POSTGRADUATE MEDICINE, 2017
VOL. 129, NO. 3, 329–331
http://dx.doi.org/10.1080/00325481.2017.1291062

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CLINICAL FOCUS: GASTROENTEROLOGY, HEPATOLOGY & NEPHROLOGY
CASE REPORT

Licorice-induced hypertension: a case of pseudohyperaldosteronism due to jelly bean ingestion

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ABSTRACT

Hypertension is one of the most common problems encountered in the primary care setting. Numerous secondary causes of hypertension exist and are potentially reversible. The ability to screen for such causes and manage them effectively may spare patients from prolonged medical therapy and hypertensive complications. Licorice can cause hypertension and hypokalemia due its effects on cortisol metabolism. We report a case of jelly bean ingestion that highlights the presentation, pathophysiology and management of licorice-induced hypertension.

ARTICLE HISTORY
Received 20 November 2016
Accepted 1 February 2017

KEYWORDS
Licorice; hypertension; aldosteronism; hypokalemia; adrenal cortex hormones

1. Introduction

Hypertension is one of the most common problems in the primary care setting, with an estimated prevalence of 23% in adults in one Canadian study [1]. Though the majority of this burden is essential hypertension, there are various secondary causes. The ability to screen for secondary hypertension quickly and efficiently may help primary care physicians offer targeted and more effective therapy to their patients. It may also help spare patients from lifelong medications and associated side effects.

Licorice is a known cause of secondary hypertension. Glycyrrhetinic acid, the active ingredient in licorice, causes hypertension through its effects on cortisol metabolism and the renin-angiotensin-aldosterone system (RAAS) (Figure 1) [2–4]. The effects are seen within 3–10 days of the start of licorice consumption and the maximal hypertensive effect occurs within 2 weeks [5,6]. Additionally, glycyrrhetinic acid has been found to effect a pro-inflammatory change in protein expression *in vitro*, likely mediated by direct action on the mineralocorticoid receptor [7].

We describe a case that demonstrates the presentation and management of licorice-induced hypertension. The patient has provided written consent for his case to be described in our manuscript and our case report was not submitted for ethics review as per institutional board guidelines.

2. Case description

A 51-year-old man presented to a community emergency department with a 3-day history of abdominal pain and 1-day history of decreased appetite, vomiting, and diarrhea. He reported dry mouth and polydipsia but no polyuria or muscle weakness. Initial workup and physical examination revealed no significant abnormalities other than an elevated blood pressure of 174/62 mmHg, tender abdomen (no obstructive or peritoneal signs), and hypokalemia with a potassium of 2.6 mmol/L (normal 3.5–5.0). Sodium was slightly elevated at 147 mmol/L (137–145) and bicarbonate was increased at 34 mmol/L (22–30). He was admitted to hospital for pain control and refractory hypokalemia. Repeated boluses of IV potassium (total of 100 mEq over 24 h) were given with marginal improvement of serum potassium to 2.8 mmol/L. Abdominal pain resolved within 24 h, but he remained both hypokalemic and hypertensive with a systolic blood pressure over 170 mmHg. This raised suspicion for hyperaldosteronism and prompted an endocrinology consult.

The patient had no history of hypertension and was on a low dose of propranolol for essential tremor. He took no diuretics and had no classical features of Cushing's disease. Upon further questioning, it was found that he had recently started eating large amounts of black licorice flavored jelly beans (one bag of approximately 50 jelly beans daily), which he continued to eat in hospital. To investigate for hyperaldosteronism, serum aldosterone, renin, and random serum cortisol were drawn prior to starting spironolactone at 50 mg daily. Abdominal computed tomography scan was negative for adrenal adenoma. While awaiting these results, he was advised to stop the black licorice intake due to its potential to cause hypertension and hypokalemia. He was discharged home with spironolactone 100 mg daily and amiloride 5 mg daily, with an improved potassium level of 3.2 mmol/L and blood pressure of 150/89 mmHg.

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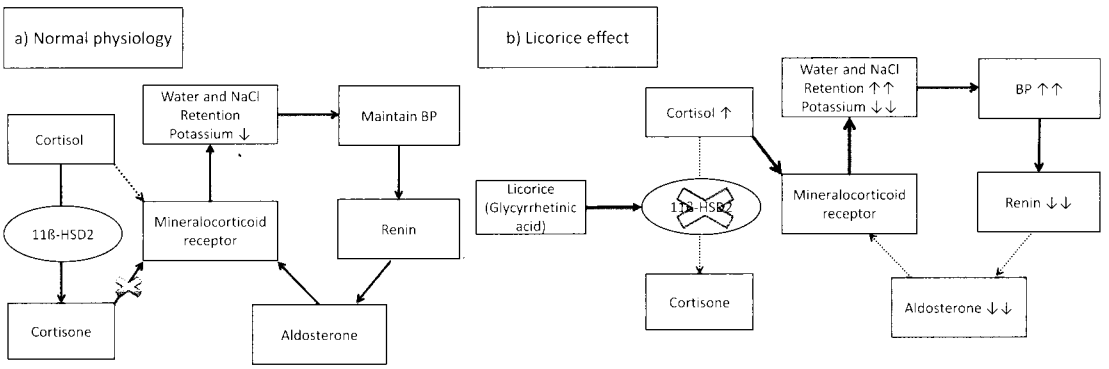

