Case report

Sweet root, bitter pill: liquorice-induced hyperaldosteronism

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In December 2002, a 49-year-old man was admitted to our hospital, with headache. He had no significant past medical history other than hypertension, diagnosed at a supermarket, while on holiday in the USA in August 2002. On admission, he was hypertensive, blood pressure (BP) 200/114 mmHg with slight ankle oedema and normal systemic examination. Blood tests showed hypokalaemia [2.2 mmol/l; normal range (NR) 3.5–5.5] plasma cortisol raised (584 nmol/l; NR 170–540), 24-h urinary cortisol raised (582 nmol;NR 100–379), 24-h urinary catecholamines normal, bicarbonate raised at the upper limit of normal (31 mmol/l; NR 19–32) with normal urea, creatinine, full blood count, erythrocyte sedimentation rate (ESR), glucose, liver, bone, thyroid profile, chest X-ray, renal ultrasound and abdominal computerized axial tomogram (CT). Hypokalaemia and uncontrolled hypertension (BP 182/102 mmHg) persisted over the next few days. He was treated with potassium supplement and alpha-blockers. Plasma renin-aldosterone studies showed both low recumbent morning renin (0.2 pmol/ml/h) and aldosterone (<70 pmol/l; NR random 100–800, recumbent 100–450) and persisted at low levels later, on the same day (renin 0.3 pmol/ml/h, aldosterone levels <70 pmol/l). Careful dietary and drug history on the ward round (Day 8) revealed that he had been taking liquorice (3 g/day) for 3 years. Liquorice-induced hyperaldosteronism was diagnosed and he was advised to stop taking liquorice. BP improved to 140/82 mmHg, potassium returned to normal 4 days after stopping liquorice and plasma cortisol was normal. One week post discharge, his BP was 165/105 mmHg. Five years later, he remains well, home BP in the range of 119–125/76–82 mmHg with normal potassium, and continues on aspirin, alpha-blockers and lansoprazole.

Discussion

Liquorice (UK) or licorice (USA) is the root of Glycyrrhiza glabra and has been used since ancient Egyptian, Greek and Roman times in the West and since the second and third centuries B.C. in ancient China. The word ‘liquorice’ is derived from the ancient Greek word ‘sweet root’. This flavour is found in a wide variety of liquorice candles, candies, herbal teas, medicines, mouth fresheners (‘jintan’, causing this syndrome at 6–10 mg of glycyrrhizic acid (GA) per day), antacids (reported with KM powder), herbal cough mixtures, throat pears, spices and alcoholic drinks. Consumption of large quantities of liquorice can cause hypokalaemia and hypertension (as observed in our patient); effects usually visible after 3–10 days.

Liquorice extract is traded both in solid and syrup form. This flavour is found in a wide variety of liquorice candies. However, in the Netherlands, liquorice candy (‘drop’) is one of the most popular forms of candy. Pontefract in Yorkshire was the first place where liquorice mixed with sugar, began to be used as a sweet. Liquorice flavouring is also used in soft drinks such as root beer and herbal teas where it provides a sweet aftertaste. This flavour is also common in medicines to disguise
unpleasant flavours. It is also popular in Italy and Spain in its natural form and the root of the plant is chewed as a mouth freshener. Liquorice is also popular in Syria where it is sold as a drink and also dried liquorice root is chewed as a sweet. Black liquorice contains ~100 calories per ounce (28 g). Chinese cuisine uses liquorice as a culinary spice for savoury foods. Other herbs and spices of similar flavour include anise, star anise, tarragon and fennel. It is also a main ingredient of a soft drink in Egypt called Erk-soos.

Consumption of large quantities of liquorice can cause hypokalaemia and hypertension as observed in our patient. It has been shown that liquorice inhibits 11β-hydroxysteroid dehydrogenase, preventing local inactivation of cortisol and allowing cortisol inappropriate access to intrinsically non-specific renal mineral or corticoid receptors. Unsweetened liquorice is also consumed in the form of small black pieces (Figure 1), made only from 100% pure liquorice extract, the taste is bitter and intense and is also popular in the UK (‘L.Imps’). This compound impairs the action of enzyme, 11β-hydroxysteroid dehydrogenase that converts cortisol to cortisone in aldosterone-responsive tissues (renal tubules). Cortisol occupies mineralocorticoid receptors, mimicking aldosterone due to equal receptor affinity and higher circulating cortisol compared with aldosterone, inducing a syndrome that mimics primary hyperaldosteronism leading to hypertension, hypokalaemia, metabolic alkalosis and a low-plasma renin activity; the unique feature to this syndrome is that plasma aldosterone level is also reduced. The direct action of GA on mineralocorticoid receptors has also been suggested. In one study, it has been shown that liquorice-induced hypertension may be the cause of 3% of all hospital cases. A hormonal assessment is characterized by low-plasma aldosterone, increased urinary-free cortisol (as in our patient), increased cortisol metabolites/cortisone metabolite ratio and reduced urinary tetrahydrocortisone/(5β-tetrahydrocortisol plus 5α-tetrahydrocortisol) < 0.5 (NR 0.7–1.2).

Cessation of liquorice is effective in patients ingesting this compound. The source of the ingested liquorice may not be obvious as sometimes, it is

![Figure 1. Liquorice tablets consumed by the patient.](image)
present in flavoured chewing gum and tobacco. ‘Asam boi’\(^3\) and ‘Shakuyaku Kanzou Tou’\(^4\) leading to pseudo-hyperaldosteronism, severe hypokalaemic paralysis and rhabdomyolysis\(^5\) due to ingestion of liquorice, liquorice-induced hypertensive encephalopathy (50 g liquorice per day, i.e. 100 mg of GA)\(^2\) and life-threatening ventricular tachycardia have been described. Liquorice-induced pseudo-hyperaldosteronism is under-diagnosed and can be easily missed without careful consideration. A good dietary and drug history on substances suspected to contain glycyrrhizic acid should be a routine aspect of investigating the causes of secondary hypertension.

Conflict of interest: None declared.

References