Reminder of important clinical lesson

Hypokalaemia with paralysis: don't forget the thyroid

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Summary

The authors report the case of a 33-year-old Italian man who had three episodes of hypokalaemia with paralysis linked to hyperthyroidism. Because of its low prevalence in western populations, the diagnosis of thyrotoxic hypokalaemic periodic paralysis can be easily missed in non-Asian countries.

BACKGROUND

Hypokalaemia linked to excessive potassium losses is a common clinical problem in medical and surgical wards. On the other hand, hypokalaemia determined by rapid intracellular shift of potassium is a far less common condition that can lead to periodic paralysis and admission in the emergency room.¹ In Western countries, the most commonly diagnosed type of hypokalaemic periodic paralysis is the familial form, which is a genetically determined channelopathy.¹ Less commonly, hypokalaemic periodic paralysis is sporadic and can be associated with thyrotoxicosis.¹ The latter syndrome is highly prevalent among Asian patients but can be encountered in non-Asian patients as well.^{1–7}

Because of its low prevalence in western populations, if the level of clinical suspicion is not high, the diagnosis of thyrotoxic hypokalaemic periodic paralysis (THPP) can be easily missed in non-Asian countries. Here, we present a case of hypokalaemia with recurrent severe muscular complications associated with thyrotoxicosis in a Caucasian patient.

CASE PRESENTATION

The patient, a 33-year-old Italian man, was admitted for the first time in the emergency room on 5 April 2010 for sudden onset of cramps and weakness of the lower limbs. Blood tests showed a serum potassium concentration of 2.6 mmol/l. The patient was treated with 500 ml of a polysaline solution, which contains 13 mmol of potassium per litre. A few hours later, serum potassium was 4.3 mmol/l and the patient was discharged without symptoms.

One week later, the same symptoms recurred. Serum potassium was 3.0 mmol/l. He received 500 ml of polysaline with rapid improvement of weakness and was discharged with oral potassium supplements. Four days later, the serum potassium was in the high normal range (5.0 mmol/l). The physician of the emergency department referred the patient to our nephrology unit for further investigations. However, the patient did not attend the scheduled visit. A few days later, the patient was admitted again in the emergency room with complete paralysis of the lower limbs. Serum potassium was 2.9 mmol/l. He was

treated with polysaline and transferred to our nephrology unit.

At admission, his body temperature was 36°C, blood pressure 135/80 mm Hg, heart rate 100 bpm and orthostatic hypotension was absent. Clinical examination was not relevant except for obesity (BMI 32 kg/m²). ECG showed absence of U waves and no signs of left ventricular hypertrophy. Serum potassium concentration was 4.1 mmol/l and muscular symptoms had completely regressed; therefore, we stopped the polysaline infusion.

During hospitalisation, the serum potassium concentration and urinary potassium excretion were normal (4.3 mmol/l and 68 mmol/day, respectively). No other electrolyte variations were noticed. Renal function was normal: serum creatinine 0.74 mg/dl (65.5 µmol/l); creatinine clearance 102 ml/min; no proteinuria. Serum bicarbonate concentration was 24 mmol/l.

Plasma renin activity (1.6 ng/ml/h normal 0.5–2.6) and aldosterone (32 pg/ml normal 30–160) were both in the normal range. On ultrasonography, kidneys were normal and no adrenal masses were identified. Clinical history was negative for vomiting, diarrhoea, diuretics, laxative or liquorice abuse.

The rapid correction of hypokalaemia with small amounts of potassium and the absence of excessive potassium excretion pointed to potassium transcellular shift as the cause of hypokalaemia. The association with lower limb weakness and paralysis in the last episode was compatible with the syndrome of sporadic periodic hypokalaemic paralysis, since family history was negative.¹

Further evaluation of the medical history revealed that in February 2010 the patient had started to complain of sweating, tachycardia and tremors. Blood tests showed thyrotoxicosis with TSH <0.01 mU/l (normal 0.3–4.6). The endocrinologist prescribed metimazole, but, 1 month later, the patient stopped taking the drug.

