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| RESEARCH ARTICLE

Periodic Paralysis and the Emergency Department: A Case Series of Thyrotoxicosis Periodic Paralysis with Literature Review

Dr. Ahmed ElKholi[1], Dr. Ali Haider Ali[2] ✉ and Dr. Maryam Mahmood Ali[3]
[1]Consultant Accident & Emergency at Salmaniya Medical Complex, Kingdom of Bahrain
[23]Accident & Emergency Resident at Slamaniya Medical Complex, Kingdom of Bahrain
Corresponding Author: Dr. Ali Haider Ali, **E-mail**: Alihaiderali97@outlook.com

| ABSTRACT
Thyrotoxic periodic paralysis is a rare but serious complication of thyrotoxic. It is an uncommon form of hypokalemic periodic paralysis characterized by proximal muscle weakness that may progress to involve distal muscle and respiratory muscle. Thyrotoxic periodic paralysis is commonly reported among Asian descent; especially the male population, between the ages of 20 and 40 years. The actual pathophysiology of Thyrotoxic periodic paralysis is unclear. However, hyperthyroidism, channelopathies, high-carbohydrate food, and hyperandrogenism are the most common predisposing factors associated with this condition. Hypokalemia and muscle weakness in Thyrotoxicosis patients result from increased shifting of K+ intracellularly. This is known to be related to increased sodium-potassium-a adenosine triphosphatase (Na/K-ATPase) pump number and activity. The proper aim of treatment in Thyrotoxicosis patients is to reach the euthyroid state. Management of Thyrotoxic periodic paralysis at the Emergency department includes establishing Intravenous potassium replacement, starting non-selective beta-blockers to reduce the phosphate and potassium intracellular shifting, and normalizing the underlying hyperthyroid state. Here, we present two cases of Thyrotoxic Periodic Paralysis. These cases reiterate the need to consider all the complications of Thyrotoxicosis, even rare ones, to treat the condition and reverse the effect of periodic hypokalemia within the Emergency Department, to prevent any inevitable complication.

| KEYWORDS
"Hyperthyroidism", "Hyperkalemia", "periodic paralysis", "Weakness", and "Electrolyte Imbalance"

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1. Introduction

Acute flaccid paralysis is an uncommon presentation in adults in the emergency department. It includes multiple etiologies such as infections, inflammatory disorders, hormonal misbalance, trauma, and electrolyte imbalance (1-2). Such hormone imbalances include thyroid disorders and associated electrolyte imbalances (1). Although thyroid disorders are regarded as common within any population, acute flaccid paralysis due to thyroid dysfunction is considered a rare presentation of the illness (1). Thyroid disorders are divided into hypothyroidism and hyperthyroidism depending on the thyroid function test, which includes thyroid stimulating hormone (TSH), Triiodothyroxine (T3), and Thyroxine (T4). More commonly, hyperthyroidism appears as acute flaccid paralysis, which is known as thyrotoxicosis periodic paralysis (2). This case study will report on two cases where the diagnosis of thyrotoxicosis periodic paralysis (TPP) was reached. Moreover, a discussion will be noted on the details of such a presentation with the proper emergency management and follow-up.

1.1 Case One

A 40-year-old South Asian Male presented to the Emergency Department with progressive muscle pain and weakness, proximal mainly, with tenderness to the touch. The patient stated he had a similar episode that spontaneously resolved a few days back and

associated it with fatigue after working out at the gym. He has no chronic illness, and this is his first presentation with such complaints. His vital signs at the time of presentation included:

Heart Rate: 110 beats per minute.

Respiratory Rate: 12 breaths per minute.

Blood Pressure: 155/110

Temperature: 37.2

Oxygen Saturation: 99% on Room Air.

During physical examination, with lower limb had a power of 0 out of 5, mainly at the level of the thighs and knee associated with hyporeflexia. The patient was able to move his feet. Other examinations seemed Unremarkable. Routine labs and venous blood gas were ordered to assess the cause of such presentation. Venous blood gas was unremarkable besides a potassium of 2.1 mmol\L. The patient was moved to a monitor bed with an electrocardiogram done and started on potassium chloride infusion at 20mEq at a rate of 2 hours. Laboratory findings can be seen in Table 1.

Table 1: Laboratory Investigations Findings.

