***Case report***

**The Root of the Problem: A case report of Licorice-Induced Hypokalemia**

**Abstract**

**Aim:**  
To highlight the importance of comprehensive medication and travel history in the evaluation of hypokalemia in returning travellers.

**Methods:**  
A case report of a 70-year-old female recently returned from China who presented with profound hypokalemia. Clinical evaluation included laboratory testing, medication review, and assessment of electrolyte levels including magnesium, renin, and aldosterone.

**Results:**

The patient was found to have severe hypokalemia requiring both intravenous and oral potassium supplementation. Magnesium was also low (0.66 mmol/L) and corrected to facilitate potassium repletion. Subsequent laboratory investigations revealed low plasma renin activity (0.16 ng/mL/hr) and low aldosterone level (<1.0 ng/dL) which suggests the possibility of herbal medications contributing to this as it was not in keeping with a primary endocrinopathy such as primary hyperaldosteronism.

**Conclusion:**  
This case underscores the need for thorough history-taking, including travel and medication use, in patients with hypokalemia. Low renin and aldosterone levels pointed to a non-renal cause, prompting consideration of exogenous substances or supplements. Identifying the underlying etiology of hypokalemia is crucial for targeted treatment and prevention of recurrence.

**Keywords:** Electrolyte, hypokalemia, licorice, acid-base

**Key Clinical Message**Hypokalemia can often be multifactorial and requires a thorough history assessing for possible causes including reduced oral intake, transcellular shift, gastric loss or renal loss. Our case highlights the significant contribution of licorice to the patient’s hypokalemia.

**INTRODUCTION**

Hypokalemia is common in hospitalized patients and can result from a variety of causes including gastrointestinal or renal losses, medication effects, endocrine disorders, and nutritional deficiencies. Identifying the underlying etiology is crucial for effective management. One of the causes of hypokalemia is the use of herbal medications and in particular licorice. Licorice has been utilized in traditional medicine since as early as 2100 BC to treat a wide range of ailments, including pain, cough, and gastrointestinal disturbances [1]. However, despite its longstanding use, licorice contains bioactive compounds that can pose significant risks in modern clinical contexts [2]. Specifically, metabolites of licorice inhibit the renal enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2), which normally converts active cortisol into its inactive counterpart, cortisone [3]. This inhibition prolongs the availability of cortisol to bind mineralocorticoid receptors, thereby inducing a state known as apparent mineralocorticoid excess (AME), also referred to as pseudohyperaldosteronism [3]. Clinically, this condition manifests as hypertension, hypernatremia, and hypokalemia [4]. Individuals particularly susceptible to severe manifestations include elderly patients, females, and those with predisposing conditions such as existing hypokalemia, hypertension, or anorexia nervosa [5].

In this report, we present the case of a 70-year-old female traveller recently returned from China, who was admitted with profound hypokalemia. This case highlights the critical importance of obtaining a comprehensive medication and travel history in evaluating returning travellers.

**CASE PRESENTATION**

A 70-year-old female returned from Guangzhou, China, where she had spent the past three months. She presented to the Emergency Department upon arrival in Australia with symptoms of persistent diarrhea, vomiting, and reduced oral intake for the preceding two weeks.

The patient had a background of seropositive rheumatoid arthritis, for which she was receiving hydroxychloroquine 200 mg daily and tocilizumab. She also had a history of total thyroidectomy, reportedly performed in China for suspected thyroid malignancy, and was maintained on levothyroxine 100 mcg daily. Her regular medications included calcitriol 0.25 µg daily, folic acid 0.5 mg daily, alprazolam 0.4 mg daily, and zolpidem 10 mg at night. She had no known drug allergies. The patient resided with her son and daughter-in-law and remained independent in her instrumental activities of daily living. She was a non-smoker and did not consume alcohol. Notably, she frequently traveled to China to fulfill ongoing family responsibilities.

