Management of life-threatening flecainide overdose: A case report and review of the literature

Nancy M. Vu, MD,[*] Terence E. Hill, MD,[†] Matthew R. Summers, MD,[†] Michael N. Vranian, MD,[†] Michael D. Faulx, MD[†]

From the [*]Internal Medicine Institute, and [†]Heart and Vascular Institute, Cleveland Clinic, Cleveland, Ohio.

Introduction

Anti-arrhythmic drug therapy carries an understood risk for toxic side effects, even at therapeutic doses. In cases of high dose ingestion these toxic effects can present rapidly with extra-cardiac symptoms, malignant arrhythmias and life-threatening hemodynamic deterioration. Prescribing clinicians should maintain familiarity with the mechanisms and kinetics of the anti-arrhythmic drugs they prescribe, as well as the clinical manifestations of anti-arrhythmic drug toxicity. Here we present a case of intentional flecainide overdose complicated by amphetamine co-ingestion. We hope this case illustrates the importance of prompt symptom recognition, mechanism-directed medical management and the utility of short term mechanical hemodynamic support in the management of anti-arrhythmic drug toxicity.

Case Presentation

A 23-year-old man with a medical history of symptomatic premature atrial complexes and paroxysmal atrial tachycardia, bicuspid aortic valve without significant stenosis or regurgitation, and severe depression with several prior suicide attempts presented to an outside hospital emergency department after ingesting a large but unknown quantity of dextroamphetamine-amphetamine and flecainide pills. An electrocardiogram (ECG) obtained 1 month prior to presentation was normal. An echocardiogram performed at that time revealed normal biventricular systolic function.

He was initially conscious but later became unresponsive. He was noted to be in a persistent wide complex rhythm (Figure 1) that quickly degenerated to pulseless ventricular tachycardia and ventricular fibrillation requiring resuscitation and multiple defibrillations. After return of spontaneous circulation, he was intubated, started on a sodium bicarbonate infusion, and transferred to our coronary intensive care unit. Urine toxicology results were positive for cannabinoids, amphetamines, and benzodiazepines. Results of a laboratory examination were significant for an elevated lactate concentration at 4.6 mmol/L, preserved renal function, and mildly elevated hepatic transaminases. His condition was initially managed with oral gastric-tube suctioning, high-dose hypertonic sodium bicarbonate, aggressive potassium and magnesium supplementation, hyperventilation to maintain a relative alkalotic state, and intravenous lipid emulsion. Although his QRS transiently narrowed with this management, he later developed progressive QRS widening (Figure 2) and recurrent hemodynamically unstable episodes of ventricular tachycardia that were refractory to intravenous amiodarone and lidocaine infusions and required progressive vasopressor support. Transvenous pacing at rates above his slow ventricular tachycardia was attempted, but his hemodynamics worsened. Given his continued clinical deterioration despite multiple and varied attempts to medically manage his overdose, we opted to pursue mechanical circulatory support with percutaneous venoarterial extracorporeal membrane oxygenation (ECMO), which was initiated approximately 8 hours after initial presentation.

Access for ECMO was obtained via the femoral artery and vein. Femoral arteriography prior to ECMO placement revealed small-caliber arteries, likely secondary to profound vasoconstriction, which restricted cannula size and subsequent flow rates. Cannulation and ECMO initiation were otherwise uncomplicated. His echocardiogram following ECMO initiation demonstrated severely reduced biventricular function and profound ventricular dyssynchrony (Video 1). He endured several hemodynamically significant wide complex rhythms necessitating repeat cardioversion though systemic perfusion was maintained via ECMO. By hospital day 3, he maintained normal sinus rhythm with narrowing of his QRS despite a persistently elevated flecainide level at 2.00 μg/mL (therapeutic range 0.20–1.00 μg/mL). His renal function remained unaffected throughout his admission and his transaminase levels improved. He tolerated an ECMO turndown and was decannulated on hospital day 5. Shortly afterward, he was extubated and transferred to the regular nursing floor. His remaining hospital course was complicated by health care–associated pneumonia, and he was discharged home on hospital day 12. Flecainide was not

KEYWORDS Flecainide; Overdose (Heart Rhythm Case Reports 2016;2:228–231)

Address reprint requests and correspondence: Dr Michael D. Faulx, Cleveland Clinic Main Campus, Mail Code J2–4, 9500 Euclid Avenue, Cleveland, OH 44195. E-mail address: faulxm@ccf.org.

http://dx.doi.org/10.1016/j.hrcr.2015.12.013

KEY TEACHING POINTS

- Lethal consequences of flecainide overdose may be more likely with coingestion of amphetamines secondary to pharmacodynamics and pharmacokinetic interactions.
- High-dose hypertonic sodium bicarbonate is the mainstay of medical therapy of flecainide overdose and should be dosed aggressively (initial 50–100 mEq bolus with subsequent therapy to get pH $>$ 7.5 and sodium concentration $>$ 150 mEq/L).
- Mechanical circulatory support should be given early consideration in cases of coingestion of medications that may potentiate the cardiotoxic effects of flecainide, such as amphetamines.

restarted on discharge, and he subsequently underwent a successful atrial tachycardia ablation. His echocardiogram prior to discharge showed a return to normal biventricular function, and his ECG also normalized (Figure 3).