Figure 1. In normal circumstances (a), cortisol is converted into inactive cortisone by 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2). In this situation, the normal function of the renin-angiotensin-aldosterone system maintains fluid and electrolyte balance with minimal effect of cortisol on the mineralocorticoid receptor (MR). Licorice (b) contains glycyrrhetinic acid which inhibits 11β-HSD2 activity, maintaining high cortisol concentration (much higher than aldosterone) so that cortisol now exerts much greater effect via binding to the MR. This results in hypertension and hypokalemia, suppressing both renin and aldosterone.

Blood work drawn a few days post-discharge, with no further jelly bean intake, revealed an elevated potassium of 6.1 mmol/L. His blood pressure was 120/86 mmHg at this time. Spironolactone and amiloride were stopped. The results of blood work from his hospital admission returned showing suppressed renin activity of <0.02 ng/L/s (recumbent 0.02–0.86; upright 0.44–2.06) and aldosterone of <83 pmol/L (118–946). Random cortisol was normal at 282 nmol/L (65–540). Follow-up studies drawn approximately 10 weeks after cessation of jelly bean intake (and 9 weeks after stopping the medications) showed normalization of potassium at 4.2 mmol/L (3.5–5.0) as well as normalization of the RAAS with direct renin concentration of 13.6 ng/L (5–60) and upright aldosterone of 300 pmol/L (83–979).

Table 1. Some potential sources of licorice.

Candies
• Jelly beans
• Licorice sticks
Licorice tea
Over-the-counter medications
• Adrenal support formulas
• Cough mixtures
Chewing gum
Chewing tobacco
Alcoholic drinks
• Belgian beers
• Anisettes

Compiled with information from references [2,8,9].

3. Discussion

This case illustrates the presentation and management of licorice-induced hypertension while highlighting the importance of a detailed dietary history in the workup of hypertension.

3.1. Identifying licorice-induced hypertension

Our patient displayed several clues for a secondary cause of his elevated blood pressure. Despite no hypertensive history, he presented with stage 2 hypertension (systolic blood pressure > 160 and/or diastolic blood pressure > 100). Initial clinical presentation was consistent with manifestations of hypokalemia. The presence of hypokalemia and metabolic alkalosis suggested a hypermineralocorticoid state that required further workup.

In patients presenting with hypertension, not the least with concurrent hypokalemia, a thorough review of the patient's diet should be conducted. Numerous dietary sources of licorice have been reported (Table 1) [2,8,9]. Licorice may even be found as an additive in chewing tobacco [8]. While not applicable to our patient, smoking cessation may be a clue to licorice consumption as patients may develop new snacking habits to satisfy cravings. Licorice-induced hypertension has been previously described in such cases [10]. Furthermore, numerous naturalist web pages promote black licorice as a smoking cessation aid due to its soothing and expectorant properties [11,12]. Patients may not be aware or properly informed of the potential side effects of licorice and are unlikely to list it among their medications. A high index of suspicion, comprehensive history, and patient education are keys.

3.2. Acute management

The first step is stopping consumption of the licorice-containing food, with potassium supplementation given if needed. Mineralocorticoid receptor antagonists (MRAs) (e.g. spironolactone) or other potassium-sparing diuretics (e.g. amiloride) can be used if hypertension and hypokalemia persist despite discontinuation of licorice. MRAs decrease cortisol's ability to stimulate the mineralocorticoid receptor. Our patient remained hypertensive and hypokalemic at the time of discharge but was not willing to remain in hospital any longer. For this reason, amiloride was added alongside the spironolactone and close outpatient monitoring of his electrolytes was arranged.

Our patient was diagnosed in hospital. However, patients with serum potassium levels less than 3.0 mmol/L should be referred to hospital for cardiac monitoring and intravenous potassium repletion due to the risk of arrhythmia. Rare but serious complications of licorice-induced hypertension

including rhabdomyolysis and hypertensive encephalopathy have been reported [13–15].

3.3. Follow-up and resolution

The effects of licorice may linger long after discontinuation. Glycyrrhetinic acid may continue to inhibit 11β-HSD2 for 2–4 weeks as it is cleared from the system and the RAAS may remain suppressed for up to 3 months [16,17]. Potassium-sparing diuretics may cause hyperkalemia as this clearance occurs, as was seen in our patient. Periodic blood pressure and electrolyte monitoring are thus important, especially during the first few weeks.

4. Conclusion

A detailed history including a dietary review for potential sources of licorice is important in patients with hypertension, not the least when a secondary cause is suspected. Prompt identification and effective management of licorice-induced hypertension may spare patients from lifelong medical therapy and prevent serious complications. An understanding of the underlying pathophysiology helps primary care physicians to achieve these goals.

Funding

This paper was not funded.

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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