On presentation, she reported gastrointestinal symptoms including diarrhea and vomiting, without associated fever, chills, or dysenteric features. She denied recent contact with ill individuals or any other signs suggestive of systemic infection. Her blood pressure on review was 181/82 mmHg.

Her investigations revealed a potassium level of 2.4 mmol/L (reference range: 3.5–5.5 mmol/L) and a sodium level of 149 mmol/L (reference range: 135–145 mmol/L), accompanied by metabolic alkalosis. Haemoglobin, white cell count, and platelet count were all within normal limits. Inflammatory markers remained normal, notably while she was receiving IL-6 inhibitor therapy, Tocilizumab. Early morning cortisol and parathyroid hormone levels were also normal. An ECG showed a QTc interval of 480 ms. A CT scan of the abdomen did not reveal any diverticular disease, which is particularly notable given her treatment with Tocilizumab. Her hypokalaemia was managed with multiple infusions of intravenous potassium as well as oral supplementation. As her magnesium level was low at 0.66 mmol/L (reference range: 0.7–1.0 mmol/L), magnesium was repleted prior to potassium to help correct the hypokalaemia more effectively. The patient’s follow-up lab results demonstrated a low plasma renin activity at 0.16 ng/ml/hr and a low aldosterone level at <1.0 ng/dL.

Upon further questioning, the patient reported using approximately 20 different herbal medications in China for a few months for general health purposes. The ingredients were not specified but suspected to contain compounds known to cause mineral imbalances. One of these compounds was confirmed to contain licorice which was consumed daily until her gastrointestinal symptoms began.

The patient’s potassium level increased to a normal value of 3.6mmol/L the next day following multiple bags of potassium replacement with additional oral supplements. Her blood pressure normalized to 131/60mmHg following a few dose of IV hydralazine. The patient was discharged the after a few days following monitoring of her potassium levels, with advice regarding the dangers of herbal medicine especially those containing licorice.

**DISCUSSION**

The renin-angiotensin-aldosterone system (RAAS) is a hormonal feedback mechanism that plays a key role in regulating sodium and potassium balance, as well as fluid homeostasis [6]. Under conditions of low blood volume, the kidneys release renin, which triggers a cascade aimed at restoring blood pressure. One of renin’s effects is the stimulation of aldosterone secretion [7]. Aldosterone, in turn, promotes sodium retention and potassium excretion, thereby increasing blood pressure [8].

This case draws parallels with reports of chronic licorice ingestion leading to mineralocorticoid excess. One such report describes a 70-year-old male with hypertension and hypokalemia due to long-term licorice consumption (60–100 g daily for 4–5 years). Licorice inhibits 11β-hydroxysteroid dehydrogenase, the enzyme responsible for converting cortisol to cortisone. This results in elevated cortisol levels acting on mineralocorticoid receptors, mimicking hyperaldosteronism—a condition referred to as apparent mineralocorticoid excess (AME) [3].

A narrative review done by Ceccuzzi et al. regarding licorice toxicity discussed how licorice, whose active component is glycyrrhizin, has long been recognized for its therapeutic benefits in conditions such as metabolic syndrome, asthma, oral ulcers, mental stress, and chronic liver disease, as well as for its lipid-lowering effects. Historically, it was used in Assyrian and Egyptian medicine for treating bruises and swelling, and in traditional Chinese medicine to enhance the efficacy of other drugs, relieve fatigue, reduce phlegm, and treat asthma. Additional uses include managing allergic skin conditions, improving gastrointestinal symptoms, and serving as a mild laxative, with possible roles in anticarcinogenic, antimicrobial, and antiviral activity [8].

A review of 104 case reports identified hypertension and electrolyte disturbances—particularly hypokalaemia—as the most frequent features of liquorice toxicity, with severe cases leading to arrhythmias, muscle paralysis, rhabdomyolysis, and coma. Diagnosis is typically based on clinical history, as glycyrrhetinic acid is rarely detected in the blood. Interestingly, this review challenges previous assumptions by suggesting that female sex and older age may not be significant risk factors for developing liquorice toxicity [8].