Investigation	Value
White Blood Cell Count	12.09 x10^9/L.
Hemoglobin	10.80 g/dL.
Potassium	2.0 mmol/L.
Sodium	144 mmol/L.
Magnesium	0.76 mmol/L.
Urea	3.3 mmol/L.
Creatinine	56.00 µmol/L.
Thyroid Stimulating Hormone	0.00 mIU/L.
Thyroxine (T4)	12.0 pmol/L.
Triiodothyroxine (T3)	24.0 mol/L.

The patient was referred to general medicine for further evaluation as a suspected case of secondary periodic hypokalemic paralysis to thyrotoxicosis. The patient's condition improved after the administration of replacement therapy, with movement increasing. Repeated serum potassium was regarded as 2.6 mmol\L with continuation of replacement therapy. Furthermore, the evaluation of renin and aldosterone was regarded as normal. The patient was discharged after a few days with full function on oral potassium chloride 500mg twice daily with follow-up for thyroid hormone.

1.2 Case Two

A 43-year-old Middle Eastern Male presented to the Emergency Department with complaints of inability to move the lower limbs bilaterally. The patient has also a mild, dry cough associated with a subjective fever at home. He has no chronic illness, and this is his first presentation with such complaints. His vital signs at the time of presentation included:

Heart Rate: 91 beats per minute.

Respiratory Rate: 12 breaths per minute.

Blood Pressure: 121 / 71

Temperature: 36.9

Oxygen Saturation: 99% on Room Air.

During physical examination, the throat was noted to be congested with the lower limb having a power of 0 out of 5 associated with hyporeflexia. Other examinations seemed Unremarkable. Routine labs and venous blood gas were ordered to assess the cause of such presentation. Venous blood gas was unremarkable besides a potassium of 1.9 mmol\L. The patient was moved to a monitor bed with an electrocardiogram done and started on potassium chloride infusion at 20mEq at a rate of 2 hours. Laboratory findings can be seen in Table 2.

Table 2: Laboratory Investigations Findings.

Investigation	Value
White Blood Cell Count	10.32 x10^9/L.
Hemoglobin	14.20 g/dL.
Potassium	2.2 mmol/L.
Sodium	139 mmol/L.
Magnesium	0.54 mmol/L.
Urea	6.4 mmol/L.
Creatinine	66.00 µmol/L.
Thyroid Stimulating Hormone	0.35 mIU/L.
Thyroxine (T4)	4.0 pmol/L.
Triiodothyroxine (T3)	12.6 pmol/L.

The patient was referred to general medicine for further evaluation as a suspected case of secondary periodic hypokalemic paralysis to thyrotoxicosis. The patient's condition improved after the administration of replacement therapy, with movement increasing. Repeated serum potassium was regarded as 2.9 mmol\L with continuation of replacement therapy. Furthermore, the evaluation of renin and aldosterone was regarded as normal. The patient was discharged after a few days with full function on oral potassium chloride 500mg twice daily with follow-up for thyroid hormone.

