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RHYTHM DISORDERS AND ELECTROPHYSIOLOGY

CLINICAL CASE

Therapeutic Flecainide Toxicity Causing VT Storm

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ABSTRACT

Ventricular tachycardia (VT) storm is a fatal arrhythmia with multiple contributory etiologies. This paper presents a case of a 71-year-old woman who developed VT storm from flecainide toxicity occurring at therapeutic flecainide levels. Flecainide toxicity should be considered in any patient on flecainide presenting with VT. (JACC Case Rep. 2025;30:102797) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 71-year-old woman presented to the emergency department with dyspnea. She reportedly experienced 4 episodes of ventricular tachycardia (VT) requiring cardioversion before arrival. She informed the medical team that she unintentionally overdosed on flecainide, taking 200 mg twice daily for at least 2 days instead of 100 mg twice daily as prescribed for increased atrial fibrillation. The patient notably tested positive for COVID-19 on a home test a week prior to presentation and was treated with molnupiravir. She noted feeling worsened malaise and generalized weakness from her COVID-19 infection. While at home, she felt progressive dyspnea and orthopnea, prompting her to seek medical attention.

TAKE-HOME MESSAGES

- Flecainide toxicity should be considered as an etiology of VT storm despite normal drug levels.
- Flecainide levels may not always be associated with electrographic abnormalities.

PAST MEDICAL HISTORY

Significant history includes hypertension, paroxysmal atrial fibrillation on anticoagulation with rivaroxaban, tachy-brady syndrome with a permanent dual chamber pacemaker, and hyperlipidemia.

DIFFERENTIAL DIAGNOSIS

The patient's cardiogenic shock from recurrent VT arrest was initially thought to be due to metabolic derangements from lactic acidosis. However, the arrhythmia persisted despite correction of the acidosis. Thus, flecainide toxicity was considered despite a normal level. Additional contributory etiologies worth considering include structural cardiac diseases, such as ischemic heart disease, nonischemic cardiomyopathy, and valvular heart dis-

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ABBREVIATIONS AND ACRONYMS

ECG = electrocardiogram

EF = ejection fraction

VT = ventricular tachycardia

eases, and abnormal electrical substrate mediated by primary conduction and secondary toxic or metabolic disorders. The patient presentation, initial laboratory tests, and cardiac diagnostic testing more strongly suggested the etiology of VT storm to be mediated by flecainide toxicity.

