The case for quinidine: Management of electrical storm in refractory ventricular fibrillation

Rebecca Pinnelas, MD,* Julie Friedman, MD,* Claudia Gidea, MD,* Eugene Yuriditsky, MD,* Larry Chinitz, MD,† Marina Cerrone, MD,† Lior Jankelson, MD, PhD†

*From the *Leon H. Charney Division of Cardiology, NYU School of Medicine, New York, New York, and †Heart Rhythm Center, Leon H. Charney Division of Cardiology, NYU School of Medicine, New York, New York.*

Introduction

Quinidine is regaining interest as a life-saving and possibly exclusive treatment for inherited arrhythmia syndromes presenting with ventricular fibrillation (VF).

In December 2017, the pharmaceutical manufacturer Eli Lilly announced they would cease manufacturing intravenous (IV) quinidine gluconate, rendering it unavailable worldwide. In March 2019, all remaining drug supply expired. Here, we present a case of idiopathic VF (IVF) and electrical storm refractory to all antiarrhythmic therapies, successfully treated with IV quinidine.

Case report

A previously healthy 27-year-old woman experienced witnessed out-of-hospital cardiac arrest, while at work. She was found in VF and return of spontaneous circulation was obtained 15 minutes later after multiple defibrillations and infusion of amiodarone and epinephrine. At admission, the electrocardiogram (ECG) (Figure 1) showed sinus rhythm at 100 beats per minute, with short-coupled premature ventricular contractions (PVCs). She demonstrated posturing of the extremities, hypokalemia, and lactic acidosis. Coronary angiography was unremarkable. Immediately after arrival to the intensive care unit she developed VF refractory to therapy with magnesium, amiodarone, lidocaine, and esmolol. She was placed on extracorporeal membrane oxygenation and hypothermia was induced (33°C). She remained in VF for another 8 hours with >20 failed cardioversion attempts. Following 2 boluses of quinidine 300 mg IV, sinus rhythm was restored with a single shock. The patient remained in sinus rhythm with no PVCs thereafter, continuing IV quinidine and finally transitioning to oral quinidine sulfate (300 mg 3 times a day). An implantable cardioverter-defibrillator was implanted for secondary prevention and magnetic resonance imaging 6 weeks later revealed normal cardiac function and absence of fibrosis. Genetic testing was uninformative, revealing 2 variants of unknown significance likely to be benign in the *FLNC* gene. She was ultimately discharged to home rehabilitative care. At 18 months follow-up she has not experienced arrhythmias and continues with oral quinidine therapy.

KEY TEACHING POINTS

- The differential diagnosis of an electrical storm includes idiopathic ventricular fibrillation (IVF).
- IVF is elicited by automatic activity arising from Purkinje fibers, which may be manifested on the surface electrocardiogram by short-coupled PVCs.
- Quinidine is a unique antiarrhythmic medication blocking both sodium and potassium channels. Its activity on the I_{to} current is effective in J-wave syndromes such as Brugada syndrome, early repolarization, and IVF.
- Intravenous quinidine supply is limited. Efforts should be taken to ensure the continuation of this life-saving medication.

Discussion

The differential diagnosis for electrical storm in a patient without ischemia falls into 2 main categories: primarily electrical and toxic-metabolic. IVF, which has been associated with short-coupled PVCs originating from the distal Purkinje fibers,[1] seemed the most likely diagnosis for the patient, considering all other negative findings. The short-coupled PVC noticed on presentation was compatible with

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Address reprint requests and correspondence: Dr Lior Jankelson, Heart Rhythm Center, Leon H. Charney Division of Cardiology, New York University School of Medicine, 550 First Avenue, New York, NY 10016. E-mail address: lior.jankelson@nyumc.org.

