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Case Report
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A Case of Severe Lower Extremity Weakness with Thyrotoxicosis – A Reminder of Hypokalemic Periodic Paralysis

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Abstract

Thyrotoxic Periodic Paralysis (TPP) is a known but rare complication of hyperthyroidism, characterized by acute onset of hypokalemia and muscle paralysis. The exact pathophysiology is still unclear, but studies suggest that thyroid hormones lead to sensitization of the Na/K-ATPase pump, leading to hypokalemia. Treatment includes potassium supplementation, as well as treating the underlying hyperthyroid state using anti-thyroid drugs, in conjunction with beta-blockers if necessary. TPP can be associated with life-threatening arrhythmias, and hence, awareness among physicians is necessary for early recognition and treatment. Here we report a case of TPP and discuss clinical features, pathophysiological hypothesis and recommended treatment options.

Keywords: Thyrotoxicosis; Periodic paralysis; Hypokalemia; Graves' Disease

Introduction

TPP is a heterogeneous group of disorders, characterized by acute flaccid muscle weakness and hypokalemia [1] and commonly affects young, otherwise healthy Asian individuals. So far, there are only few reports in Caucasians over the years, with the onset being around 30 years of age, which intriguingly coincides with the age of presentation with Grave's disease. There are two main subtypes described: Primary (hereditary) and secondary (acquired), with the latter being more common. Secondary PP often occurs in the context of hyperthyroidism and is termed Thyrotoxic Periodic Paralysis (TPP) and is defined by 3 characteristic features: Thyrotoxicosis, hypokalemia, and acute painless muscle weakness. TPP has a male preponderance, affecting males 26 times more frequently than their female counterparts [2]. Since this condition is rare, diagnosing this condition may be challenging and can go unrecognized, which may delay treatment leading to worse outcomes and could potentially be life-threatening.

Case Presentation

A 39-year-old Caucasian Albanian male presented to the Emergency Department with acute onset lower limb weakness and gait instability, which started on waking up. The patient denied any problems with his upper limbs, had no history of low back pain, sphincter disturbance, or sensory disturbance. He claimed to have had two episodes of loose stools the day prior to presentation, but denied nausea or vomiting, or febrile episodes. The patient was on carbimazole 10 mg daily, which his general practitioner had initiated back in Albania few weeks before after presenting with unintentional weight loss secondary to Graves' Disease. Mr. FH is a smoker and had no relevant surgical or family history.

At his initial assessment, he was clinically stable, with no hemodynamic compromise. Cardiovascular, respiratory and abdominal systems were unremarkable on examination. Neurological examination revealed reduced proximal power proximally in the lower limbs, with symmetrical weakness (⅘ on MRC Power Scale) in the iliopsoas, quadriceps, and hamstring muscle groups. Sensation and tone were preserved. Cranial nerves' examination was normal throughout.

Urgent blood tests and venous blood gases were sent for analysis (Table 1). These found the patient to be severely hypokalemic, with a potassium (K+) level of 2.1 mmol/L.

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Table 1: Venous blood gas results.

	At presentation	Reference Range
pH	7.32	7.35-7.45
Na^+	146	135-145 mmol/L
K^+	2.1	3.5-5.1 mmol/L
Lactate	1.5 mmol/L	
Glucose	6.1 mmol/L	
HCO_3^-	22.1	18-22 mmol/L

Table 2: Thyroid function tests.

	At presentation	Reference Range
Thyroid Stimulating Hormone (TSH)	<0.008	0.3-3 mic IU/ml
Free Thyroxine (T4)	40.59	11-21 p mol/L
Free Tri-iodothyronine (T3)	17.62	03.5-6.5 p mol/L

A provisional diagnosis of hypokalemia related muscle paralysis was made, and the patient was started on standard potassium replacement regimes with combined Intravenous (IV) and oral replacement. This consisted of intravenous administration of 40 mmol of 15% potassium chloride, diluted in 1 liter of 0.9% normal saline, administered at 160 ml/h. He was also given oral potassium supplementation (20 mmol every 8 hours). Mr. FX improved considerably once potassium replacement was commenced and weakness resolved completely within a few hours, once potassium levels normalized.

No clear cause for the hypokalemia was at first apparent. The patient had only had one low volume bout of loose stools the day before presentation, was on a healthy diet, and had no medications that could precipitate hypokalemia. Urinary electrolytes showed no renal potassium loss. He had an elevated serum creatinine kinase (517 U/l, reference 39-308 U/l) with a normal aldolase. His morning serum cortisol was also within range. Further testing including thyroid function tests showed that the patient was hyperthyroid (Table 2) despite being compliant to Anti-Thyroid Drugs (ATD).

He was reviewed by the endocrinologists who doubled the carbimazole dose. The history, presence of biochemically severe hyperthyroidism, and lack of other causes for hypokalemia was consistent with a diagnosis of Thyrotoxic Periodic Paralysis (TPP) was put forward. TSH receptor antibodies were strongly positive at 33.7 IU/L (reference 0.1-1.0 IU/L). The patient was discharged after one further night of observation, and is being regularly followed up at out-patients. He remains well and has no residual weakness. Biochemically, his thyroid function tests have also improved on a daily dose of 20 mg carbimazole.

Discussion

TPP commonly affects adolescent males, with an incidence of around 2% in the Asian population [3]. The characteristic features include thyrotoxicosis (and related symptoms such as weight loss), acute painless paralysis and hypokalemia. Attacks commonly initially involve the lower limits, without sensory involvement [4,5], with the severity of weakness being correlated to the degree of hypokalemia. Most cases of TPP are found in patients with Graves' disease. Other associated conditions include thyroiditis and toxic multinodular goiter.

The exact mechanism of TPP is still not well understood. Skeletal muscles contain a large amount of potassium and are crucial in maintaining extracellular potassium homeostasis through Sodium-Potassium-Adenosine Triphosphate (Na/K ATPase) pumps (which regulate intracellular potassium shifts) and potassium channels which shift K+ extracellularly [6,7].

It is thought that thyroid hormones sensitize the Na/K-ATPase pump activity in skeletal muscle, liver and kidney *via* both transcriptional and post-transcriptional methods [4,8]. This translates in an increase in the genetic transcription of genes coding of the Na/K+ pump, augmenting its intrinsic activity [9,10]. Enhanced beta-2 adrenergic stimulation also potentiates the hypokalemic effects of adrenaline and insulin, which explains why triggering factors include stress, exercise or large meals [11].

The goals of treatment are rapid, but safe, normalization of potassium. Any underlying cause should ideally be identified and treated. Rebound hyperkalemia may occur if potassium is supplemented hastily. Patients should have cardiac monitoring whilst potassium is being supplemented IV, at a dose that usually varies between 40 mmol to 200 mmol. Oral or IV beta-adrenergic blockers such as propranolol can be beneficial. ATDs are useful in the setting of Graves' Disease. Radioactive iodine or surgery might be required in some scenarios. Patients should avoid precipitating factors such as intensive exercise or heavy carbohydrate meals.

Conclusion

TPP is a rare condition characterized by acute painless lower limb paralysis in patients with thyrotoxicosis. Patients with hyperthyroidism should be educated about precipitating causes such as strenuous activity and high carbohydrate meals, since these lead to a rise in epinephrine levels and resultant hypokalemia through shift of potassium into the cells. Early identification and treatment of TPP is crucial, since hypokalemia may be life-threatening. The mainstay of treatment involves identification and treatment of the underlying cause, with urgent potassium supplementation to avoid arrhythmias, with possible addition of IV beta blockers as necessary.

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