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Teaching Point
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Lower limb monoparesis due to liquorice consumption

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Introduction

Since more than six decades ago, liquorice extracts have been used as treatment of gastroduodenal ulcers or Addison's disease, as adjuvant sweetener in medical mixtures and even as a sweet for children. However, the first case reports on severe side effects of liquorice consumption were observed in the Netherlands back in the 1940s [1]. Hypokalaemic respiratory muscle paralysis due to liquorice consumption remains a rare but potentially life-threatening condition, usually accompanied by a generalized muscle weakness or flaccid tetraparesis [2–5]. Here, we report an unusual presentation of this disorder as monoparesis of the lower limb.

Case report

A 70-year-old male patient presented to the emergency room with a 1-week history of painful progressive weakness of the right leg that developed after a night of step dancing. His past medical history was unremarkable apart from arterial hypertension that was firstly diagnosed 3 weeks prior to admission. He had been started on an angiotensin-converting enzyme inhibitor (ramipril 5 mg/day) and a diuretic (hydrochlorothiazide 25 mg/day). The patient denied any other medications. The patient did not report vomiting or diarrhoea.

On examination, flaccid monoparesis of the right leg (proximal muscles MRC grade 3 and distal muscles MRC grade 4) with decreased patellar reflex was found. Sensory examination was completely normal. Blood pressure was elevated at 164/94 mmHg. Heart rate was 88 per minute. Laboratory studies revealed severe hypokalaemia (1.5 mmol/L; normal values 3.5–5.5 mmol/L), an elevated creatine kinase level (6265 U/L; normal values <171 U/L), elevated myoglobin (3074 μg/L; normal values <70 μg/L), and a reduced serum phosphate level (0.47 mmol/L; normal values 0.8–1.5 mmol/L). Blood gas analysis showed a metabolic alkalosis (pH 7.50; normal values 7.34–7.42), a base excess of 6.1 mmol/L (normal values 2–3 mmol/L), standard bicarbonate of 29.9 mmol/L (normal values 22–27 mmol/L), a pO_2 of 61.3 mmHg (normal values 55–83 mmHg) and a pCO_2 of 38.5 mmHg (normal values 38–52 mmHg).

Serum sodium (146 mmol/L), calcium (2.1 mmol/L), magnesium (1.07 mmol/L), creatinine (63.3 μmol/L; estimated glomerular filtration rate 98 mL/min), blood urea nitrogen (2.8 mmol/L) and thyroid-stimulating hormone (3.17 mIU/L) were all normal. Urinary dipstick was unremarkable. Haemoglobin was 134 g/L, white blood cell count 5.6×10^9/L and platelets 323×10^9/L. Morning cortisol level (246 nmol/L; normal values 171–536 nmol/L) was normal, while renin (<0.06 pmol/L) and aldosterone levels (<75 pmol/L) were below the detection level. Ultrasound examination of the abdomen was unremarkable.

On further questioning, the patient admitted taking large amounts of liquorice extract (Radix Liquiritae) as a herbal remedy. He had taken liquorice for 5 years without professional supervision to alleviate minor epigastrial discomfort, which he supposed to be due to gastritis. In the last 3 months prior to the admission, he had been taking at least one spoonful of liquorice extract (~10 mg) daily as a tea. He purchased the liquorice extract over the counter without prescription at his local pharmacy.

Liquorice and the antihypertensive medications were discontinued, and potassium was replaced. Five days after admission, the patient was discharged with full strength in his right leg, normotensive (136/82 mmHg) and normokalaemic (potassium 3.8 mmol/L).

Discussion

Hypokalaemic neuromuscular disorders due to liquorice consumption usually present as flaccid tetraparesis [2–4] or generalized muscle weakness [5]. To our knowledge, this is the first case of a focal presentation of this disorder as monoparesis of the lower limb. In our patient, a chronic consumption of large amounts of liquorice as herbal medication resulted in hypertension, hypokalaemia and rhabdomyolysis. Discontinuation of liquorice and the diuretic

along with potassium replenishment therapy resulted in a full recovery.

Large doses of glycyrrhizic acid and glycyrrhetinic acid in liquorice extract can lead to hypokalaemia and serious increases in blood pressure. These side effects are caused by inhibition of the enzyme 11β-hydroxysteroid dehydrogenase (type 2), which is responsible for renal conversion of cortisol to locally inactive cortisone. A subsequent cortisol increase further activates renal mineralocorticoid receptors, resulting in a state of apparent mineralocorticoid excess, known as pseudohyperaldosteronism [6], while the plasma aldosterone level is low as was found in our patient. Due to the mineralocorticoid excess, potassium excretion through renal tubuli is higher, while sodium uptake is increased. It should be noted that development of hypertension is not constant, while hypokalaemia is.

Regular intake of glycyrrhizic acid can produce hypokalaemia in sensitive individuals even in the absence of factors that contribute to potassium loss. In one study, regular intake of 100 or 200 g liquorice (equivalent to 0.7 and 1.4 g glycyrrhizic acid) for 1–4 weeks resulted in a plasma potassium fall of >0.3 mmol/L in most subjects [7]. In our patient, the hypokalaemia was probably further exacerbated by the diuretic drug hydrochlorothiazide, added as a part of his antihypertensive regimen. It is likely that the hypertension itself was a result of liquorice ingestion for several years [8], as it resolved after the discontinuation of the herbal remedy.

Hypokalaemia increases the risk of developing rhabdomyolysis by several mechanisms [9,10]. One direct mechanism of damage might be the depolarization of muscle membranes [11]. Hypokalaemia also impairs muscle blood flow during exercise due to failure of potassium-mediated arteriolar dilatation, which might result in ischaemia [12]. In our patient, the excessive leg exercise (step dancing) appears to have triggered the rhabdomyolysis and paresis. Of interest, the patient presented with a monoparesis of his dominant leg, supporting the possibility that the exercise contributed to the muscle damage.

In conclusion, our patient presented with a monoparesis of the right leg due to liquorice-induced hypokalaemic rhabdomyolysis after exercise. Our case highlights the possibility of a focal presentation of this disorder. The case also emphasizes the importance of obtaining a detailed history of all medication, especially considering the increasing use of liquorice-containing herbal products obtainable over the counter.

Teaching points

(1) Hypokalaemic neuromuscular disorders due to liquorice consumption can present as generalized muscle weakness, tetraparesis and also monoparesis.

(2) One should notice that hypertension after liquorice consumption is not constant, while hypokalaemia is.

(3) Liquorice extracts were introduced for treatment of peptic ulcers more than six decades ago; however, these therapies have experienced a renaissance in paramedicine and are being discussed in the Internet.

(4) A detailed history of all medications, especially herbal products obtainable over the counter, should be collected in all unusual cases.

Conflict of interest statement. None declared.

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