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CASE REPORT

Severe hypokalaemic paralysis and rhabdomyolysis due to ingestion of liquorice

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ABSTRACT

Chronic ingestion of liquorice induces a syndrome with findings similar to those in primary hyperaldosteronism. We describe a patient who, with a plasma K^+ of 1.8 mmol/l, showed a paralysis and severe rhabdomyolysis after the habitual consumption of natural liquorice. Liquorice has become widely available as a flavouring agent in foods and drugs. It is important for physicians to keep liquorice consumption in mind as a cause for hypokalaemic paralysis and rhabdomyolysis.

KEYWORDS

Hypokalaemia, liquorice consumption, paralysis, rhabdomyolysis

INTRODUCTION

Chronic ingestion of liquorice or liquorice-like compounds induces a syndrome with findings similar to those in primary hyperaldosteronism. This syndrome is characterised by sodium retention, hypertension, hypokalaemia, metabolic alkalosis and low plasma renin activity. The hypokalaemia is usually mild; nevertheless it could become extremely severe and even life threatening. A frequently undiagnosed serious complication of hypokalaemia is rhabdomyolysis.[1,2] Here, we describe a patient who showed a plasma K^+ of 1.8 mmol/l, paralysis and severe rhabdomyolysis after the habitual consumption of natural liquorice.

CASE REPORT

A 59-year-old Caucasian man presented to the neurological outpatient department with muscular weakness that progressed to paralysis involving all extremities. He was unable to stand up from the sitting position (Gower's phenomenon). He denied nausea, vomiting, diarrhoea or the use of drugs, including diuretics. However, he had been eating nearly 200 g of liquorice a day during the last four weeks after quitting smoking. His family and past medical histories were unremarkable. He did not use alcohol.

On physical examination, his blood pressure was 187/87 mmHg, heart rate 83 beats/min, respiratory rate 15/min, and body temperature 37.9°C. His thyroid gland was not enlarged. Cardiopulmonary examination was unremarkable. There was a symmetric flaccid paralysis with areflexia in the lower and upper extremities. Fasciculations, myoclonus and muscular atrophy were not observed. The remainder of the physical examination was normal. The major biochemical abnormalities are shown in *table 1*. Laboratory tests showed severe hypokalaemia (1.8 mmol/l), metabolic alkalosis and extreme enzyme abnormalities (CK 35.063 U/l) compatible with rhabdomyolysis. Urinary potassium excretion was low. Plasma renin activity and aldosterone levels were far below the plasma level of normal. As a conformation of our diagnosis, we found a very high plasma level of glycyrrhetic acid at 257 μg/l (normal range <5 μg/l). Hypokalaemia was associated with typical electrocardiographic changes. Computed tomography scanning showed normal adrenal glands.

Table 1
Laboratory data on admission

PLASMA	
Na^+ (mmol/l)	147
K^+ (mmol/l)	1.8
HCO_3^- (mmol/l)	40
pH	7.54
Magnesium (mmol/l)	1.00
Urea (mmol/l)	3.6
Creatinine (µmol/l)	83
Creatinine kinase (u/l)	35,063
Renin activity (ng/ml/h)	3.9 (10-60)*
Aldosterone (ng/dl)	<0.04 (0.04-0.35)*
Glycyrrhetic (µg/l)	257 (<5)*

URINE	
Potassium (mmol/l)	12
Osmolality (mOsm/kg)	350

**Normal range for laboratory data.*

His initial therapy included 10 mmol of potassium chloride (KCl) per hour given by the intravenous route, and a potassium-sparing diuretic (spironolactone 100 mg/day) was prescribed. Within one week, serum levels of potassium normalised and all clinical symptoms improved. Nevertheless, potassium chloride supplementation was needed for several weeks. The serum creatine kinase isoenzymes (CK total and MB) returned to normal during a prolonged period (*figure 1*).

