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Therapy & Toxicology



Lethal Arrhythmia Induced by Licorice

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OPEN ACCESS

Received: Jan 15, 2023

Accepted: Mar 9, 2023

Published online: Mar 21, 2023

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Disclosure

The authors have no potential conflicts of
interest to disclose.

Author Contributions

Conceptualization: Han EJ, Park JS. Writing
- original draft: Han EJ. Writing - review &
editing: Park JS.

An 89-year-old woman was referred to our clinic for recurrent syncope. The patient had felt general weakness and easy fatigue for 5 days.

On admission, she developed seizure-like movements. The monitor showed an irregular polymorphic ventricular arrhythmia (Fig. 1). Defibrillation was immediately done. After 1st



Fig. 1. On admission, monitoring HR showed repetitive polymorphic ventricular tachycardia of different types.

defibrillation, repetitive polymorphic ventricular arrhythmias of different types occurred. Over 10 hours, more than 30 defibrillations were needed. Twelve-lead electrocardiogram showed polymorphic ventricular tachycardia (Fig. 2A). After defibrillation, QT interval prolongation, junctional escape beats and premature ventricular complexes with R-on-T were observed (Fig. 2B). Corrected QT interval was 686 ms.

Initial laboratory tests revealed severe hypokalemia (potassium, 1.5 mmol/L), which might lead to QT interval prolongation. The patient had not taken any medications, possible exogenous causes of hypokalemia such as laxatives or diuretics. Laboratory test for investigating other causes of hypokalemia was performed. As plasma renin activity was suppressed (0.2 ng/ml/hr) and serum aldosterone was in normal range (206.67 pg/ml),

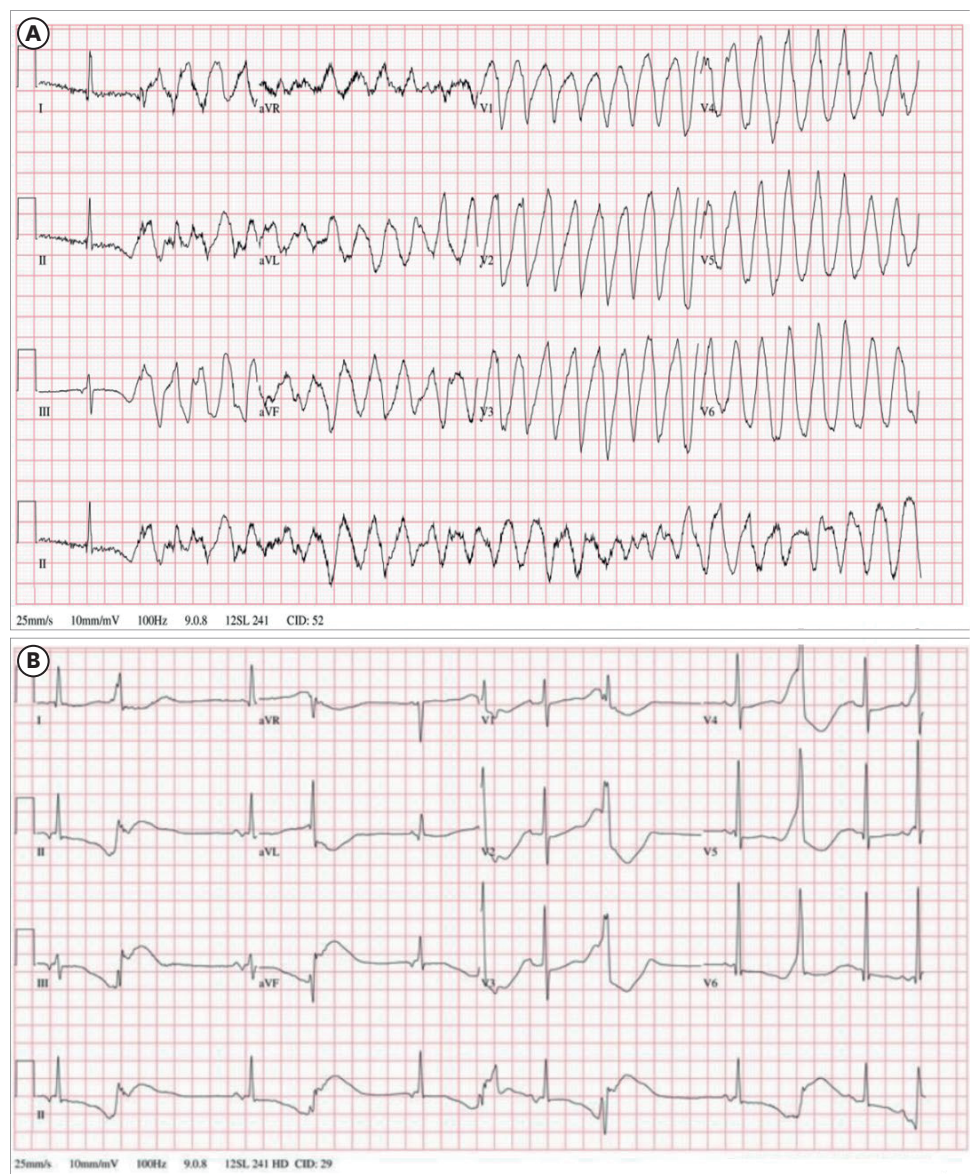


Fig. 2. Twelve-lead electrocardiogram on admission. Twelve-lead electrocardiogram showed polymorphic ventricular tachycardia (A). After defibrillation, 12-lead electrocardiogram showed prolonged QT interval, junctional escape beat and premature ventricular complexes with R-on-T (B).

