Spectrum of cardiac manifestations from aconitine poisoning

Swetha P. Karturi, MD,[*] Hjalti Gudmundsson, MD,[*] Masood Akhtar, MD,[†] Arshad Jahangir, MD,[†‡] Indrajit Choudhuri, MD[†]

From the [*]Gundersen-Lutheran Health, La Crosse, Wisconsin, [†]Aurora Cardiovascular Services, Aurora Sinai/Aurora St. Luke's Medical Centers, University of Wisconsin School of Medicine and Public Health, Milwaukee, Wisconsin, and [‡]Center for Integrative Research on Cardiovascular Aging (CIRCA), Aurora Research Institute, Aurora Health Care, Milwaukee, Wisconsin.

Introduction

Aconite is a potentially toxic root from which herbal preparations are used to treat common somatic ailments from headache to heartburn in the Southeast Asian population. Lack of awareness of aconite root use in the growing Hmong population in the United States (US) poses a potential for loss of life. We present a case of acute aconitine poisoning in a middle-aged Hmong man in whom (1) a broad spectrum of electrocardiographic changes and dysrhythmias manifested, and (2) critical illness and shock developed, requiring aggressive life support to prevent loss of life.

Case report

A 62-year-old Hmong man presented to the local emergency room with complaints of sudden-onset chest pain, dizziness, and palpitations. Little other history was obtainable owing to language barrier. The patient appeared in mild distress, exhibiting generalized weakness. Initial vital signs demonstrated hypotension and tachycardia with systolic blood pressure 60–80 mm Hg and heart rate 150–220 beats per minute. His initial electrocardiogram (ECG) (Figure 1, *top*) demonstrated sinus rhythm with low-amplitude P waves and junctional rhythm conducting with narrow QRS complex, followed by ventricular ectopics or couplets with right bundle branch block (RBBB) morphology and left axis deviation suggestive of left posterior fascicular origin. Diffuse ST-segment depression was present and the QT interval was prolonged. Ventricular ectopics occurred during the terminal phase of the T wave.

KEYWORDS Aconite; Aconitine; Conduction disturbance; Ventricular tachycardia; Long QT; Shock; Hmong
(Heart Rhythm Case Reports 2016;2:415–420)

Dr. Jahangir's research effort was, in part, supported by the National Heart, Lung, and Blood Institute grants RO1 HL101240 and R01 HL089542. **Address reprint requests and correspondence:** Dr Indrajit Choudhuri, Aurora Cardiovascular Services, 2801 W Kinnickinnic River Parkway, 840, Milwaukee, WI 53215. E-mail address: publishing6@aurora.org.

Initial blood tests revealed hypokalemia (2.9 mmol/L) and acidosis (pH 7.21) with increased anion gap (17) and elevated lactate levels (9.7 mmol/L). Troponin T (<0.01 ng/mL) and digoxin levels (0.1 ng/mL) were not elevated. Intravenous saline was administered. Bedside echocardiography demonstrated hyperdynamic left ventricular function with no regional wall motion abnormalities and no evidence of pericardial effusion. There were no findings of Takotsubo cardiomyopathy. Concern for coronary ischemia and lactic acidosis prompted urgent coronary angiography, which demonstrated nonobstructive coronary atherosclerosis with slow coronary flow. Ventriculography confirmed echocardiographic findings, demonstrating hyperdynamic left ventricular function with no wall motion abnormalities.

Vasodilatory shock was diagnosed. Poor response to fluids necessitated hemodynamic support with intravenous pressors and intraaortic balloon pump. The patient was intubated for impending respiratory failure. Blood cultures were drawn and empiric antibiotics initiated.

Incessant dysrhythmias continued, including progressive atrioventricular (AV) conduction delay, left axis deviation in beats conducting with variable QRS morphologies including left bundle branch block (LBBB), RBBB ventricular ectopy, nonsustained monomorphic ventricular tachycardia (VT) (Figure 1, *bottom*), sustained monomorphic VT (Figure 2, *top*), and bidirectional VT characterized by RBBB morphology and alternating QRS axis (Figure 2, *bottom*). Ventricular ectopy and sustained arrhythmias persisted despite treatment with intravenous amiodarone. Cardioversion restored sinus rhythm but with generally little impact on hemodynamics and with continued recurrence of dysrhythmias. Hence, further cardioversion was avoided. Empiric use of hemodynamic dialysis was considered but was deferred because of ongoing hemodynamic instability.

