

## RHYTHM DISORDERS AND ELECTROPHYSIOLOGY

### THE FOUR CORNERS: DIAGNOSTIC CHALLENGE CORNER

# Acute Electrocardiographic Changes Coincident With Dofetilide Overdose and Acute Coronary Syndrome



David J. King, MD,<sup>a</sup> Mudit Dutta, MD,<sup>a</sup> Ramil Goel, MD,<sup>b</sup> Kun Xiang, MD<sup>c</sup>

#### ABSTRACT

A 73-year-old man with atrial fibrillation and coronary disease requiring stenting to the right coronary artery 7 months prior was admitted for observation after taking an extra dofetilide dose. Troponins trended upward, and electrocardiogram demonstrated QT prolongation to 502 ms as well as T-wave inversions. The patient underwent cardiac catheterization, which revealed severe distal left main disease. (JACC Case Rep. 2024;29:102709) Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

#### HISTORY OF PRESENTATION

A 73-year-old man presented with anxiety and “heartburn” after taking an extra dose of dofetilide 500 µg. History included atrial fibrillation on apixaban and dofetilide, sick sinus syndrome requiring dual-chamber pacemaker, gastroesophageal reflux, and coronary disease with stenting to a 99% lesion of the right coronary artery 7 months before admission. Previous catheterization showed 50% left main stenosis, 30% left anterior descending stenosis, and 80% first diagonal stenosis that did not require intervention. He denied alcohol, tobacco, and illicit substance use. On examination, the patient had an anxious affect without cardiopulmonary abnormalities.

#### INVESTIGATIONS

Electrocardiography (ECG) showed an atrial-paced ventricular-sensed rhythm at 72 beats/min with normal QT interval (**Figure 1A**). High-sensitivity troponin I was 18 pg/mL (upper reference limit = 15 pg/mL), with unremarkable metabolic panel and complete blood count. The patient was admitted for QT interval observation

#### TAKE-HOME MESSAGES

- Dofetilide affects the QT interval through modification of the  $I_{K_R}$  potassium channel, while NSTEMI does so via the  $I_{Na}$  sodium channel.
- It is important to maintain a broad differential diagnosis when determining the cause of QT prolongation.

From the <sup>a</sup>Department of Medicine, University of Florida, Gainesville, Florida, USA; <sup>b</sup>VAMC and the University of Florida, Division of Cardiovascular Medicine, Gainesville, Florida, USA; and the <sup>c</sup>Division of Cardiovascular Medicine, University of Florida, Gainesville, Florida, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

Manuscript received July 9, 2024; revised manuscript received September 5, 2024, accepted September 16, 2024.

**ABBREVIATIONS  
AND ACRONYMS****ACS** = acute coronary  
syndrome**ECG** = electrocardiography

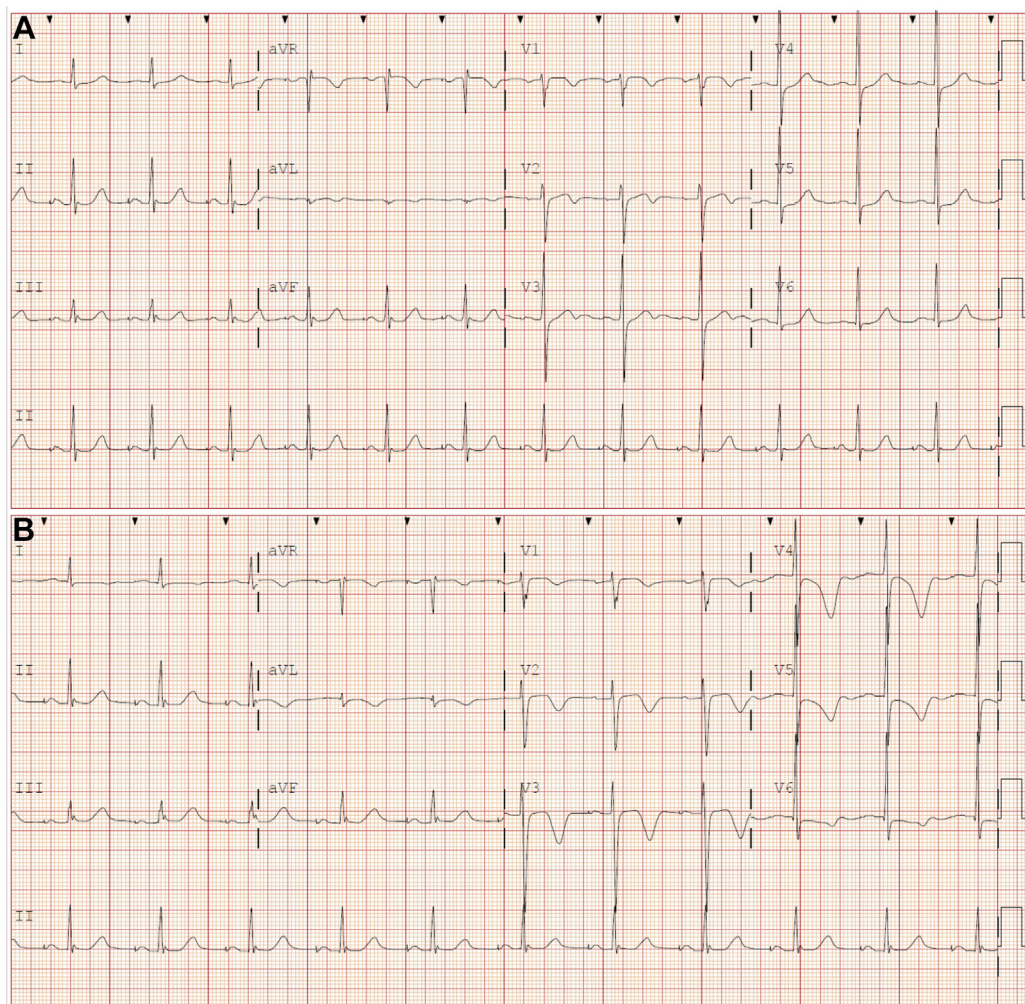
following dofetilide overdose. He continued to experience “heartburn” and received pantoprazole. Repeat ECG demonstrated QT prolongation to 502 ms, precordial T-wave inversions (**Figure 1B**), and repeat troponin was 108 pg/mL.

