Unusual presentation of more common disease/injury

An unusual cause of muscle weakness: a diagnostic challenge for clinicians

Sayantan Ray,¹ Supratip Kundu,¹ Manas Goswami,¹ Subhasis Maitra,¹ Arunansu Talukdar,¹ Animesh Maiti²

¹Department of Medicine, Medical College and Hospital, Kolkata, West Bengal, India;

²Department of Endocrinology, Medical College and Hospital, Kolkata, West Bengal, India

Correspondence to Dr Arunansu Talukdar, arka_talukdar@yahoo.com

Summary

The authors describe a 27-year-old male who presented with acute flaccid quadriparesis. The patient denied any history of similar episodes in the past. At presentation, the patient was tachycardiac with normal systolic blood pressure. He had marked flaccid weakness of both upper and lower limbs and furthermore, he was hypotonic and without tendon reflexes. Biochemical analyses revealed severe hypokalaemia (1.9 meq/l). The patient was given potassium supplementation. He showed complete recovery after the medical intervention. Successive investigations documented an undiagnosed case of Graves' disease. Hypokalaemia secondary to thyrotoxicosis was diagnosed as the cause of the paralysis. Thyrotoxic periodic paralysis is a rare neurologic manifestation of thyrotoxicosis. Absence of obvious signs of thyrotoxicosis poses a diagnostic challenge for the clinicians.

BACKGROUND

Thyrotoxic periodic paralysis (TPP) is a potentially reversible metabolic disorder characterised by acute, episodic, transient, muscle paralysis and severe hypokalaemia due to a massive intracellular shift of potassium.¹ Male patients of Asian descent are mainly affected. Many affected patients do not have obvious symptoms and signs of hyperthyroidism. Hence it is frequently overlooked and misdiagnosed at presentation. Effective control of hyperthyroidism is indicated to prevent the recurrence of paralysis. Here we are presenting a case of 27-year-old male who presented with acute quadriparesis and subsequently diagnosed as having TPP. The article aims at highlighting the importance of suspecting thyrotoxicosis in cases of acute onset muscular weakness especially in absence of any clue towards recurrent periodic paralysis and recognising these clinical settings in hypokalaemic patients to avoid risks of late diagnosis.

CASE PRESENTATION

A 27-year-old male presented to the emergency department for sudden onset weakness of all four limbs and respiratory distress. He first noticed weakness while getting up from the bed in the morning. The patient denied any history of trauma, fever, vomiting, diarrhoea, alcohol or illicit drug use or diuretic abuse. No family member had similar symptoms. The patient denied any history of similar episode in the past.

On examination, the patient was tachycardiac (pulse rate 110/min) with normal systolic blood pressure. He was tachypnoeic but his respirations were shallow. Head and neck examination findings were normal, with no exophthalmos, masses or bruits. The thyroid gland was not obviously enlarged. He was alert and orientated. Neurological examination showed marked flaccid weakness of both upper and lower limbs (grade 1/5). Deep tendon reflexes were absent, with normal plantar response. Cranial nerves

Figure 1 (a) Initial electrocardiogram of the patient with thyrotoxic periodic paralysis showing sinus tachycardia and U wave in precordial leads; (b) Radioiodine uptake scan showing diffuse, homogenous radiotracer uptake.

were intact, as were sensation and proprioception. Lungs were clear, with diminished chest wall excursions bilaterally. Auscultation of the heart revealed rapid but regular heartbeats. The remainder of the physical examination was unremarkable.

INVESTIGATIONS

Investigations after admission to medical ward showed profound hypokalaemia with serum potassium (K^+) of 1.9 meq/l. Serum sodium and calcium concentrations were normal, as was the glucose level. The creatine-kinase level was not elevated. These findings were consistent with hypokalaemic periodic paralysis. Further investigation was aimed at establishing the cause of hypokalaemia. ECG at presentation showed sinus tachycardia with presence of U-wave in the precordial leads (figure 1a). Assessment of arterial blood gases (ABG) on room air revealed hypercapnia and respiratory acidosis. Urine electrolytes test was done to rule out renal tubular acidosis.

