CASE REPORT

Generalised weakness in a young patient: a cause for concern?

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SUMMARY

Muscular weakness in young patients is usually due to mild, self-limiting causes. Nonetheless, it is important to remember other, more serious aetiologies which can cause this clinical picture. Thyrotoxic hypokalaemic periodic paralysis (THPP) is a rare disease in Europe and the USA, with fatal cardiovascular and respiratory complications. It is characterised by recurrent episodes of generalised muscular weakness, especially in the legs, with an associated hypokalaemia and hyperthyroidism. Diagnosis is based on clinical history, laboratory tests and an ECG. Early treatment focused on cautious correction blood potassium and non-cardiac selective β -blockers. Additionally, it is imperative to normalise thyroid function to prevent relapses. We present a young, healthy man to the emergency department with episodes of intermittent leg weakness. The history and the ECG findings allowed for the diagnosis of THPP to be reached with early treatment causing remission.

BACKGROUND

This case highlights an infrequent disease which can be diagnosed with simple tests available in the accident and emergency (A&E) department. Reaching the right diagnosis of thyrotoxic hypokalaemic periodic paralysis (THPP) is difficult as the symptoms are vague and non-specific, and may be the first clinical presentation of underlying hyperthyroidism, of which a cause as to be found. This case is interesting not only for endocrinologists, but also doctors working in the emergency department who should keep in mind the diagnosis in a patient who presents with generalised weakness especially of the legs, tachycardia and reduced lower limb reflexes, and can lead to fatal complications.

CASE PRESENTATION

A 28-year-old man with no medical history presented to the emergency department with a 2-day history of generalised muscular weakness, predominantly in both legs, with difficulty in walking. The patient had consumed alcohol the night before symptom onset. He had similar, less marked episodes over the course of the year without consulting with his local doctor. The patient had no relevant family history and a focused history of thyroid pathology was undertaken. The patient referred having palpitations, sweating, anxiety, increased bowel movements, weight loss and insomnia in the previous months. On physical examination, the patient was tachycardic at 120 bpm, proximal leg weakness with a

symmetrical power score of 3/5 bilaterally and reduced knee and ankle reflexes. The rest of the examination was normal.

INVESTIGATIONS

An ECG was performed which showed sinus rhythm with amplified voltages, ST depression in the anterior leads, with Q waves, and a QT interval on the upper limit of normal (figure 1). An electrolyte abnormality was initially suspected which was confirmed on blood testing with a potassium level of 1.9 mEq/L. He also had an elevated creatinine kinase phosphate (CKP) level (487 U/L), with a normal anion gap and no other abnormalities. On the basis of generalised muscular weakness, hyporeflexia, hypokalaemia and an abnormal ECG, THPP was suspected and thyroid function tests were conducted which showed primary hyperthyroidism (free T4 5.14 ng/dL, thyroid-stimulating hormone (TSH) 0.009 μ U/mL).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a young man with bilateral leg weakness included Guillain-Barré syndrome, although the patient did not recount an ascending weakness, and did not have a previous infectious disease; myasthenia gravis but there was no progressive fatigue. Spinal cord compression was ruled out as there was no history of trauma and conversion syndrome was unlikely as there was no psychiatric history. Myelitis due to ischaemia was unlikely due to the lack of cardiovascular risk factors. None of these could account for the tachycardia, and low potassium levels and the latter could not account for the reduced reflexes. Familial hypokalaemic periodic paralysis was also ruled out as the patient had an unremarkable family history. Additionally, there were no potassium losses as demonstrated in the urine test nor did the patient have vomiting or diarrhoea which could explain the hypokalaemia. Hyperaldosteronism could not be ruled out in the A&E department as this requires more extensive hormonal testing. Although hyperaldosteronism could cause hypokalaemia, it would have also given rise to hypertension which the patient did not have. A diagnosis of periodic paralysis was considered which would explain the weakness, tachycardia and low potassium levels.

TREATMENT

The patient was started on a slow rate of intravenous potassium under continuous ECG monitoring

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Figure 1 ECG showing sinus tachycardia with high voltages, ST depression and U waves which are signs of hypokalaemia.

and an oral β -blocker (propranolol 20 mg/6 h). After a few hours in the short-stay observation ward normalisation of the potassium level and ECG tracing were achieved ([figure 2](#)), as well as resolution of the leg weakness. Once stable, a thyroid echogram showing a hypervascularised goitre, a gammagraphy demonstrating a generalised increased uptake and positive anti-TSH receptor antibodies confirmed the diagnosis of Graves' disease.