What is the most appropriate next step in management?

- A) Consent the patient for cardiac catheterization
- B) Contact poison control and pursue gastric lavage
- C) Inpatient pharmacologic stress testing
- D) Neurology consultation given development of neurogenic T waves
- E) Watchful waiting strategy for dofetilide washout

**DISCUSSION**

The correct answer is A. The patient had “heartburn,” ECG changes, and uprending troponins suggesting acute non-ST-segment elevation myocardial infarction. Subsequent urgent cardiac catheterization revealed

**FIGURE 1** Presenting and Follow-Up ECGs

(A) Presenting electrocardiogram (ECG) demonstrating an atrial-paced ventricular-sensed rhythm, normal QTc, and anteroseptal T-wave abnormalities. (B) Repeat ECG with anterolateral T-wave inversions and QT prolongation to 502 ms.

severe distal left main disease. Answers B and C would be appropriate for intermediate-risk patients, but this presentation should raise suspicion for acute coronary syndrome (ACS) as opposed to dofetilide overdose alone. Watchful waiting (E) would have missed the true culprit of his symptoms. Last, the patient had no evidence of a neurologic deficit to prompt consultation (D).

In ACS, QT prolongation is considered the earliest sign of myocardial ischemia.<sup>1</sup> This ECG abnormality is due to modification of the inward sodium current ( $I_{Na}$ ), increasing action potential duration and prolonging repolarization.<sup>1</sup> QT prolongation from dofetilide use is secondary to its effect on the rapid delayed outward rectifier potassium current ( $I_{KR}$ ); decreased potassium efflux increases time taken by the myocyte to reach resting membrane potential, slowing repolarization.<sup>2,3</sup> Causes of QT prolongation include congenital channelopathies, left ventricular hypertrophy, hypokalemia, hypomagnesemia, hypocalcemia, and numerous medications. Although perturbation of the  $I_{KR}$  potassium channel is the most common cause of acquired QT prolongation—the mechanism shared by most QT-prolonging medications<sup>3</sup>—it was not the etiology of this patient's presentation. The case highlights that early ACS can present with QT prolongation, and that dofetilide use could mask interpretation.

### FUNDING SUPPORT AND AUTHOR DISCLOSURES

---

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

---

**ADDRESS FOR CORRESPONDENCE:** Dr David J. King, Department of Medicine, University of Florida, 1600 SW Archer Road, Gainesville, Florida 32608, USA. E-mail: [David.King@medicine.ufl.edu](mailto:David.King@medicine.ufl.edu).

---

### REFERENCES

1. Kenigsberg DN, Khanal S, Kowalski M, Krishnan SC. Prolongation of the QTc interval is seen uniformly during early transmural ischemia. *J Am Coll Cardiol*. 2007;49(12):1299-1305. <https://doi.org/10.1016/j.jacc.2006.11.035>
2. McClellan KJ, Markham A. Dofetilide: a review of its use in atrial fibrillation and atrial flutter. *Drugs*. 1999;58(6):1043-1059. <https://doi.org/10.2165/00003495-199958060-00007>
3. Redfern WS, Carlsson L, Davis AS, et al. Relationships between preclinical cardiac electrophysiology, clinical QT interval prolongation and torsade de pointes for a broad range of drugs: evidence for a provisional safety margin in drug development. *Cardiovasc Res*. 2003;58(1):32-45. [https://doi.org/10.1016/s0008-6363\(02\)00846-5](https://doi.org/10.1016/s0008-6363(02)00846-5)

---

**KEY WORDS** acute coronary syndrome, dofetilide,  $I_{KR}$  potassium channel,  $I_{Na}$  sodium channel, non-ST-segment elevation myocardial infarction, NSTEMI, QT prolongation, Tikosyn