Even though the patient did not have goitre or typical symptoms of thyrotoxicosis except for tachycardia, we proceed with a thyroid function test, which showed thyroid stimulating hormone level of <0.005 μ IU/ml (normal range 0.35–4.94 μ IU/ml), free T4 of 2.78 ng/dl (normal range 0.7–1.48 ng/dl) and free T3 of 4.90 pg/ml (normal range 1.71–3.71 pg/ml), suggestive of thyrotoxicosis. Radioiodine uptake scan revealed diffuse, homogenous radiotracer uptake (figure 1b).

DIFFERENTIAL DIAGNOSIS

- ▶ Guillain–Barré syndrome
- ▶ Myasthenia gravis
- ▶ Acute transverse myelitis
- ▶ Acute spinal cord compression

TREATMENT

We send the patient to intensive care unit for possible need of ventilator support and intravenous potassium supplementation started immediately (10 meq/h in 5% mannitol) and continued until serum potassium level reached >2.0 mmol/l. Thereafter oral potassium replacement was done with about 60 meq over next 24 h. Fortunately, he did not need ventilator support and ABG revealed normal parameters after correction of hypokalaemia.

OUTCOME AND FOLLOW-UP

He showed complete recovery with this intervention and his serum potassium was increased to 3.9 meq/l. The patient was diagnosed as a case of hypokalaemic TPP associated with Graves' disease. He was started on oral carbimazole 10 mg three times a day and propranolol 40 mg three times a day and was scheduled for follow-up. After 6 months of follow-up the patient remains euthyroid and no further episodes were reported.

DISCUSSION

TPP a special form of secondary hypokalaemic periodic paralysis and occurs mainly in young adult males. It is characterised by recurrent, transient episodes of skeletal muscle weakness associated with hypokalaemia (potassium level <3.0 mmol/l).¹ The muscle weakness may range between

mild weakness to severe paralysis with respiratory failure and life-threatening cardiac arrhythmia. Patients with TPP are usually in the age group of 20–40 years.² In a recent study from north India, thyrotoxicosis was found in nearly 17% of patients with secondary hypokalaemic periodic paralysis.³

Patients with TPP have significantly higher number of Na/K ATPase pump activity than other thyrotoxic patients, which helps to mobilise extracellular potassium into the cell leading to hypokalaemia and resultant muscle paralysis.⁴ According to some recent work excess T_3 modifies insulin sensitivity in skeletal muscles and pancreatic cells and thus altering potassium homeostasis.⁵ A recent study identified an inward rectifying potassium channel, Kir 2.6 mutations of which predispose to periodic paralysis in patients with hyperthyroidism.⁶ Precipitating factors of hypokalaemic TPP include strenuous exercise followed by rest, excessive carbohydrate-rich food ingestion, administration of insulin or epinephrine, emotional stress, trauma and infection.⁷

The initial symptom of TPP may only be a sensation arising in the affected muscle presented as a cramp, pain, ache or stiffness.¹ The weakness usually starts in the lower limbs, followed by involvement of girdle muscles and then upper limbs. Although rare but in severe attack respiratory⁸, bulbar and ocular muscles can be involved. Attacks may resemble other conditions simulating periodic paralysis like Guillian–Barre syndrome, myasthenia gravis, acute transverse myelitis, acute spinal cord compression or hysteria.⁸ Other causes of periodic paralysis must be ruled out before committing to the diagnosis of thyrotoxic hypokalaemic periodic paralysis (HPP). TPP should be distinguished from familial HPP. Clinically, the attacks of paralysis are much the same as those of familial hypokalaemic type. The difference between these two clinical entities is addressed in table 1.