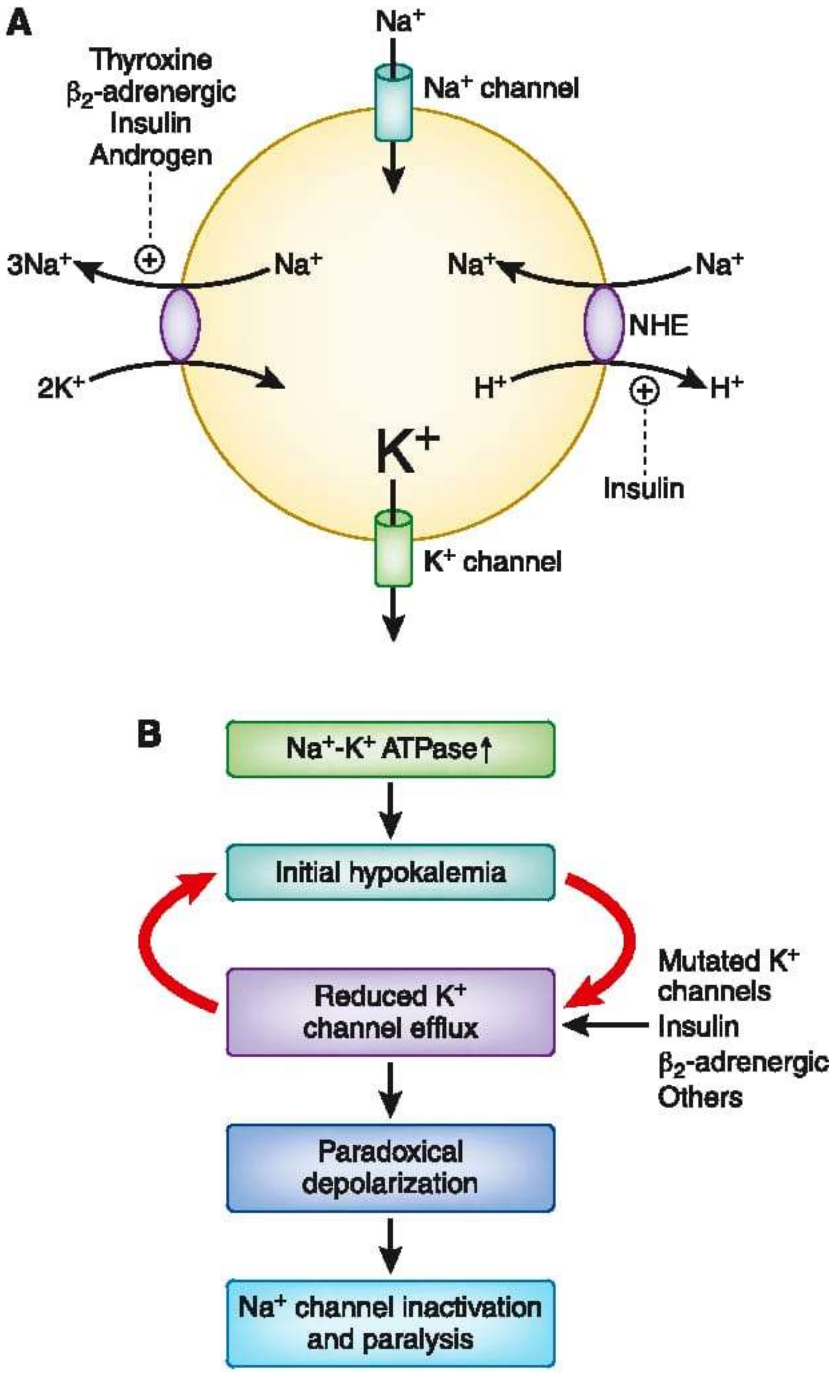
2. Discussion

As previously mentioned, such presentation of thyrotoxicosis is extremely rare. In terms of epidemiology, such cases have been rarely reported in the Middle East, with only 0.1% of presentations within the geographic area (2-3). Although rare in the Middle East, it is regarded as more common in the South Asian community, with literature regarding 1.9 – 3% of reported cases, with higher incidence rates between men, a ratio of 2:1 as compared to women within the same demographic area (2). The incidence is reported to be about 10 to 20 times more common among the Asian community as compared to the non-Asian community (3). Therefore, due to the rarity of the disorder and its presentation, the pathophysiology is not well understood, with multiple theories proposed. Although most of the literature agrees that the main cause of paralysis is related to the intracellular shift of potassium induced by sodium\potassium ATPase, rather than depletion of total body potassium, it is debated on the mechanism of hypokalemia (3). It is important to note that the skeletal muscle within the body plays a major role in the storage and control of extracellular potassium. Thus, the loss of potassium will mainly affect the skeletal muscle. Figure one gives a summary of the mechanism that occurs in the depletion of potassium. Such theories include the following (3-5):

1. The stimulation of the Sodium Potassium ATPase pumps through the overstimulation of the thyroid hormone. This will lead to loss of extracellular potassium from the serum, due to the effect on the influx and efflux of potassium within the cells. Research has noted increased activity in muscle cells during TPP. They upregulate the transcription of the pump through genomic factors therefore enhancing the activity of the pump.
2. Hyperthyroidism has been noted to affect the stimulation of the pump due to beta 2 adrenergic agonist activity. They increase the production of intracellular cAMP leading to the increase in pump activity.
3. Hyperinsulinemia may be regarded as an acute thyroid attack. There is an exaggerated response if an oral glucose test is done. It is known that insulin will lead to intracellular potassium shift, which in turn induces hypokalemia.

A newer theory notes a genetic mutation that was isolated in TTP patients. Two papers published in 2020 and 2023 respectively (1, 3-5), noted mutations in the Kir2.6 gene, which is responsible for encoding the skeletal muscle-specific potassium channels. There were correlated in both papers to increase the likelihood and risk of TPP.