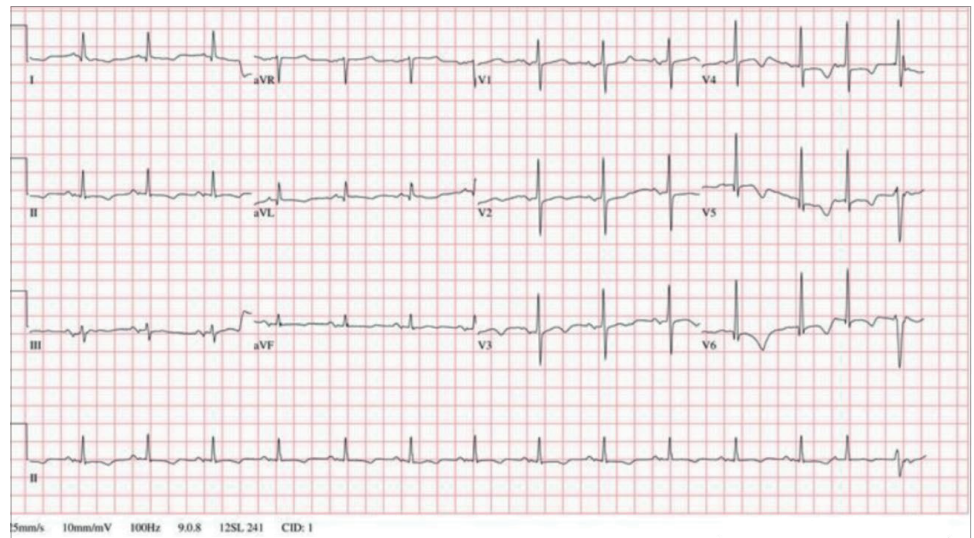


Fig. 3. After potassium replacement, 12-lead electrocardiogram showed that QT interval shortened compared with initial electrocardiogram.

pseudoaldosteronism was suspected. We rechecked her medications which could cause pseudoaldosteronism. The patient revealed taking herbal medicine containing licorice to treat chronic constipation for 2 months. She was diagnosed as licorice-induced intractable hypokalemia leading to lethal arrhythmia.

Potassium replacement was done by intravenous administration. With 10 hours' continuous infusion of potassium, her potassium level reached 3.9 mmol/L. Electrocardiogram showed QT interval shortened (**Fig. 3**). Corrected QT interval was 500 ms. After potassium replacement, no further ventricular arrhythmia occurred.

Licorice is widely used as herbal medications for indigestion and constipation, food additives and cosmetics.¹ Glycyrrhetic acid, an active metabolite of licorice, can cause mineralocorticoid overload by inhibiting the enzyme 11- β -hydroxysteroid dehydrogenase enzyme type 2.² Mineralocorticoid reaction results in pseudoaldosteronism characterized by hypertension, metabolic acidosis, sodium elevation and potassium reduction. A daily consumption of glycyrrhetic acid of 95 mg or more may cause an increase in blood pressure.^{3,4,5} In the present case, long-term use of licorice may induce pseudoaldosteronism with intractable hypokalemia, resulting in lethal polymorphic ventricular arrhythmias. As licorice could be taken without any prescription, final diagnosis was delayed due to unawareness of taking licorice.

As the class Ia antiarrhythmic drugs, such as quinidine, procainamide, and class III drugs, such as sotalol, amiodarone, prolong the repolarization phase of the cardiac action potential, antiarrhythmic drugs could worsen lethal polymorphic ventricular arrhythmias in patients with QT interval prolongation. Overdrive pacing, which can shorten the QT interval, would be another treatment option of polymorphic ventricular arrhythmias associated with prolonged QT interval.

Including licorice, there are lots of herbal medicine or their derivatives with arrhythmogenic effects, such as aloe vera, moonseed, aconitum, horny goat weed, curcumin, hawthorn

and ginseng.⁶ In addition to the medical history, herbal therapies or food additives should be taken into consideration in patients with unexplained hypokalemia or ventricular arrhythmias. To avoid unnecessary evaluation or antiarrhythmic therapy, correctable cause for ventricular arrhythmias should be fully identified. Although it is a rare case of licorice-induced intractable hypokalemia causing lethal ventricular arrhythmia, it might be getting more prevalent with increasing use of licorice.

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