

# Amiodarone for the Successful Management of Caowu Poisoning – Induced Cardiac Arrhythmia

Ming-Fu Chen,<sup>1</sup> Cheng-Hsuan Ho,<sup>2</sup> Tsung-Neng Tsai,<sup>2</sup> Pai-Shan Chen<sup>3</sup> and Sy-Jou Chen<sup>2</sup>

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## INTRODUCTION

A 61-year-old man visited the emergency department for dizziness, diaphoresis and chest pain at 1 h after ingestion of 10 g Caowu decoction (Figure 1) for his myofascial pain. The patient is a traditional Chinese medicine physician with no previous medical record. On arrival, his vital signs were as follows: body temperature, 36.6 °C; blood pressure, 106/65 mmHg; pulse rate, 43 beats/min; and respiration rate, 19 breaths/min. Electrocardiography (ECG) revealed an irregularly irregular rhythm containing multifocal atrial premature complexes (APCs) with aberrant conduction and polymorphic ventricular ectopic beats (Figure 2A). The serum levels of creatinine, alanine aminotransferase, troponin-I, sodium, potassium, free calcium, and magnesium as well as the arterial blood gas findings were unremarkable. For the symptomatic dysrhythmia with a fluctuant rhythm on bedside ECG, intravenous amiodarone (150 mg) for 10 min was prescribed, and the heart rhythm was successfully restored to normal sinus rhythm (Figure 2B), with symptomatic relief. Coronary computed tomography angiography revealed no obstructive lesion on the coronary artery, and a 24-hour Holter monitoring

showed no arrhythmia episode, except for few single ventricular premature contractions. Liquid chromatography mass spectrometry determined the serum level of aconitine, a major compound of Caowu, to be 2.45 ng/mL. In outpatient department follow-ups, the patient was noted to be asymptomatic for 6 months.

## DISCUSSION

Aconitum plants such as Caowu (dry rootstocks of



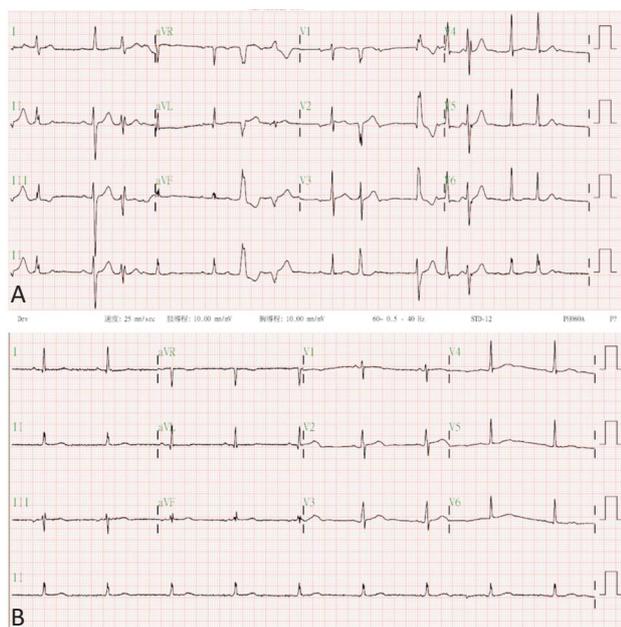
Figure 1. Sample of processed dry roots (Caowu) decocted for the patient.

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<sup>1</sup>Emergency Department, Tri-Service General Hospital, Songshan Branch, National Defense Medical Center; <sup>2</sup>Emergency Department, Tri-Service General Hospital, National Defense Medical Center; <sup>3</sup>Department and Graduate Institute of Forensic Medicine, National Taiwan University, Taipei, Taiwan.

Corresponding author: Dr. Sy-Jou Chen, Department of Emergency Medicine, Tri-Service General Hospital, National Defense Medical Center, No. 325, Section 2, Cheng-Kung Road, Neihu, Taipei 114, Taiwan. Tel: 886-937455230; E-mail: syjou.chen@gmail.com



**Figure 2.** (A) First electrocardiogram (taken at the emergency department) showing multifocal atrial premature complexes with aberrant conduction and polymorphic ventricular ectopic beats. (B) Post-amiodarone electrocardiogram showing regular sinus rhythm.

