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*Case Reports*

# Periodic Paralysis: An Unusual Presentation of Thyrotoxicosis

L Chapman & S Miller

**Key Points**
- Consider Thyrotoxic periodic paralysis (TPP) in any patient presenting with muscle weakness and symptoms suggestive of thyrotoxicosis
- Serum potassium is often low (but can be normal or elevated)
- Thyrotoxic Periodic Paralysis is more common in men and in Asian, Latino and Pacific Island racial groups
- Paralysis often follows vigorous exercise or excessive intake of carbohydrate or alcohol
- Treatment is with beta-blockers, correction of any electrolyte abnormality and by treatment of the underlying thyroid disorder

## Abstract
*Thyrotoxic Periodic Paralysis (TPP) is a rare complication of thyrotoxicosis and is up to 20 times more common in males. Cases usually present with painless muscle weakness precipitated by heavy exercise, fasting, an alcohol binge or large carbohydrate meal. Serum potassium is low in the majority, but normokalaemic (or even hyperkalaemic) TPP is recognised. Acute treatment of any electrolyte disorder, administration of a beta-blocker and treatment of the thyrotoxicosis leads to complete resolution. This rare diagnosis should be considered by the Acute Physician when confronted with any case of muscle weakness.*

## Keywords
*Thyrotoxicosis, Hyperthyroidism, Muscle weakness, Periodic Paralysis, Hypokalaemia.*

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## Case 1
A 31 year old Samoan male presented after awakening in the early hours of the morning with bilateral leg weakness and inability to walk. He described an identical episode which had occurred 8 days earlier. On both occasions he was awakened by the urge to urinate but found himself unable to mobilise with consequent incontinence. There were no sensory symptoms. On the first occasion the weakness gradually fully resolved over a 5 hour period. At presentation the weakness was felt to have ascended to involve both arms and a medical opinion was sought.

On direct questioning he admitted to weight loss of up to two years duration, with accompanying heat intolerance and restlessness. Systems enquiry was otherwise unremarkable.

He had no relevant past medical history and took no regular medication. He was a recent ex-smoker, consumed occasional alcohol in binges and he lived with his wife and their children aged 6 years and 13 months. There was no family history.

Other than a relative tachycardia of 90 bpm, vital signs were normal. He was alert and oriented to time, place and person. Examination of the cardiovascular, respiratory and gastrointestinal systems was unremarkable. Tone was normal throughout. Upper limb power was normal. Power was reduced (4/5) in both proximal lower limbs with preserved reflexes, bilateral flexor plantar response and intact cranial nerve function. He was clinically thyrotoxic with a fine resting tremor, sweaty palms and a collapsing pulse. A soft systolic bruit was heard over a moderate-sized non-tender, firm goitre. There were no signs of opthalmopathy.

The ECG confirmed sinus rhythm at a rate of 84bpm. Laboratory investigations (Table 1) revealed suppressed thyroid stimulating hormone (TSH) and elevated free T4 (fT4).

The diagnosis of thyrotoxic periodic paralysis was made. Further enquiry ascertained that the first stereotyped episode followed a large carbohydrate meal accompanied by 12 unit alcohol binge and the second followed a similarly large carbohydrate intake. He was started on a beta-blocker and carbimazole. Subsequent TSH receptor antibodies were positive confirming Graves thyrotoxicosis. Given his young children the planned treatment is with 12 months carbimazole with radioiodine reserved as second line therapy.

## Case 2
A 32 year old Samoan male presented to the Emergency Department with a 1 year history of intermittent bilateral leg weakness, most marked in the evening and following morning, with gradual resolution throughout the day. There were no sensory

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symptoms. Episodes occurred every few weeks. He had noticed his weakness was more severe on Friday nights and Saturday mornings following a habitual large carbohydrate meal (pizza) and 16 unit alcohol binge. He presented on a Saturday morning with weakness that was more severe then usual.

On direct questioning he admitted to heat intolerance and 7 kg weight loss over 12 months. He complained of an itchy rash on both shins. Systems review did not elicit any additional information of note.

There was no significant drug history or past medical history. He was a lifelong smoker of roll-up cigarettes and worked as a driver. He lived with his wife and their 2 year old son. There was a family history of primary hypothyroidism in a maternal aunt.

On examination he was alert and orientated. Vital signs were normal. There was early bilateral pretibial myxoedema on the anterior shins. Examination of the cardiovascular, respiratory and gastrointestinal systems was unremarkable. Power was reduced (4/5) in both proximal lower limbs and proximal upper limbs with preserved reflexes, bilateral flexor plantar response and intact cranial nerve function. He was clinically thyrotoxic with a fine resting tremor, sweaty palms and a collapsing pulse. There was no goitre, and no signs of opthalmopathy.

The ECG was normal. Laboratory investigations (Table 1) showed hypokalaemia, suppressed TSH and elevated fT4 in keeping with primary hyperthyroidism.