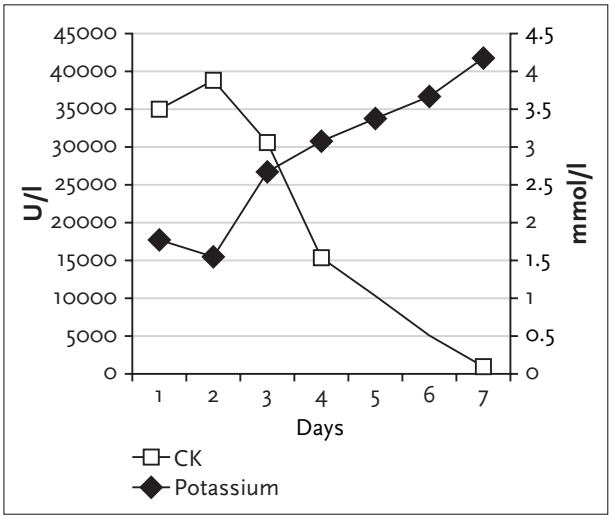

Figure 1
Time course, in days, of the patients' serum creatine kinase and potassium

DISCUSSION

Hypokalaemic paralysis and rhabdomyolysis due to liquorice consumption are rare. The potential dangers of ingesting liquorice, even in small amounts such as 50 g daily after only two weeks, are discussed here.[3] Liquorice-induced hypokalaemia is a rare disorder first described by Revers in 1946; since that time the potential neuromuscular complications of severe hypokalaemia have been demonstrated in a number of case reports.[4-7]
To mention just some examples: regular ingestion of natural liquorice, flavoured tea, white beer, grapefruit or even alternative medications has been complicated by severe hypokalaemia.
Our patient had an extreme degree of hypokalaemia and rhabdomyolysis in combination with metabolic alkalosis. This, together with the mild hypertension found on physical examination, suggested that he had a condition with high mineralocorticoid activity. Measurements of renin and aldosterone plasma levels are helpful at this point. Low plasma renin and aldosterone levels suggested an apparent mineralocortoid excess-like disorder. Diagnosis depends on elicitation of a thorough history and laboratory evidence of hypokalaemia. In this patient, it quickly became evident that this was caused by liquorice consumption.
The mechanism behind liquorice-induced hypokalaemic hypertension was briefly reviewed in this journal.[8] Liquorice causes hypokalaemia through its active metabolite, glycyrrhetic acid, which inhibits the renal enzyme 11β-hydroxysteroid dehydrogenase. This enzyme is responsible for renal conversion of cortisol to cortisone, which is inactive and does not bind to the mineralocorticoid receptor.[9] The acquired dehydrogenase inhibition due to liquorice thus leads to activation of renal mineralocorticoid receptors by cortisol, resulting in a state of apparent mineralocorticoid excess. Hypokalaemia is caused by renal and extrarenal loss of potassium or by an acute shift of potassium into the cells. Hypokalaemia is associated with typical electrocardiographic changes and marked acid-base disturbance. Incidentally paralysis and even rhabdomyolysis have been reported. The most frequent symptoms of rhabdomyolysis are fatigue, weakness, muscular pain and swelling, although it is possible that some patients are completely asymptomatic.[6,7] The severity of neuromuscular disorders tends to be proportionate to the rate at which hypokalaemia develops. Muscle destruction due to rhabdomyolysis causes the release of large amounts of potassium into the circulation. Consequently, when the clinical syndrome of hypokalaemia and rhabdomyolysis develops, the absolute concentration of potassium is far below the normal limits. Large amounts of KCl supplementation are necessary.

A liquorice-induced excessive mineralocorticoid effect usually responds to spironolactone and is reversible upon cessation of liquorice ingestion.[10] In addition to KCl supplementation and spironolactone, the administration of dexamethasone should be considered. Dexamethasone causes suppression of endogenous cortisol production and thus reduces the cortisol-mediated stimulation of the mineralocortcoid receptor.

After liquorice consumption was discontinued and KCl and spironolactone were taken, the plasma K^+ of our patient rose to normal levels and hypertension resolved, but the time required for these to occur was more than two weeks. This can be explained by glycyrrhetic acid having a large volume of distribution, a long biological half-life, and undergoing substantial enterohepatic circulation. Therefore, physicians should anticipate that the effects might take a considerable time to abate as documented in our patient.

CONCLUSION

In conclusion, severe hypokalaemia with paralysis and rhabdomyolysis is a potentially life-threatening medical emergency. Besides KCl supplementation, a vigorous search for the underlying cause is necessary to avoid missing treatable causes – in this case, liquorice consumption. Given the diagnosis, large doses of KCl supplementation for weeks are necessary because of the long half-life of glycyrrhetic acid. Liquorice has become widely available as a flavouring agent in foods and drugs. It is important for physicians to keep liquorice consumption in mind as a cause for hypokalaemic rhabdomyolysis.

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