*Aconitum kusnezoffii*), Chuanwu (the root tuber of *A. carmichaeli*), and Fuzi (lateral root tuber of *A. carmichaeli*) are widely used as analgesics, anti-inflammatory drugs, and even cardiotoxic drugs in traditional Chinese herbal medicine. Raw aconitum roots are extremely toxic and should only be administered after properly processing the preparation to reduce and hydrolyzetoxic alkaloid content.<sup>1</sup>

Aconitine alkaloid, the main toxic ingredient of Cao-wu, has a half-life ranged from 3 to 15.4 hours. Normally, it became undetectable after 24 h. Severity of symptoms may correlate with plasma aconitine level. A blood aconitine concentrations at 3.6 ng/mL may be lethal if not treated.<sup>2</sup> In a report by Moritz et al. using highly sensitive and specific analysis method, liquid chromatography coupled with turbo ion spray tandem mass spectrometry, sinus bradycardia with polymorphic and bigeminal ventricular extrasystole were observed at the aconitine level of 1.75 ng/mL, which was measured 7 h after ingestion of aconitum napellus capsules. Cardiovascular symptoms were disappeared at calculated concentration of 0.65 ng/mL 11 h later.<sup>3</sup> Our case indicated a toxic aconitine level of 2.45 ng/mL that induced cardiovascular symptoms of both atrial and ventricular dysrhythmias.

Inappropriate aconite administration can induce cardiotoxicity and neurotoxicity through the persistent activation of voltage-sensitive sodium channels in the cell membranes because of the sodium channel-binding property of this compound; aconitine keeps the channels open, resulting in continued sodium influx and sustained depolarization, which in turn leads to the cells becoming refractory to excitation. During late phase 2 or early phase 3 of the action potential, aconitine can induce intracellular  $\text{Na}^+$  and  $\text{Ca}^{2+}$  accumulation as well as inhibit the  $\text{K}^+$  current that causes early after-depolarization. This could result in long QT intervals and increase the risk of torsades de pointes. In addition, aconitine increases sodium influx, inhibits the transient  $\text{K}^+$  current, and elevates intracellular  $\text{Ca}^{2+}$  concentrations during late phase 4 of the action potential, thereby inducing delayed after-depolarization (DAD). This effect increases the automaticity of the myocardium and the occurrence of premature ventricular beats or bidirectional ventricular tachycardia. In the present case, ECG revealed no QTc prolongation (423 ms), but several polymorphic ventricular premature complexes were observed in long lead II, which may have been related to DAD. In addition to causing ventricular arrhythmia, aconitine suppresses sinoatrial node automaticity through vagal stimulation and induces enhanced abnormal automaticity of the atrial ectopic pacemaker to generate APCs. In our case, ECG revealed several APCs with aberrant conduction in long lead II. Bedside continuous cardiac monitoring revealed intermittent bradycardia, and the lowest heart rate was approximately 30-40 beats/min. Hence, both the phenomena of vagal bradycardia and increased excitability were present in this case.

Currently, the antidote for aconite poisoning remains unknown. The management is limited to maintaining the vital signs and treating sequelae such as cardiac arrhythmia. For the treatment of aconitine-induced arrhythmia, amiodarone and flecainide are reasonable antiarrhythmic drugs because of their action on sodium channel blocking. In the report by Tai et al., ventricular arrhythmia was successfully controlled by amiodarone in five of 23 patients.<sup>4</sup> Although the exact dosage of amiodarone and temporal response was not reported, it is likely that the dose of amiodarone for correction of aconitine-induced ventricular arrhythmia depends on the amount of exposure and its toxicokinetics.<sup>5</sup> Moreover, amiodarone is a

class III agent, with Na<sup>+</sup>, K<sup>+</sup>, and Ca<sup>2+</sup> channel-blocking properties. Amiodarone mainly affects the repolarization stage, with prolongation of the action potential duration and refractory periods, thus leading to a reduction in membrane excitability. Therefore, amiodarone should be used cautiously due to side effects such as potential QT prolongation and torsades de pointes.

The present case indicates that both atrial and ventricular dysrhythmias can be observed in aconitine intoxication, and successfully restored to sinus rhythm by amiodarone. Our case highlights the efficacy of amiodarone for aconitine-induced ventricular, atrial, or even both types of arrhythmias.

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#### DECLARATION OF INTEREST

The authors declare that there are no conflicts of interest.

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