The differential diagnoses for our patient centered around causes of low-renin hypertension, including conditions such as Conn syndrome, Liddle syndrome, enzyme deficiencies like 11β-hydroxylase and 17α-hydroxylase deficiency, and Apparent Mineralocorticoid Excess (AME) [9]. Conn syndrome, also known as primary hyperaldosteronism, is typically caused by an aldosterone-producing adenoma in the adrenal gland [10]. This condition leads to autonomous aldosterone secretion, which suppresses plasma renin activity. Consequently, it is characterized by elevated aldosterone levels and low renin. Given that our patient does not exhibit elevated plasma aldosterone, Conn syndrome is unlikely to be the underlying cause. Enzyme deficiencies, specifically of 11β-hydroxylase and 17α-hydroxylase, represent forms of congenital adrenal hyperplasia. These are inherited in an autosomal recessive manner and result from mutations in the *CYP11B1* and *CYP17* genes, respectively [11]. Both enzyme defects impair cortisol synthesis, leading to reduced serum cortisol levels.

In our patient, the etiology of the hypokalemia and hypomagnesemia could be multifactorial, with potential contributions from herbal compounds (licorice), gastrointestinal losses, and reduced intake.

**CONCLUSION**

Hypokalemia can result from various causes, including gastrointestinal or renal losses, transcellular shifts, or reduced oral intake, making a thorough history essential for identifying the underlying etiology. Additionally, the use of herbal medications, particularly those containing licorice, can exacerbate hypokalemia.

**Ethical statement and Consent**

The author has obtained written informed consent from the patient. Patient information has been deidentified for confidentiality purposes.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

**REFERENCE**

1. Shibata S. A drug over the millennia: pharmacognosy, chemistry, and pharmacology of licorice. Yakugaku Zasshi. 2000;120:849–862. doi:10.1248/yakushi1947.120.10\_849.
2. Bush TM, Rayburn K, Holloway SW, et al. Adverse interactions between herbal and dietary substances and prescription medications: a clinical survey. Altern Ther Health Med. 2007;13:30–35.
3. Farese RV Jr, Biglieri EG, Shackleton CHL, Irony I, Gomez-Fontes R. Licorice-induced hypermineralocorticoidism. N Engl J Med. 1991;325:1223–1227. doi:10.1056/NEJM199110243251706.
4. Deutch MR, Grimm D, Wehland M, Infanger M, Krüger M. Bioactive candy: effects of licorice on the cardiovascular system. Foods. 2019;8:495. doi:10.3390/foods8100495.
5. Nazari S, Rameshrad M, Hosseinzadeh H. Toxicological effects of *Glycyrrhiza glabra* (licorice): a review. Phytother Res. 2017;31:1635–1650. doi:10.1002/ptr.5893.
6. Baudrand R, Vaidya A. The low-renin hypertension phenotype: genetics and the role of the mineralocorticoid receptor. Int J Mol Sci. 2018;19:546. doi:10.3390/ijms19020546.
7. Xu N, Hirohama D, Ishizawa K, et al. Hypokalemia and pendrin induction by aldosterone. Hypertension. 2017;69:855–862. doi:10.1161/HYPERTENSIONAHA.116.08519.
8. Cappellini F, Molinaro A, Montagnani A, et al. Liquorice toxicity: a comprehensive narrative review. Nutrients. 2023;15(18):3866. doi:10.3390/nu15183866.
9. Ganguly A. Primary aldosteronism. N Engl J Med. 1998;339(25):1828–1834. doi:10.1056/NEJM199812173392507.
10. White PC. Inherited forms of mineralocorticoid hypertension. Hypertension. 1996;28(6):927–936. doi:10.1161/01.hyp.28.6.927.
11. Abriel H, Loffing J, Rebhun JF, et al. Defective regulation of the epithelial Na⁺ channel by Nedd4 in Liddle's syndrome. J Clin Invest. 1999;103(5):667–673. doi:10.1172/JCI5713.