He was diagnosed with Hypokalaemic Thyrotoxic Periodic Paralysis and treatment with a beta-blocker and Carbimazole was commenced. Subsequent TSH receptor antibodies were positive confirming Graves Thyrotoxicosis and as with the patient described in case 1, planned treatment is with 12 months of carbimazole to maintain euthyroidism.

| | | Measured Value | Normal range |
|---|---|---|---|
| **Case 1** | K+ | 4 mmol/l | 3.5-5.2 mmol/l |
| | TSH | <0.08 mU/l | 0.4-4 mU/l |
| | fT4 | 82 pmol/l | 9-19 pmol/l |
| **Case 2** | K+ | 2.1 mmol/l | 3.5-5.2 mmol/l |
| | TSH | <0.08 mU/l | 0.4-4 mU/l |
| | fT4 | 28 pmol/l | 9-19 pmol/l |

**Table 1.** Laboratory findings: K+ - Serum potassium; TSH : thyroid stimmulating hormone; fT4 - free thyroxine

## Discussion

Periodic Paralysis (PP) accompanying thyrotoxicosis was first described in 1931[1] and is the commonest acquired form of periodic paralysis. Clinical features are indistinguishable from those of the inherited forms of periodic paralysis, although affected individuals tend to present in the 3rd to 5th decade (compared to 1st or 2nd decade for the inherited forms).[2,3] There is a clear male predominance with up to 20 times higher prevalence in men.[4] When considered alongside the increased incidence of thyrotoxicosis in females, this suggests a role for androgens in the pathogenesis of TPP.

Salient clinical features include transient, recurrent episodes of paralysis which are brisk in onset (over minutes to hours) and which last for hours to days. Proximal muscle groups are affected more than distal, and the lower limbs are affected more than the arms. Muscle tone and tendon reflexes are often diminished but can be unaffected. Peripheral sensory and higher brain functions are preserved. Hypokalaemia is usually present (but can be absent) and the severity of weakness often correlates with the degree of hypokalaemia. In very severe cases profound weakness involving bulbar muscles necessitates intubation and ventilatory support.[5]

Cardiac involvement in TPP can be demonstrated by the presence of abnormalities of the electrocardiograph (ECG). Changes seen are most often those associated with thyrotoxicosis and hypokalaemia (sinus tachycardia, atrial tachyarrhythmia, U waves, QRS prolongation, QT prolongation, T wave flattening) but may include atrioventricular block, ventricular tachycardia, ventricular fibrillation and cardiac arrest.[6] Treatment of hypokalaemia leads to resolution of the ECG abnormalities.

The precise pathophysiology of TPP is incompletely understood. The combination of a thyrotoxic state superimposed upon susceptible sodium and potassium ion channel genetic polymorphisms has been proposed.[7] This leads to a large intracellular shift of potassium ions and hypokalaemia, which then causes impaired skeletal muscle depolarisation and consequent muscle weakness. Moreover, thyrotoxicosis is known to increase skeletal muscle $Na^+/K^+$ ATP-ase expression, the activity of which is also increased by b-adrenergic stimulation[8] and thyrotoxicosis.[9] Postprandial glucose transport into skeletal muscle (and adipocytes) leads to a corresponding intracellular shift of potassium and can result in hypokalaemia.[10] It is recognised that TPP individuals are hyperinsulinaemic and insulin resistant compared to thyrotoxic controls,[11] and that the $Na^+/K^+$ ATP-ase activity in TPP is further increased following an oral glucose load.[12] This implies a role for insulin resistance in the pathogenesis of TPP.

TPP is more common in certain ethnic groups. The incidence in thyrotoxic patients in China and in Japan is around 2%[13,4] whereas a non-Asian (predominantly Caucasian) series reported an incidence of just 0.2%.[14] Other ethnicities recognised to be at increased risk of TPP are New Zealand Maori, and Pacific Islanders (as in the 2 cases described above).[15]

The muscle paralysis is due to intracellular potassium shifts rather than total body potassium deficiency, however correction of hypokalaemia leads to an improvement in muscle function.[16] Correction of hypokalaemia also stabilises the myocardium and prevents fatal arrhythmia. Care should be taken to prevent iatrogenic rebound hyperkalaemia. Beta-blockers at the doses normally used for control of thyrotoxic symptoms (eg. Propranolol 20-40mg tid) are effective[17] and probably mediate their effect via the $Na^+/K^+$ ATP-ase channel.[18]

Control of thyrotoxicosis by antithyroid drugs, radioiodine or thyroidectomy appear to be equally

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effective in treating TPP, implying that control of the thyrotoxic state is an essential component of therapy. Until thyroid function tests are normal patients should be advised to avoid precipitants such as vigorous exercise, excessive intake of carbohydrate or alcohol. PP will remain in complete remission once euthyroidism is restored.

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