A sweet tooth as the root cause of cardiac arrest

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A 71-year-old woman was admitted with hypotension and bradycardia. An electrocardiogram showed flattened T waves and increased U wave prominence, resulting in a long QT(U) syndrome. Her initial serum potassium level was 1.6 mmol/L (all other electrolytes, including magnesium, were normal). She suffered recurrent ventricular tachycardia and ventricular fibrillation arrest requiring direct current cardioversion and high-dose intravenous potassium chloride replacement. Systematic enquiry revealed that she had been constipated for a number of months and had resorted to consuming large quantities of liquorice on a daily basis for its laxative effects. Endocrinology review identified no primary abnormality of the renin-angiotensin-aldosterone axis, and the patient was diagnosed with hypokalemia secondary to liquorice overindulgence. Liquorice has a mineralocorticoid effect. If chronically consumed in large quantities, this effect may lead to severe depletion of whole-body potassium stores. The present case highlights a rare but important cause of hypokalemic cardiac arrest of which all acute care physicians should be aware.

Key Words: *Cardiac arrest; Hypokalemia; Liquorice; Pontefract cake*

Une dent sucrée à l'origine d'un arrêt cardiaque

Une femme de 71 ans a été hospitalisée en raison d'une hypotension et d'une bradycardie. L'électrocardiogramme a démontré des ondes T aplaties et une proéminence accrue des ondes U, entraînant un syndrome du QT(U) long. Son taux de potassium sérique initial était de 1,6 mmol/L (tous les autres électrolytes, y compris le magnésium, étaient normaux). Elle souffrait d'une tachycardie ventriculaire récurrente et d'un arrêt de la fibrillation auriculaire qui a exigé une cardioversion et un traitement de substitution à fortes doses de chlorure potassique intraveineux. Une exploration systématique a révélé que la femme était constipée depuis plusieurs mois et qu'elle avait recouru à une importante consommation quotidienne de réglisse en raison de ses effets laxatifs. Le bilan endocrinologique n'a révélé aucune anomalie primaire de l'axe rénine-angiotensine-aldostérone, et la patiente a obtenu un diagnostic d'hypocalcémie secondaire à une surconsommation de réglisse. La réglisse a un effet minéralocorticoïde. S'il est consommé de manière chronique en grandes quantités, il peut être responsable d'une grave déplétion des réserves totales de potassium. Le présent cas faire ressortir une cause rare mais importante d'arrêt cardiaque hypocalcémique que tous les médecins de soins aigus devraient connaître.

It has long been known that liquorice can induce a hypermineralocorticoid syndrome. We describe a case of severe liquorice-induced hypokalemia leading to recurrent nonsustained ventricular tachycardia and ventricular fibrillation (VF).

CASE PRESENTATION

A 71-year-old Yorkshire (United Kingdom) woman collapsed unconscious at home and required direct current cardioversion for VF by the paramedic ambulance crew. On arrival at the hospital, the patient was intubated and was determined to be hypotensive (66/43 mmHg). The initial 12-lead electrocardiogram showed a junctional bradycardia of 40 beats/min, with flattened T waves and increased U wave prominence, resulting in a long QT(U) syndrome (Figure 1). Intravenous atropine had no appreciable effect; therefore, temporary transcutaneous pacing was used for 10 min, before the eventual return to sinus rhythm. The initial serum potassium level was 1.6 mmol/L (all other electrolytes, including magnesium, were within the normal range; estimated glomerular filtration rate was 55 mL/min/1.73 m^2). The acid-base balance was undisturbed. Therefore, high-dose potassium supplementation was started through a central venous line and she was transferred to the intensive care unit for further management.

The patient's medical history included hypertension and a 'small' myocardial infarction in 2002. There was no antecedent history of gastrointestinal symptoms or conventional laxative use to account for her low serum potassium level. Her long-standing medications were bendroflumethiazide 2.5 mg once daily and lisinopril 20 mg once daily. All serum electrolytes were normal when they were checked by her general practitioner six months previously. However, systematic enquiry revealed that she had been constipated for a number of months and had resorted to consuming large quantities of liquorice on a daily basis for its laxative effects. It transpired that she had favoured a local Yorkshire delicacy – Pontefract liquorice cakes.