Figure One: Mechanism of Sodium\Potassium ATPase effect on potassium shift in TPP.



In terms of etiology, most cases are related to the causes of hyperthyroidism which include and not limited to (1-5):

- Graves' disease, is the most common cause of hyperthyroidism worldwide (4).
- Toxic Nodular Goiter.
- Iodine-induced Thyrotoxicosis.
- Excessive thyroid use.
- Pituitary adenoma.

The difficulty in diagnosis is related to the lack of obvious symptoms of hyperthyroidism. Most patients may only present with symmetrical bilateral weakness of the lower limbs, therefore making it indistinguishable from familial period paralysis, which is also associated with hypokalemia (4). Other prodromal symptoms include and are not limited to muscle cramps, muscle pain, and stiffness as presented in one of the cases above (3). Furthermore, such illness may be exacerbated by intensive labor and activity

as seen with our young patient above (4). Moreover, most symptoms appear after a heavy meal or are related to waking up in the morning (3-4). An interesting aspect of TPP, less than 5% of patients may present with typical symptoms of hyperthyroidism which include sweating, tachycardia, hypertension, palpitations, tremors, and more (5-6). It is important to note that TPP usually occurs in young males, between the ages of 20 to 40 years old, with about more than 50% of reported cases occurring in patients younger than 20 (5, 7). These attacks are also recurrent and transient, mainly affecting the limbs more than the trunk (5). A defying aspect that aids in differtionation with familial periodic paralysis is that TPP may affect respiratory muscles leading to respiratory distress, and ultimately respiratory failure which may require intubation to prevent deterioration (5-6). Furthermore, familial periodic paralysis is seen mainly in caucasian individuals, with equal distribution between both genders and is more likely to appear in ages less than 20 years old (4).

The differential diagnosis of TPP is summarized in Table 3. As noted, electrolyte abnormalities, muscular disorders, neuromuscular junction disorders, central nervous disorders, and polynueropathies play a major role in cases of such presentation (5-6). Mianloy most can be excluded by history, physical examination, and laboratory investigation. In terms of treatments, some literature has been able to divide it into multiple sections of management. These sections include emergency management, prevention of recurrent attacks, and treatment of underlying hyperthyroidism (1, 4, 6-7).

Table 3: Differential Diagnosis of TPP.

Differtional Diagnosis	Disease
Electrolyte Abnormalioties	Hypo or hyperkalemia. Hypercalcemia. Hypo or Hypernatermia. Hypophosphotemia. Hypo or hypermagnesemia.
Muscle Disorders	Channelopathies. Metabolic defects within the muscle. Myopathies.
Neuromuscular Junction Disorders	Myasthesia Gravis. Eaton-lambort syndrome. Organophosphate poisoning. Botulism.
Centeral Nervous System Disorders	Transient Ischemic Atatck. Transient Global Cerebral Ischemia. Multiple Sclerosis.
Polyneuropathies	Gillian-Barre Syndrome. Infections. Toxins.

In terms of emergency management, it mainly consists of potassium replacement. The patient will be placed on a monitor bed, with potassium replacement started either potassium chloride 10mEq per hour through intravenous access or potassium chloride 2 grams every two hours per oral (7). Furthermore, potassium is monitored to avoid recurrent hyperkalemia or rebound hypokalemia (7). Proponalol, a beta-adrenergic antagonist, can be started to decrease the effect of thyroid hormones and improve symptoms, with a dose of 3 to 4 mg per kilogram orally (6-7). In terms of prevention of recurrent attacks, patients are advised to avoid precipitating factors until euthyroidism is achieved with 20 to 80mg propranolol to decrease symptoms of hyperthyroidism (7). Anti-thyroid medications are started to control the excess production of thyroid hormone (7). Overall, the prognosis of TPP is considered as good with patients gaining back full motor function with potassium replacement in the emergency department (5-7).

3. Conclusion

TPP is generally a benign case of flaccid paralysis and muscle weakness. It is completely reversible leading to a favorable prognosis. In the cases discussed above, such rare presentations must be managed properly and swiftly within the emergency department to avoid respiratory distress and mortality among patients. With proper management and swift recognition of signs and symptoms, the patient can be managed properly within the emergency department and referred to the appropriate specialty for further workup and follow-up.

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