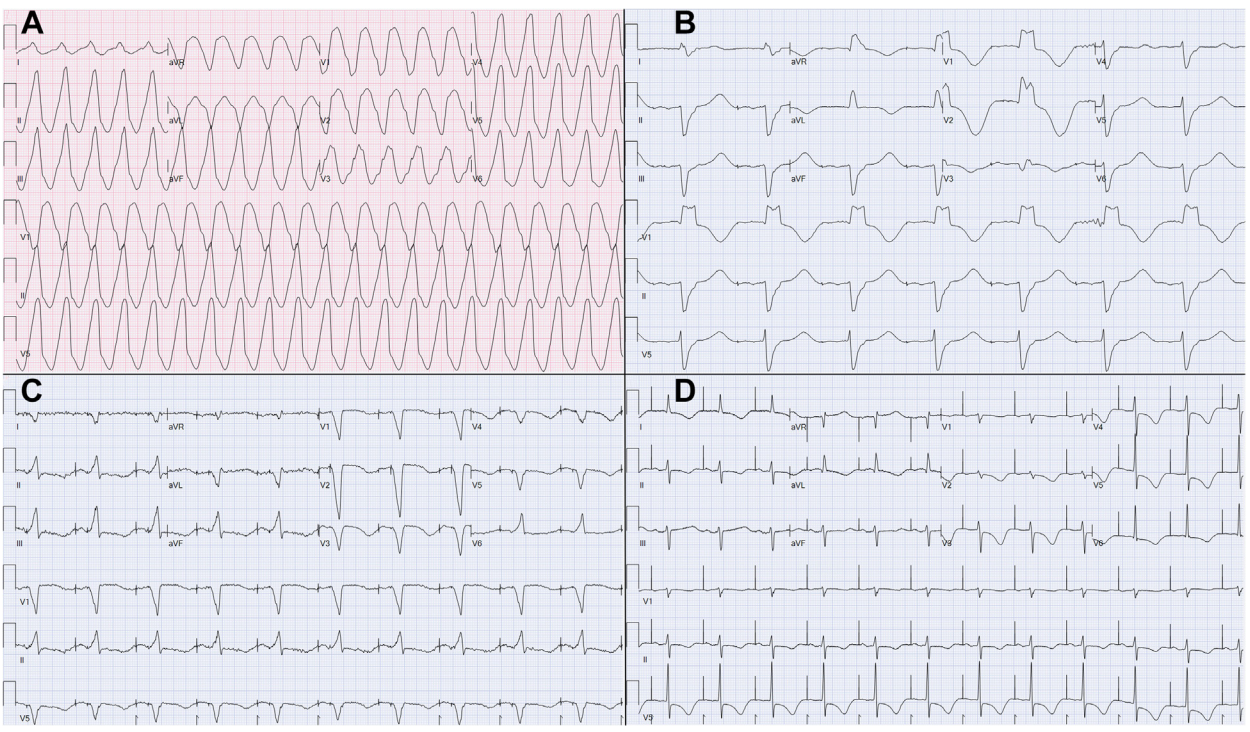
INVESTIGATIONS

The patient's initial electrocardiogram (ECG) showed a VT with QRS duration of 180 ms and QTc interval of 773 ms (Figure 1A), and repeat ECG showed a new right bundle branch block with a slower heart rate of 44 beats/min and QRS duration of 168 ms (Figure 1B). Lactic acidosis was noted on admission arterial blood gas (pH 7.33, pCO_2 23, bicarbonate 11.8, lactate 8.0). QRS slurring suggested flecainide toxicity (Figure 1C). High-sensitivity troponin assay peaked at 411. Flecainide level on admission to the intensive care unit the following day was 0.64 μg/mL (normal limits between 0.2 and 0.99 μg/mL). Point of care ultrasound suggested mildly reduced ejection fraction (EF) and right ventricular dysfunction. A formal transthoracic echocardiogram was completed, showing a new reduced EF of 25% to 30% and right ventricular wall motion abnormalities of mid to distal free wall and apex akinesis (Figure 2A). Repeat transthoracic echocardiogram showed improved EF and resolution of wall motion abnormalities (Figure 2B), and resolution of wide QRS morphology (Figure 1D). Subsequent cardiac catheterization (Figure 3) was completed, and there was no evidence of a culprit lesion to suggest acute ischemic pathology.

