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CASE REPORT

Thyrotoxic hypokalaemic periodic paralysis in a Caucasian man who had already started treatment for hyperthyroidism

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Abstract

Thyrotoxic hypokalaemic periodic paralysis (THPP) is characterised by the triad hyperthyroidism, hypokalaemia and brief transient paralysis with proximal muscle weakness. It is a rare disease worldwide, but particularly prevalent in Asian men. The symptoms arise as a result of increased sodium-potassium adenosine triphosphatase (Na/K-ATPase) pump activity on the cell membrane, probably influenced by thyroid hormone, insulin and β-adrenergic impulses. An intracellular shift of potassium occurs and consequently leads to paralysis. We describe a Caucasian man who had already started treatment for hyperthyroidism, including propranolol, which is assumed to have a protective effect against recurrent paralytic attacks in THPP.

Introduction

Thyrotoxic hypokalaemic periodic paralysis (THPP) is a rare disease, especially in non-Asian populations. The transient paralysis is caused by a rapid intracellular shift of potassium. As a result of the sometimes very severe hypokalaemia, serious and potentially fatal complications may occur. Therefore, recognition and acknowledgement of the clinical picture is of the utmost importance.

Case report

A 38-year-old man presented to the emergency department with loss of strength in both arms and legs. A week before, he was diagnosed with hyperthyroidism after which treatment with methimazole 30 mg once daily and propranolol 40 mg three times per day was started. He was not on any other medications. For the last two days he had noticed transient weakness and sensory loss in the extremities, especially in the evening around nine o'clock and in the morning after waking up. Until then, the attacks of weakness and sensory loss had stopped on their own after about one hour, without residual symptoms. Furthermore, he had suffered from stiff muscles and muscle pain for the last few days. In the morning on the day of presentation, the loss of strength was so severe that he could not walk and he could only move by crawling. Except for a slight visual impairment for several months, there was no diplopia, no headache, no tingling, no difficulty swallowing, no difficulty breathing, no nausea, no vomiting and no fever.

On examination, the patient did not appear to be acutely ill; he was alert and oriented with a blood pressure of 155/70 mmHg, a regular pulse of 84 beats/min, 99% saturation at room air and a temperature of 36.5 °C. A diffusely enlarged thyroid gland was palpable. No abnormalities were found on further physical examination of heart, lungs and abdomen.

Neurological examination showed a completely reduced sensibility of the right arm and leg. The patient experienced a dull feeling, but discrimination tests were intact. Muscle strength, measured using the Medical Research Council (MRC) scale, in particular showed proximal weakness: biceps 1/1, triceps 1/1, pinch force 4-/4-, iliopsoas 1/1, hamstrings 1/1, foot flexors 4-/4-, and foot extensors 4-/4-. Reflexes: biceps tendon reflex -4/-4, triceps tendon reflex -4/-4, patellar tendon reflex 0/0, Achilles tendon reflex 0/0, and plantar reflex of the foot on both sides.

Laboratory findings showed hypokalaemia (potassium 2.2 mmol/l), a slightly decreased bicarbonate (20.2 mmol/l), mild hypophosphataemia (phosphate 0.6 mmol/l) and a low normal level of magnesium (0.73 mmol/l). In addition, a slightly increased level of glucose (7.3 mmol/l) and elevated cholestatic liver function tests was found: alkaline phosphatase 122 U/l and gamma glutamyl transferase 148 U/l with normal transaminases and bilirubin. Creatine kinase was 110 U/l and myoglobin 118 µg/l. The patient appeared to have good renal function (creatinine 56 µmol/l), normal coagulation and haematological results. Blood results were found to correspond with hyperthyroidism: thyroid stimulating hormone <0.02 mU/l and free T4 34.2 pmol/. A sample of urine was examined and showed the following values: creatinine 16.2 mmol/l, sodium 106 mmol/l, potassium 11 mmol/l, calcium 21.6 mmol/l and

phosphate 8 mmol/l. The calculated urine calcium to phosphate ratio was 2.7 mmol/mmol.

The electrocardiogram showed sinus rhythm 82 beats/min with a normal heart axis, flat T segments and the following conduction times: PR 186 ms, QRS 128 ms, and QTc 624 ms (*figure 1*).

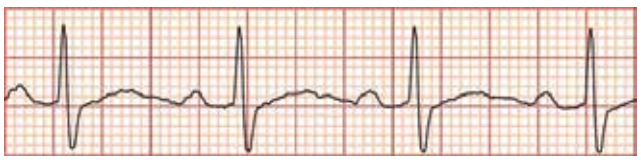

Figure 1. Detail of the ECG at presentation (lead II): heart rate 82 beats/min, PR interval 186 ms, QRS interval 128 ms, QT interval 534 ms (QTc 624 ms)

Owing to the seriousness of the loss of strength, the severe hypokalaemia and ECG abnormalities, the patient was transferred to the intensive care unit. Given the recent history of hyperthyroidism, the clinical features and laboratory test results, the diagnosis of thyrotoxic hypokalaemic periodic paralysis was made. The patient was given potassium chloride 60 mmol and his strength recovered almost completely within one hour. The serum potassium level was determined again and was found to be 4.1 mmol/l. A subsequent ECG showed normalisation of the previously recorded abnormalities: QRS 104 ms, QTc 421 ms and normalisation of the T wave (*figure 2*). When checking the serum after six hours, the potassium level remained 4.3 mmol/l without further supplementation.