Discussion

Flecainide is a Vaughan Williams class IC lipophilic antiarrhythmic agent indicated for patients with supraventricular arrhythmias without evidence of ischemic or structural heart disease. Flecainide exerts its action by delaying phase 0 depolarization through its high-affinity binding for open-state sodium channels. Physiologically, this results in a slowing of conduction in the atria, ventricles, and His-Purkinje system along with an increased refractory period in ventricular tissue.[1] The sodium channel–blocking properties of flecainide are use-dependent in that the effects are potentiated by increasing heart rate.

Flecainide is known to have proarrhythmic potential even at usual doses, particularly in patients with underlying coronary artery disease or structural heart disease.[2] Bradyarrhythmias and QRS widening result from slowing of conduction in the atrial and ventricular myocytes as well as the His-Purkinje fibers in a dose-dependent fashion. Additionally, tachyarrhythmias, particularly ventricular tachycardia, frequently complicate flecainide overdose, and an increased propensity toward ventricular tachycardia may even be seen at normal doses. There are limited experimental data regarding the mechanism, but it has been proposed that the cause is nonuniform conduction slowing and prolonging of the ventricular myocyte refractory period, leading to the development of reentrant circuits.[3,4]

Flecainide toxicity is rare but potentially fatal, with a mortality rate upward of 10%.[5] Symptoms of toxicity include noncardiac manifestations, such as nausea, vomiting, and seizures, as well as cardiac manifestations, including bradycardia, widening of the QRS complex, and ventricular tachyarrhythmia.[5] The management strategy for flecainide toxicity has been studied only through case reports, and successful management can be extremely challenging given its high oral bioavailability (approximately 90%) and slow rate of elimination. Flecainide is not effectively dialyzed, likely because of its large volume of distribution. The mainstay of medical therapy has been the use of high-dose sodium bicarbonate to offset the cardiotoxic effects of the drug by inducing a high-dose sodium load along with serum

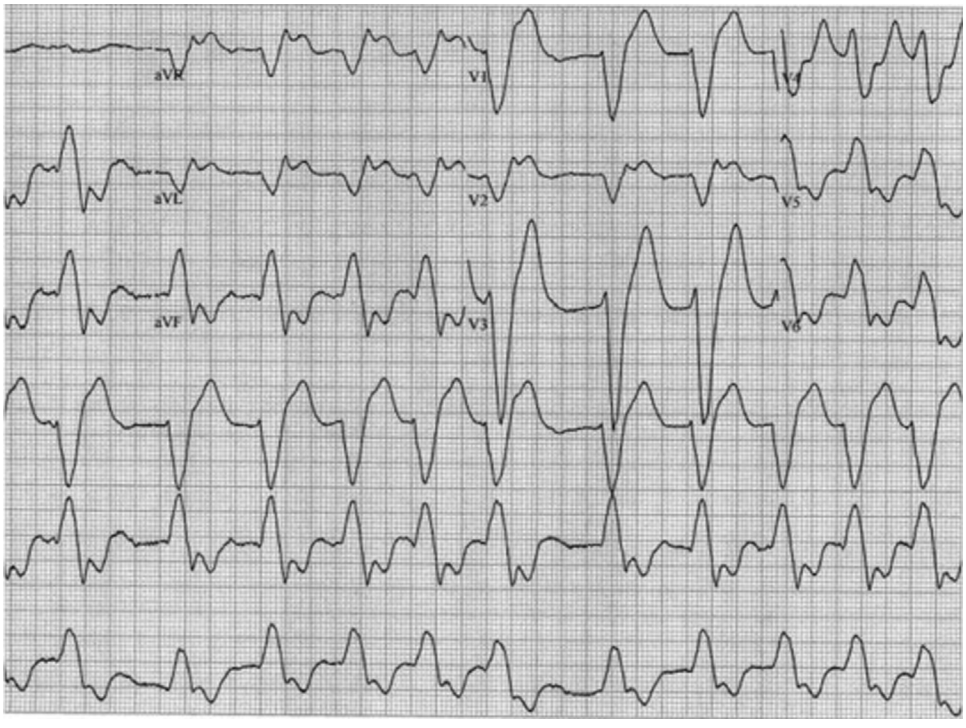

Figure 1. Electrocardiogram obtained upon arrival to the outside hospital emergency department.