Hyperthyroidism may be clinically silent. The subtlety of this condition together with its rarity makes it difficult to diagnose at presentation. These patients may have sinus tachycardia, prolonged QT-U interval, and cardiac arrhythmias on ECG. Electromyography is diagnostic if done during attack, showing complete electrical silence.⁹ Molecular genetic testing identifies the mutation in the disease causing gene (KCNE 3).¹⁰

Treatment for an acute attack is determined by severity of symptoms, serum potassium levels and the ECG changes, if any. Potassium supplementation should be given with caution to avoid rebound hyperkalaemia. Non-selective β -blockers like propranolol are useful to prevent

Table 1 Distinguishing features between thyrotoxic periodic paralysis and familial hypokalaemic periodic paralysis

Parameters	Thyrotoxic periodic pparalysis	Familial periodic paralysis
Age	20–40 years	<16 years
Sex	Male predominant (70:1)	M>F (3:1)
Heredity	Sporadic	Autosomal dominant
Ethnicity	Asian	Caucasian
Hyperthyroidism	Present	Absent
Acetazolamide	No definitive effect	Crisis prevention
Propranolol	Preventing crisis	No definitive effect
Antithyroid	Definitive effect	No definitive effect

attacks until euthyroid state is achieved. Since attack does not occur after patient has reached euthyroid state so, adequate control of thyroid function is of prime importance. Effective preventive measures include a low carbohydrate, low salt, potassium rich diet and using potassium-sparing diuretics.

In conclusion, TPP should be kept in mind as a cause of acute onset quadriparesis to avoid delayed diagnosis and improper management. The early identification and prompt treatment of this entity is important in preventing patients from developing life-threatening complications respiratory failure and fatal arrhythmias. The authors suggest that a thyroid function test may be rewarding even in absence of any suggestive history of recurrent periodic paralysis as in the present case.

Learning points

- ▶ Thyrotoxicosis is an important cause of acute onset flaccid quadriparesis in Asian descent males.
- ▶ Although rare, this entity should be considered in differential diagnosis of quadriparesis with acute onset, and thyroid function should be evaluated.
- ▶ Severe cases may be life threatening due to progression to respiratory paralysis and cardiac arrhythmias.
- ▶ Manifestation of thyrotoxicosis is often subtle making the diagnosis difficult.
- ▶ Adequate control of thyrotoxicosis is necessary to prevent further attacks.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **McFadzean AJ**, Yeung R. Periodic paralysis complicating thyrotoxicosis in Chinese. *Br Med J* 1967;**1**:451–5.
2. **Lin SH**. Thyrotoxic periodic paralysis. *Mayo Clin Proc* 2005;**80**:99–105.
3. **Maurya PK**, Kalita J, Misra UK. Spectrum of hypokalaemic periodic paralysis in a tertiary care centre in India. *Postgrad Med J* 2010;**86**:692–5.
4. **Magsino CH Jr**, Ryan AJ Jr. Thyrotoxic periodic paralysis. *South Med J* 2000;**93**:996–1003.
5. **Maciel RM**, Lindsey SC, Dias da Silva MR. Novel etiopathophysiological aspects of thyrotoxic periodic paralysis. *Nat Rev Endocrinol* 2011;**7**:657–67.
6. **Ryan DP**, da Silva MR, Soong TW, *et al*. Mutations in potassium channel Kir2.6 cause susceptibility to thyrotoxic hypokalemic periodic paralysis. *Cell* 2010;**140**:88–98.
7. **Ober KP**. Thyrotoxic periodic paralysis in the United States. Report of 7 cases and review of the literature. *Medicine (Baltimore)* 1992;**71**:109–20.
8. **Liu YC**, Tsai WS, Chau T, *et al*. Acute hypercapnic respiratory failure due to thyrotoxic periodic paralysis. *Am J Med Sci* 2004;**327**:264–7.
9. **Puvanendran K**, Cheah JS, Wong PK. Electromyographic (EMG) study in thyrotoxic periodic paralysis. *Aust N Z J Med* 1977;**7**:507–10.
10. **Dias Da Silva MR**, Cerutti JM, Arnaldi LA, *et al*. A mutation in the KCNE3 potassium channel gene is associated with susceptibility to thyrotoxic hypokalemic periodic paralysis. *J Clin Endocrinol Metab* 2002;**87**:4881–4.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit

<http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Ray S, Kundu S, Goswami M, Maitra S, Talukdar A, Maiti A. An unusual cause of muscle weakness: a diagnostic challenge for clinicians.

BMJ Case Reports 2012;10.1136/bcr.01.2012.5625, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow

Keep up to date with all published cases by signing up for an alert (all we need is your email address) <http://casereports.bmj.com/cgi/alerts/etoc>