Thyroid status evaluation in our Unit showed persistent hyperthyroidism: TSH was <0.01 mU/l (normal 0.3–4.6), FT3 28 pg/ml (normal 4.2–8.1) and FT4 61 pg/ml (normal 10–28). We found very high values of autoantibodies: anti-TSH receptor 15 U/l (normal <1.5), anti-TPO 9741 U/ml (normal <60), anti-TG 6325 U/ml (normal <60) and antimicrosomal 3980 U/ml (normal <50).

OUTCOME AND FOLLOW-UP

We started therapy with 15 mg/day of metimazole in three divided doses. Serum potassium, a few days after discharge, was about 5.0 mmol/l. The patient completely recovered and he had no muscular symptoms in the following 8 months.

DISCUSSION

THPP is a rare manifestation of thyrotoxicosis, characterised by hypokalaemia, recurrent episodes of muscular weakness and complete inability to walk, which regress with correction of hypokalaemia.^{1 2} THPP is most widely reported and studied in Asian populations, in whom there is a 10-fold higher incidence of this complication than in Caucasian populations.¹⁻³

Only few cases of THPP have been described in non-Asian populations including the Italians.¹⁻⁷ However, THPP is becoming more frequent in western countries because of immigration. Most cases of THPP occur in men despite the higher incidence of hyperthyroidism in women. The age of onset of symptoms is between 20 and 39 years in approximately 80% of patients. This later age of onset is helpful to distinguish THPP from the familial periodic paralyses, which present at a younger age but adolescents with THPP have been reported too.²

Symptoms of THPP usually appear when serum potassium concentration is lower than 3 mmol/l. Paresis or paralysis is the most recurrent symptom. It generally appears after physical exertion or during the warm season, affecting mainly the lower extremities and the proximal muscles and possibly preceded by lower limbs cramps, stiffness or pain. The episodes are self-limiting and stop spontaneously after few hours with complete recovery.¹⁻³ In some cases, THPP can be a life-threatening syndrome because of the involvement of the respiratory muscles.⁶

Before making a diagnosis of THPP, it is necessary to exclude other causes of paralysis and other and more common causes of hypokalaemia.

Therapy is based on both correcting thyroid hyperactivity and providing oral or intravenous supplements of potassium until complete recovery of the symptoms and improvement of clinical status.

Because of its rare prevalence especially in the western population, THPP could not be easily recognised. For this reason, an assessment of thyroid function must be performed in all young or middle-aged men who have recurrent episodes of severe muscular weakness.

The aetiology of THPP is not completely clear. It has been suggested that it is caused by an increase in intracellular shift of potassium due to hyperactivity of Na/K ATPase pump. Na/K ATPase, in fact, is activated by insulin and β 2 adrenergic receptor stimulation. Thyroid hormones seem to increase the number of β 2 adrenergic receptors in

the skeletal muscles and, consequently, the Na/K ATPase activity.^{3 4} Hyperthyroidism, moreover, increases not only Na/K ATPase activity, but also the passive transmembrane flux of these ions.³

It has also been suggested that there is a genetic predisposition to thyrotoxic periodic paralysis. Because of the similarity with familial periodic paralysis, genetic studies have focused on mutations of genes involved in the familial paralysis, like calcium (CACN1AS), potassium (KCNE3) and sodium (SCN4A) channel genes. However, investigations have not yet clarified the role of such polymorphisms in the disease pathogenesis or genetic differences between Asians and Caucasians who suffer from this condition.^{3 7}

Learning points

- Hypokalaemia linked to excessive potassium losses is a common clinical problem in medical and surgical wards.
- Hypokalaemia determined by rapid intracellular shift of potassium is a far less common condition, which can lead to periodic paralysis and admission in the emergency room.
- In Western countries, the most commonly diagnosed type of hypokalaemic periodic paralysis is the familial form, which is a genetically determined channelopathy. Less commonly, hypokalaemic periodic paralysis is sporadic and can be associated with thyrotoxicosis.
- Because of its low prevalence in the western population, the diagnosis of THPP can be easily missed in non-Asian countries.

Competing interests None.

Patient consent Obtained.

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