Figure 1) A *Paramedic ambulance electrocardiogram strip showing ventricular fibrillation. This was followed by direct current cardioversion to a junctional bradycardia* (**B**)

The following day, her serum potassium level increased to 2.9 mmol/L. Despite this, runs of nonsustained ventricular tachycardia continued. A further VF arrest followed, requiring intubation, direct current cardioversion and 2 min of cardiopulmonary resuscitation to restore cardiac output. Further aggressive intravenous potassium supplementation and intravenous magnesium sulphate was required to abolish ventricular arrhythmias. In total, 720 mmol intravenous and 312 mmol oral potassium chloride were required to restore serum potassium levels to the normal physiological range. During this time period, oral spironolactone and lisinopril were administered as an adjunct to maintain serum potassium levels and control arterial hypertension (bendroflumethiazide was temporarily stopped).

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By day 3, she was hemodynamically stable. Endocrinology review identified no primary abnormality of the renin-angiotensin-aldosterone axis and a diagnosis of hypokalemia secondary to liquorice overindulgence was made. A six-month outpatient review revealed that she remained asymptomatic and her serum potassium levels remained within the normal physiological range on the same combination of diuretic and angiotensin-converting enzyme inhibitor as at the time of admission. Unsurprisingly, she no longer has the same enthusiasm for Pontefract cakes.

DISCUSSION

Liquorice has long been associated with the county of Yorkshire, where it was cultivated as early as the 17th century by Dominican monks who settled around Pontefract castle. It was noted for its medicinal properties and was often prescribed by apothecaries for abdominal complaints. Nonetheless, its effects are not uniformly benign. The active ingredient of liquorice – glycyrrhizin (derived from the Greek words 'glukos' meaning 'sweet', and 'rhiza' meaning 'root') – may induce a mineralocorticoid excess syndrome producing clinically significant hypokalemia, as well as sodium retention, peripheral edema and hypertension (1). Cases of liquorice-induced cardiac arrhythmia (2) and reversible dilated cardiomyopathy (3) have been described.

In 1977, Epstein and Espiner (4) studied the effects of ingesting 100 g to 200 g of liquorice daily for one to four weeks among 14 healthy volunteers. Serum potassium concentrations fell by more than 0.3 mmol/L in 11 people, including four who had to be withdrawn from the study due to marked hypokalemia (4). These findings will not surprise senior physicians, who may recall episodes of serious potassium loss secondary to carbenoxolone, which is a liquorice-containing medication used within the past 20 years for the treatment of gastric ulceration.

In the present study, diuretic-induced hypokalemia was not considered to be a significant contributory cause. The patient was taking the lowest prescribable dose of bendroflumethiazide, which is very widely used in the United Kingdom and does not cause significant potassium loss, particularly when prescribed in tandem with an angiotensin-converting enzyme inhibitor, as in the present case.

Liquorice-induced hypokalemia is only rarely encountered in North America, where the majority of liquorice products contain flavouring but not glycyrrhizin. This is in contrast to European liquorice products. However, European immigrants (especially Dutch or English) may continue to indulge in imported delicacies, highlighting the need for awareness of this rare complication.

CONCLUSION

This is not the first time that Pontefract cakes have been implicated in the production of severe hypokalemia (5). We are aware, however, of only one other description of liquorice-related cardiac arrest in the literature (6). We suggest that a history of liquorice ingestion should be actively sought in all cases of hypokalemia, especially in the elderly population, in whom low potassium levels may be wrongly ascribed to diuretic medications alone. Patients potentially susceptible to cardiac dysrhythmias should be advised to moderate their liquorice intake, particularly if they are already on medication that may potentially lower serum potassium levels.

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