

## Licorice Consumption Causing Severe Hypokalemic Paralysis

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**Hypokalemic paralysis due to licorice consumption is extremely rare, with only 40 cases in the English literature describing paralysis secondary to exposure to licorice in candies, medications, chewing tobacco, and herbal preparations. We describe a patient who suffered life-threatening hypokalemic paralysis caused by consumption of licorice in the form of a tea sweetener superimposed on long-term consumption of licorice candy. Aggressive fluid and potas-**

**sium replenishment produced complete and lasting recovery. To our knowledge, this is the first report of hypokalemic paralysis due to exposure to licorice as a tea sweetener, a common custom among the Arab population. The case emphasizes the importance of considering patients' cultural backgrounds and local customs, which often may lead the treating physician to the correct clinical diagnosis.**

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**H**ypokalemic paralysis due to licorice consumption is extremely rare. We describe a patient who experienced a life-threatening event after exposure to licorice as a tea sweetener, a common custom among the Arab population.

### REPORT OF A CASE

A 36-year-old previously healthy Palestinian man from Eastern Jerusalem presented to the emergency department with a 4-day history of rapidly progressive limb weakness. Bilateral paresis first developed in his legs and hands, progressed to his arms, thighs, and torso, and caused extreme difficulty in walking. On the day of his admission, the patient had difficulty sitting up or raising his hands from the bed.

On examination, the recumbent patient was unable to move yet was fully alert, cognizant, and afebrile. Mild hypertension (blood pressure, 150/100 mm Hg) was noted. Neurologic examination revealed severe bilateral weakness of the proximal and distal muscles of all 4 limbs and bilaterally absent patellar, ankle, and triceps reflexes; plantar responses were flexor. The patient had no evidence of meningeal, cranial nerve, or central nervous system involvement, sphincter disturbance, muscle wasting, or muscle tenderness.

Results of laboratory studies (blood cell count, erythrocyte sedimentation rate, toxic screen, arterial blood gas, urinalysis), lumbar puncture, chest radiography, and computed tomography of the head showed no abnormalities. Electrocardiography revealed a mildly elongated QT interval. Serum biochemistry was remarkable only for severe hypokalemia (potassium, 1.7 mEq/L) and a mildly elevated creatine kinase level (800 U/L).

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The patient's weight was stable, he consumed a balanced diet, and he did not have diarrhea, excessive sweating, or symptoms of hyperthyroidism, Cushing syndrome, or pheochromocytoma. He had no previous episodes of muscular weakness or known personal or family history of renal disease, endocrine disorders, propensity for electrolyte disturbances, or periodic paralysis. He denied use of licorice, chewing tobacco, and prescribed, over-the-counter, natural, or herbal medications or abuse of drugs, alcohol, or laxatives and had no risk factors for human immunodeficiency virus.

A 24-hour urine collection study revealed high urinary excretion of potassium relative to blood levels, sodium excretion of 400 mEq/L, no amino acid excretion, and normal levels of catecholamines. Results of thyroid function and low-dose dexamethasone suppression tests were normal. Abdominal ultrasonography, including a duplex scan of the renal arteries, was unremarkable.

The patient was treated with large amounts of intravenous and oral potassium chloride, which resulted in normalization of the serum potassium and creatine kinase levels after 3 days and concomitant complete restoration of muscle strength and motor reflexes. He was gradually weaned from all potassium supplements, and his electrolyte levels remained stable and normal throughout the rest of his hospitalization.

On further questioning, the patient admitted that during the previous year he and his 3 sons had consumed a half bag (25 g) of licorice candy daily. He also noted that during the 2 weeks before his admission he drank large amounts of tea prepared from an extract purchased at one of East Jerusalem's popular "sus houses" specializing in the production of licorice-sweetened tea ("sus" is Arab slang for licorice). We estimate that the patient consumed an additional 100 mg of glycyrrhizic acid daily with the tea, which aggravated his hypokalemia and resulted in the development of the progressive life-threatening paralysis. Our unfamiliarity with Arab

slang (“sus” for licorice) and the unique local customary usage of the substance resulted in a delayed diagnosis.

The patient’s children (who did not drink the tea) remained asymptomatic and refused to be examined or to have blood withdrawn for testing. The patient was discharged after 10 days of hospitalization with strict precautions to avoid licorice and licorice-flavored products. At 18-month follow-up, he was normotensive, normokalemic, and free of any residual weakness.

## DISCUSSION

Licorice-induced hypokalemia is a rare disorder first described by Revers in 1946<sup>1,2</sup>; only 40 cases have been reported in the English literature. Previous publications have reported exposure through licorice consumption as a candy or by ingestion of licorice-containing products such as the antituberculosis medication *p*-aminosalicylic acid,<sup>3,4</sup> the anti-peptic ulcer medication carbenoxolone sodium,<sup>5</sup> the French alcoholic beverage *boisson de coco*,<sup>6,7</sup> chewing tobacco,<sup>8</sup> and some Oriental herbal preparations.<sup>9</sup> Symptoms of the disorder include mild hypertension, muscular weakness, flaccid quadriplegia, and, less frequently, myalgia, peripheral dysesthesia, and cranial nerve involvement. Laboratory tests reveal hypokalemia, mildly elevated creatine kinase levels, and decreased plasma renin activity.<sup>10,11</sup>

The mechanism by which licorice’s active ingredient, glycyrrhizic acid, causes hypokalemia is through inhibition of the renal enzyme 11  $\beta$ -hydroxysteroid dehydrogenase, which is responsible for renal conversion of cortisol to locally inactive cortisone. This inhibition leads to activation of renal mineralocorticoid receptors by cortisol, resulting in a state of apparent mineralocorticoid excess.<sup>12-14</sup> Diagnosis depends on elicitation of a thorough history and laboratory evidence of hypokalemia. Treatment with potassium supplementation and discontinuation of licorice consumption usually lead to complete recovery.