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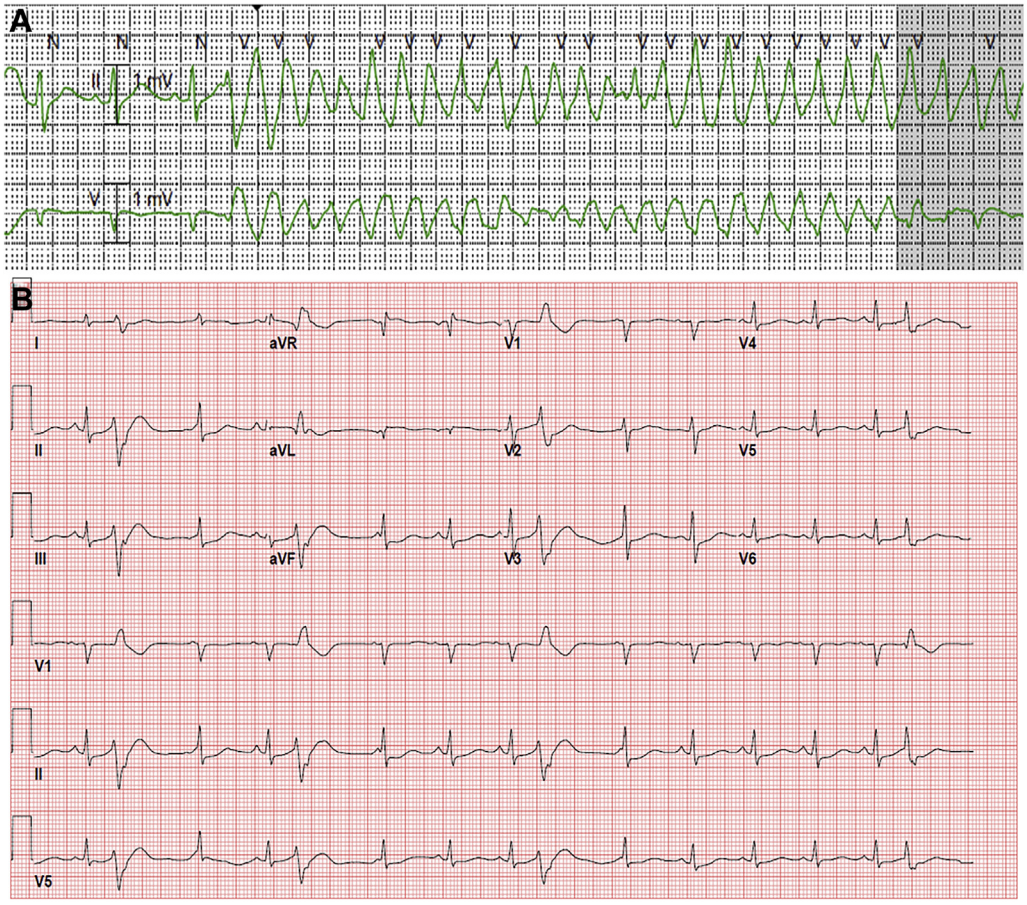

Figure 1 Electrocardiogram (ECG) recordings. **A:** Telemetry strip demonstrating sinus rhythm with short-coupled premature ventricular contraction (PVC)–initiated polymorphic ventricular tachycardia. **B:** ECG immediately after initial cardioversion with short-coupled (240 ms) PVCs. Note the right bundle branch block, left anterior hemiblock morphology of the PVC, typical for Purkinje ectopy in the distal left posterior fascicle region.

a left posterior fascicle morphology (right bundle branch block, left anterior hemiblock), typical for Purkinje fibers supplying the posteromedial papillary muscle.[2] IVF is a rare cause of sudden death, with an incidence between 1.2% and 6.8%.[3] Haissaguerre and colleagues[4] demonstrated that repetitive activity from the distal Purkinje fiber network may cause VF even with minimal or no PVCs at baseline. Quinidine is a class Ia sodium channel blocker that also reduces the inward and outward potassium currents IK1 and IK_{to}.[5] This combined effect may make quinidine uniquely effective in controlling arrhythmias associated with action potential duration dispersion and phase 2 reentry, postulated in IVF. Particularly, I_{to} is highly expressed in Purkinje fibers, possibly explaining the unique effect of quinidine.[6] Several studies have now demonstrated reduced incidence of ventricular arrhythmias in patients with IVF treated with quinidine.[7,8] In addition to medical therapy, radiofrequency ablation has been shown to effectively suppress Purkinje fiber–triggered ectopy and IVF.[9] In our case, PVCs were not observed following the initiation of Quinidine therapy. Additional primary electrical etiologies of electrical storm include QT interval abnormalities (short and long QT syndrome), catecholaminergic polymorphic ventricular tachycardia, early repolarization syndrome,[10] and Brugada syndrome. The latter may be elicited even in the presence of a normal baseline ECG by placing the precordial leads at an elevated sternal position or by administration of a sodium channel blocker such as procainamide or ajmaline.[11] In our patient we did not observe a change to the ECG with these interventions.

The worldwide discontinuation of IV quinidine is alarming. Its demonstrated effectiveness for various malignant ventricular arrhythmias expanded its in-hospital use, while availability kept decreasing progressively. Critically ill patients cannot easily absorb oral quinidine, and the lack of a parenteral option leaves them without access to a potentially life-saving medication. Our patient may not have survived her acute illness if IV quinidine was unavailable.

Quinidine's disappearance has impacted the infectious disease community as well. Owing to the lack of the drug, severe cases of malaria are now treated with IV artesunate, which is not yet approved by the Food and Drug Administration and must be obtained through the Centers for Disease Control. The restored availability of IV quinidine would hence serve different patients with life-threatening conditions and should be advocated by the medical community.

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