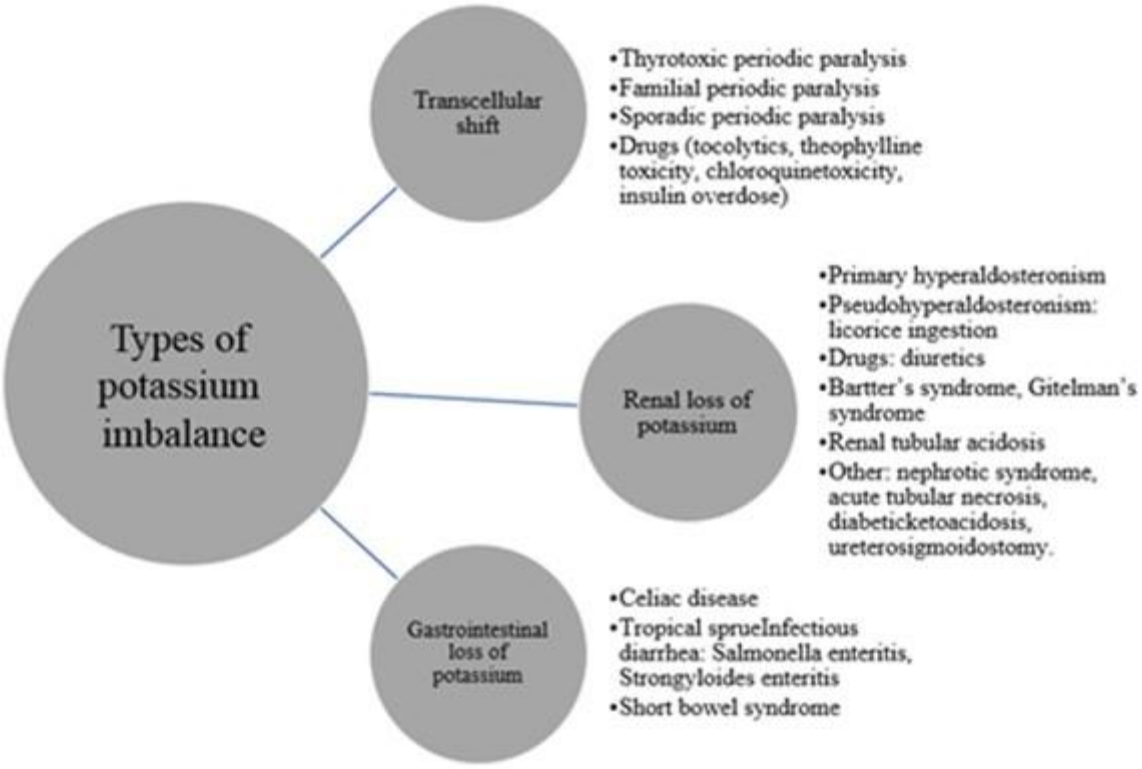
Hypokalaemia is the hallmark characteristic of TPP [9]. Normally in TPP, the potassium level is <3 mmol/L and the urinary potassium is < 20 mmol/L, which has been observed in this patient. This was supported by electrocardiogram (ECG) findings that showed prolonged QT intervals as previously reported.[10]

Besides hypokalaemia, hypophosphataemia and hypomagnesaemia may also be present due to intracellular shifts of phosphate and magnesium that follow potassium transport across the cellular membrane.[11] However in our patient, the serum phosphate and magnesium level were within normal limits.

In a patient who presents with hypokalaemia, a few differential diagnoses should be considered (Figure 2). Drug history and family history should be elicited to rule out toxicities and familial disorders. Besides, laboratory investigations, such as urinary potassium and arterial blood gases are also crucial to differentiate TPP from other causes of hypokalaemia such as renal and gastrointestinal loss of potassium.

Urgent correction of hypokalaemia is required, together with antithyroid drugs for the underlying hyperthyroid state, in the management of TPP. Euthyroidism restoration will prevent future attacks; however, non-selective β-blockers can be used until a euthyroid state is achieved. In addition, precipitating factors such as exercise or high carbohydrate diet should be avoided.

Figure 2 Differential diagnosis of hypokalaemic paralysis



Conclusion

TPP should be considered, even in the absence of thyrotoxic state, in all cases of acute hypokalemic paralysis, especially in young male patients. Thyroid function tests should be performed in all cases of periodic paralysis to allow an early diagnosis of TPP and initiate definite treatment.

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