The patient improved both hemodynamically and electrically, and supportive care was weaned successfully over the next 48 hours. Ventricular ectopy and VT resolved and the rhythm transitioned through AV block with junctional broad and narrow escape rhythm (Figure 3, *top*) back to sinus

 http://dx.doi.org/10.1016/j.hrcr.2016.05.007

KEY TEACHING POINTS

- Narrow QRS complex beat or tachycardia is not diagnostic of supraventricular origin. In particular, narrow QRS complexes can arise from the ventricle in close proximity to the His-Purkinje system that activates right and left ventricular muscle in a balanced manner, or owing to ventricular ectopy occurring ipsilateral to bundle branch block *and simultaneous with intrinsic conduction*.
- Ventricular ectopy and ventricular tachycardia are not always the cause of hemodynamic collapse. Rather, as seen in this case, ventricular arrhythmias can be a *manifestation* of broader physiologic derangement.
- Herbal and "natural" remedies have the potential to cause lethal physiologic derangement and must be considered in the differential when traditional or more common medical etiologies are excluded.

rhythm with intact conduction and normal PR and QRS intervals with nonspecific T-wave abnormalities (Figure 3, *bottom*). The patient was discharged uneventfully and counseled against aconite root use. In follow-up, the patient has not had a recurrence of dizziness or weakness. He does still use aconite root, but only in limited amounts.

English-speaking family members were eventually found and presented to provide additional history. The patient has a history of "heartburn" but was not taking any prescription medications. He had been in his usual health on the day of presentation. Later he developed his usual heartburn symptom and ingested an herbal decoction made from boiling various herbs and roots. His symptoms did not improve over an hour and he repeated the elixir 3–4 times. Over the next half-hour, he developed chest pain, dizziness, and generalized weakness with severe nausea, vomiting, and abdominal pain. The family confirmed use of aconite root. Serum aconitine level was not obtained, owing to the late discovery of this information.

Discussion

Aconitine is a toxin found in the Aconitum plant, also known as "devil's helmet" or "monkshood" (*Aconitum napellus*) and wolfsbane (*Aconitum vulparia*), known for its toxic properties. The use of aconite root for medicinal purposes is common in the Hmong, Asian, and Indian populations to treat various ailments, including heartburn and headache.[1] Raw aconite roots are extremely toxic and must be processed to reduce the alkaloid content before use. Inadequate processing or ingestion of higher doses of the decoction of aconite roots increases the risk of poisoning.[2]

Pure aconitine has low bioavailability with little variability in the pharmacokinetic behavior after single or multiple administrations. In contrast, multiple administrations of processed Fuzi extract, the processed lateral roots of *Aconitum,* could increase the bioavailability of aconitine, which results in toxicity.[3]

Cellular mechanisms

Aconitine interacts with the voltage-dependent sodium channel present on cell membranes of excitable tissues, including myocardium, striated and smooth muscle, and neurons, altering membrane depolarization and repolarization. Aconitine binds with high affinity to the voltage-sensitive sodium channel in its open state and suppresses the conformational change to the inactive state,[4] delaying repolarization by prolonging sodium influx and membrane depolarization. Conformational changes to the channel induced by aconitine binding shift the activation threshold of the channel to a more negative potential,[2] while the inactivation curve is shifted toward a more positive potential, resulting in prolonged opening of the channel that predisposes to the development and persistence of triggered activity.[1]

At lower concentrations, aconite increases the strength of muscle fiber contraction by increasing acetylcholine release from nerve endings owing to depolarization. In synaptic clefts, the released acetylcholine binds to postsynaptic cholinergic receptors to activate sodium channels, generating action potential and muscle contraction. At higher concentrations, persistence of sodium channels in the open state results in suppression of action potential transmission and reduced axonal end-terminus acetylcholine release and depression of muscle contraction.[2]

In addition, the powerful increase in late sodium channel current owing to delayed sodium channel inactivation promotes conditions for early afterdepolarization development by prolonging depolarization, as well as activation of the sodium-calcium exchanger generating a transient inward current and development of delayed afterdepolarization;[1] thus, aconitine-induced triggered activity is related to increased late I_{Na}.

Electrocardiographic manifestations and possible underlying mechanisms

Important ECG manifestations observed in this case were supraventricular abnormalities, including low-amplitude P waves and sinus bradycardia; AV conduction abnormalities with conduction prolongation and fascicular and bundle branch block; repolarization abnormalities with QT prolongation; and ventricular ectopy and nonsustained and sustained VT with monomorphism, as well as bidirectionality that exhibited sharp, rapid QRS onset with RBBB morphology suggesting left fascicular origin.

The binding of aconitine to the sodium channel promoting persistence of the activated state can explain the ECG findings in this patient. The AV interval was observed to prolong with LBBB, suggesting conduction delay within and/or below the His bundle.[5] Preferential block in the left system fascicles or proximal block in the left bundle system