OUTCOME AND FOLLOW-UP

Forty-eight hours after admission the patient was discharged with tiamazol 10 mg/8 h and propranolol 40 mg/8 h with follow-up in the endocrinology outpatient clinic to determine whether he is a candidate for radioiodine. A hormone analysis including cortisol, aldosterone, catecholamines, adrenocorticotrophic hormone and renin levels were requested in the clinic, which were subsequently shown to be normal.

Figure 2 ECG showing normalisation of the ST segment, resolution of U waves and reduction of the voltages after correcting the potassium level.

DISCUSSION

THPP is an uncommon disease, more frequently seen in Asia than in Western countries. Although thyroid pathology has a female predisposition, THPP is more commonly seen in men, especially between 20 and 40 years old.¹ It usually presents as recurrent and intermittent episodes of muscular weakness affecting the legs, with occasional myalgia, asthenia and muscle cramps. Hyporeflexia is another important finding with normal sensitivity on neurological examination. Symptoms usually resolve completely within 72 h. Precipitating factors include physical exercise, infection, surgery, carbohydrate or alcohol consumption.¹

The associated hypokalaemia is not due to a deficit in potassium as such, but rather an extracellular shift intracellularly due to an increased activity of the Na⁺/K⁺ ATP pump caused by the β -adrenergic properties of hyperthyroidism. For this reason there is no detectable increase in urinary or faecal potassium levels. The degree of hypokalaemia correlates with the severity of the leg weakness. It is not unusual for potassium levels to descend below 3 mmol/L, with levels down to 1.1 mmol/L being reported.^{1 2}

The differential diagnosis of bilateral leg weakness include Guillain-Barré syndrome, transverse myelitis, spinal cord compression, conversion disorder, familial and sporadic hypokalaemic periodic paralysis.¹

Diagnosis of THPP is challenging due to the rarity of the disease and also because there is frequently no previous symptoms of hyperthyroidism.¹ History, examination findings and ECG changes can be sufficient in establishing the diagnosis before confirming with laboratory tests if the disease is highly suspected. Common ECG changes include tachycardia (due to hyperthyroidism), prolonged PR interval, high voltages and U waves with a prolonged QT interval.³ These tests allow early diagnosis which is essential to avoid possibly fatal complications such as ventricular arrhythmias due to hypokalaemia, rhabdomyolysis or respiratory muscle compromise. It is important to emphasise that THPP is potentially a fatal condition that is reversible if it is detected early.^{4 5} Diagnosis is confirmed by the presence of hypokalaemia, elevated T3 and T4 levels, TSH level and frequently and elevated CKP. The majority of cases of hyperthyroidism with periodic hypokalaemic paralysis are associated with Grave's disease. Although this is a rare manifestation of Grave's disease, hypokalaemic periodic paralysis is well-known entity to occur in Grave's disease. THPP has also been associated with thyroiditis, nodular thyroid, T4 ingestion and TSH-secreting pituitary tumours have also been reported.^{1 2}

Hypophosphataemia and hypomagnesaemia is seen in two-thirds of cases with a normal acid-base balance.¹ Electromyography studies show signs of myopathy with a

reduction of the amplitude of muscular action potentials which do not change after the administration of epinephrine.²

Treatment is based on the slow and cautious administration of potassium chloride (either orally or intravenously) to prevent fatal cardiovascular complications. A non-cardioselective β -blocker such as propranolol also increases the blood potassium levels due to its inhibitory effects on the ATPase pump without causing a rebound hyperkalaemia as well as preventing future relapses.¹⁻³ Glucose solutions should be avoided as these stimulate insulin secretion and can aggravate the hypokalaemia. Once the potassium level is normalised, oral supplementation is not necessary as this does not prevent further episodes of muscular paralysis.^{1 5} Definite prevention is achieved by treating the hyperthyroidism and restoring thyroid function.²

Learning points

- Thyrotoxic hypokalaemic periodic paralysis is a rare disease in Western countries.
- It is characterised by leg weakness, hypokalaemia and ECG changes which are precipitated by hyperthyroidism.
- The disease is also difficult to diagnose as few patients experience symptoms of hyperthyroidism. If suspected, prompt treatment is required to prevent serious, cardiovascular complications which can be fatal.
- THPP is known to occur, as shown in this case, in Grave's disease.

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Competing interests None.

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