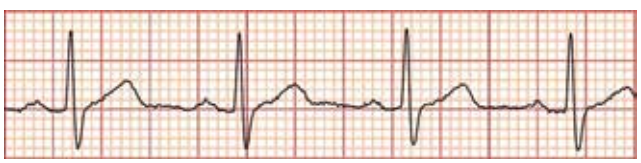

Figure 2. Detail of the ECG just after potassium chloride suppletion and recovery of muscle weakness (lead II): heart rate 84 beats/min, PR interval 165 ms, QRS interval 104 ms, QT interval 356 ms (QTc 421 ms)

The patient stayed in the intensive care unit for 24 hours. In this period, the loss of strength and reduced sensibility did not occur again. No heart rhythm disturbances were observed. Once again, the serum potassium level was measured and found to remain stable at 4.3 mmol/l. The phosphate level appeared to be corrected to 1.4 mmol/l without supplementation. Also, the bicarbonate level was slightly increased to 21.0 mmol/l. Finally, the patient was discharged from the hospital without any physical symptoms.

Discussion

Thyrotoxic hypokalaemic periodic paralysis (THPP) is a rare disease. Although still without a genetic explanation, its incidence clearly differs between ethnic groups.[1] THPP occurs in 2% of male Asians with hyperthyroidism, but only in 0.1 to 0.2% of Caucasian male patients. Even though hyperthyroidism is more common in women, most patients with THPP are men, 20 to 40 years of age.[2,3]

THPP is characterised by the triad hyperthyroidism, hypokalaemia and brief transient paralysis with proximal muscle weakness. In addition, the following symptoms may be present: mild myalgia, loss of muscle tone with hyporeflexia or areflexia and tachycardia. Due to the sometimes severe hypokalaemia, serious cardiac problems may occur. Attacks can persist for minutes, hours or sometimes even days. The frequency of attacks ranges from once only to several times a day.[3]

Until now, pathogenesis of the disease has not been fully clarified. It is assumed that thyroid hormone increases the sodium-potassium adenosine triphosphatase (Na/K-ATPase) pump activity on the cell membrane.[4] As a result, the potassium is driven intracellularly. This will lead to hyperpolarisation and inexcitability of the muscle fibres. The intracellular potassium shift results in hypokalaemia and paralysis. In addition, it is assumed that genetic factors are contributory, but the exact mechanism is not clear.[1,5]

At least three mechanisms can activate the Na/K-ATPase pump. Besides thyroid hormone, insulin and β-adrenergic impulses can also cause this increased activity. There may be an association with hyperinsulinaemia, since insulin also activates the sodium-potassium ATPase pump and creates an intracellular shift of potassium. For this, attacks of paralysis would occur more frequently after eating carbohydrate-rich meals or sweet snacks.[6]

Moreover, hyperthyroidism causes an increased β-adrenergic response and, as a result, increases the Na/K-ATPase pump activity even further.[1,7] Physical exercise causes potassium release from the skeletal muscle cells. On the other hand, resting after exercise results in potassium re-entering the cell. Owing to this mechanism, attacks of paralysis may occur when a person is recovering from physical exertion.

In the above-described case, hypokalaemia was accompanied by low potassium excretion in the urine, suggesting that there was no excessive loss of potassium in the urine but a massive intracellular shift of potassium.[8] Slight hypophosphataemia was also found, which was presumed to be an intracellular shift as well, because the phosphate transport is associated with potassium transport.

Given the proximal muscle weakness without an increased creatine kinase level, a myasthenia-like condition due to propranolol use was considered. However, there was no ptosis, diplopia or weakness of facial, bulbar or respiratory muscles.

The spot urine calcium to phosphate ratio was determined, since this can differentiate between THPP and familial hypokalaemic periodic paralysis.[9] As a result of the hypophosphataemia, which is caused by an intracellular shift of phosphate, a

significantly decreased renal excretion of phosphate occurs. In turn, thyroid hormone stimulates osteoblasts and bone remodelling, resulting in a high renal calcium excretion. This is possibly even further stimulated by increased glomerular filtration and reduced tubular reabsorption of calcium. Using a spot urine calcium to phosphate ratio cut-off value of 1.4 mmol/mmol (1.7 mg/mg), the sensitivity and specificity for THPP are 100% and 96%, respectively.[9] The calcium to phosphate ratio in the above-described case was 2.7 mmol/mmol and so it is well above the cut-off point of 1.4 mmol/mmol.

Treatment of THPP consists of the restoration of an euthyroid state. Furthermore, nonselective β-adrenergic blockers (such as propranolol) could have a protective effect for recurrent paralytic attacks.[7] The assumption is that this β-adrenergic blocker can reverse the excessive stimulation of the sodium-potassium ATPase pump and consequently the intracellular shift of potassium. Despite the fact that our patient had already started treatment with propranolol a week ago, he still suffered from paralytic attacks. Perhaps the treatment was started too recently to have a protective effect in this respect. Treatment in the acute phase consists of potassium supplementation, taking into account that a rebound hyperkalaemia can occur, because there is an intracellular shift of potassium and not an absolute potassium deficiency.[10]

Conclusion

Thyrotoxic hypokalaemic periodic paralysis (THPP) is a rare disorder, which is particularly prevalent in Asian men, but is also described in other races. THPP is characterised by the triad hyperthyroidism, hypokalaemia and brief transient paralysis with proximal muscle weakness. As a result of the sometimes severe hypokalaemia, serious cardiac complications may occur. It is presumed that an intracellular shift of potassium arises as a result of increased Na/K-ATPase pump activity, caused by thyroid hormone and possibly affected by insulin and β-adrenergic impulses also. A spot urine calcium to phosphate ratio may be used to differentiate between THPP and familial hypokalaemic periodic paralysis.

Treatment consists of restoring the euthyroid state. During the acute phase, potassium supplementation may be given, taking into account the risk for rebound hypokalaemia. In addition, β-blockers could have a protective effect for recurrent paralytic attacks.

Disclosures

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