Hypokalemia is caused by renal or extrarenal loss of potassium or by an acute shift of potassium into cells. Paralysis has been reported in some, but not all, cases of hypokalemia. Although most cases are due to familial periodic paralysis, sporadic cases have been associated with diverse underlying etiologies, including thyrotoxic periodic paralysis, barium poisoning, renal tubular acidosis, primary hyperaldosteronism, licorice ingestion, and gastrointestinal potassium losses.<sup>15</sup>

Regular daily intake of 100 mg of glycyrrhizic acid produces adverse effects in sensitive individuals, and consumption of 400 mg/d produces adverse effects in most subjects.<sup>16</sup> Therefore, in patients with hypokalemic paralysis who consume relatively low amounts of glycyrrhizic acid, the physician should seek additional contributing factors that can affect potassium balance, such as diarrhea or

the use of diuretics. Increased salt intake may potentiate the adverse effects of glycyrrhizic acid.<sup>17</sup> Our patient’s elevated urinary excretion of sodium suggests that he had consumed large amounts of salt before admission.

## CONCLUSION

Our patient’s consumption of licorice candy and tea sweetener resulted in severe symptomatic hypokalemic paralysis. The use of licorice in tea, prevalent among the Arab population, is generally unknown in Western countries and, to the best of our knowledge, has not been described previously as a cause of severe hypokalemic paralysis. Our case emphasizes the importance of thorough history taking. Information about a patient’s cultural background, local customs, and slang language can greatly enhance communication with the patient and may yield important clues to the cause of the patient’s complaints. In addition, patients’ ethnic backgrounds may profoundly influence their perception of the illness and their compliance with medical treatment.

## REFERENCES

1. Revers FE. Question of therapeutic action of licorice juice on gastric ulcer [in Dutch]. *Ned Tijdschr Geneesk.* 1946;90:135-137.
2. Revers FE. Licorice juice in therapy of ventricular and duodenal ulcers [in Dutch]. *Ned Tijdschr Geneesk.* 1948;92:2968-2972.
3. Cayley FE. Potassium deficiency in *p*-aminosalicylic acid therapy: cardiac and paralytic effects. *Lancet.* 1950;1:447-448.
4. Heard KH, Campbell AH, Hurley JJ. Hypokalemia complicating sodium para-amino-salicylate therapy for pulmonary tuberculosis. *Med J Australia.* 1950;2:606-612.
5. Baron JH. Side-effects of carbonoxolone. *Acta Gastroenterol Belg.* 1983;46:469-484.
6. Mollaret P, Goulon M, Tournilhac M. Quadriplegie avec hypokaliemie et alcalose metabolique secondaire a l’ingestion massive et prolongee d’extraite de réglisse chez un psychopathe ethylique et potomane. *Bull Mem Soc Med Hop Paris.* 1960;1:491-512.
7. Jenny M, Muller AF, Fabre J, Mach RS. Hypokaliemie et alcalose par ingestion abusive d’extraite de réglisse (Liquorice) et d’eau bicarbonatée. *Schweiz Med Wochenschr.* 1961;91:869-875.
8. Blachley JD, Knochel JP. Tobacco chewer’s hypokalemia: licorice revisited. *N Engl J Med.* 1980;302:784-785.
9. Sugimoto K, Shionoiri H, Inoue K, Kaneko Y. A case report of hypokalemic myopathy due to ingestion of large dose of “jintan” [in Japanese]. *Nippon Naika Gakkai Zasshi.* 1984;73:66-70.
10. Card WI, Mitchell W, Strong JA, Taylor NRW, Tompsitt SL, Wilson JMG. Effects of liquorice and its derivatives on salt and water metabolism. *Lancet.* 1953;1:663-668.
11. Epstein MT, Espiner EA, Donald RA, Hughes H. Liquorice toxicity and the renin-angiotensin-aldosterone axis in man. *BMJ.* 1977;1:209-210.
12. Molhuysen JA, Gerbrandy J, deVries LA, et al. A liquorice extract with deoxycortone-like action. *Lancet.* 1950;2:381-386.
13. Stewart PM, Wallace AM, Valentino R, Burt D, Shackleton CH, Edwards CR. Mineralocorticoid activity of liquorice: 11-beta-hydroxysteroid dehydrogenase deficiency comes of age. *Lancet.* 1987;2:821-824.
14. Farese RV Jr, Biglieri EG, Shackleton CH, Irony I, Gomez-Fontes R. Licorice-induced hypermineralocorticoidism. *N Engl J Med.* 1991;325:1223-1227.
15. Ahlawat SK, Sachdev A. Hypokalaemic paralysis. *Postgrad Med J.* 1999;75:193-197.
16. Stormer FC, Reistad R, Alexander J. Glycyrrhizic acid in liquorice—evaluation of health hazard. *Food Chem Toxicol.* 1993;31:303-312.
17. Ferrari P, Sansonnens A, Dick B, Frey FJ. In vivo 11beta-HSD-2 activity: variability, salt-sensitivity, and effect of licorice. *Hypertension.* 2001;38:1330-1336.