MANAGEMENT

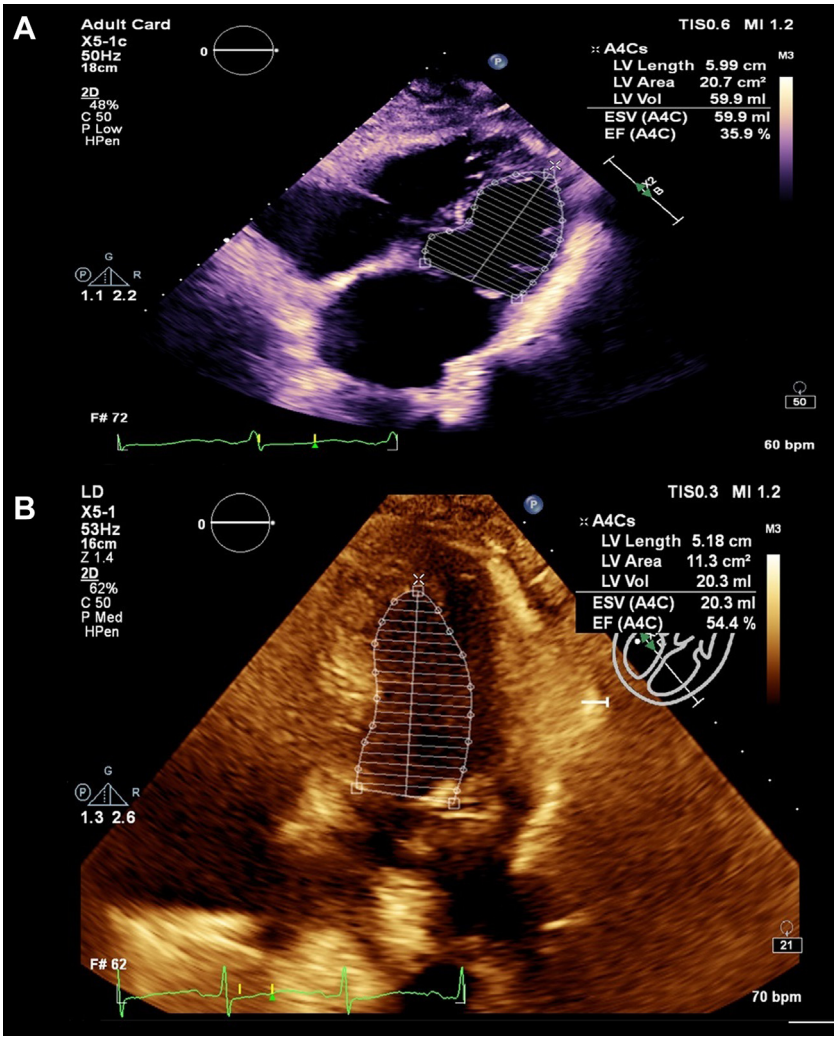
On presentation to the emergency department, the patient was found to be in shock. Intravenous fluids, vasopressor support with norepinephrine, and broad-spectrum antibiotics were started to treat presumed septic shock. Additionally, she received 2 ampules of sodium bicarbonate to treat her metabolic acidosis, resulting in improved heart rate allowing pacemaker

FIGURE 1 Electrocardiograms During Hospital Course



(A) Ventricular tachycardia with QRS duration of 180 ms and QTc interval of 773 ms. (B) Repeat electrocardiogram (ECG) showing right bundle branch block, rate of 44, and QRS duration of 168 ms. (C) Subsequent ECG, after sodium bicarbonate administration, showed improved heart rate and pacemaker recapture. QTc interval remained prolonged at 772 ms, and QRS slurring suggested flecainide toxicity. (D) ECG 2 days after initial presentation, showing narrowing of QRS interval and atria-paced rhythm.

FIGURE 2 **Transthoracic Echocardiography Images**



(A) Transthoracic echocardiogram in the apical 4-chamber view from admission, showing a newly reduced ejection fraction (EF) along with right ventricular wall motion abnormalities. (B) Repeat echocardiogram in the apical 4-chamber view, 4 days after admission, showing EF recovery and resolution of wall motion abnormalities.

capture, although QTc interval remained prolonged at 772 ms (Figure 1C). The patient was admitted to the intensive care unit for treatment of cardiogenic shock and placed on dobutamine and furosemide continuous infusions. Her course was complicated by 3 additional episodes of VT requiring defibrillation despite treatment of the acidosis. She was treated with amiodarone and lidocaine continuous infusions briefly for undifferentiated ventricular arrhythmia at that time. She was briefly intubated and sedated to attenuate the catecholaminergic surge. Electrophysiology was consulted and increased the lower pacing rate to 70 beats/min and the atrioventricular delays on the patient's pacemaker to promote more native conduction. Interrogation of the device showed a slower VT that was below the detection limit. Additionally, telemetry showed premature ventricular contractions triggering the VT. Emergent left heart catheterization did not reveal any culprit coronary lesions to suggest acute ischemia. With

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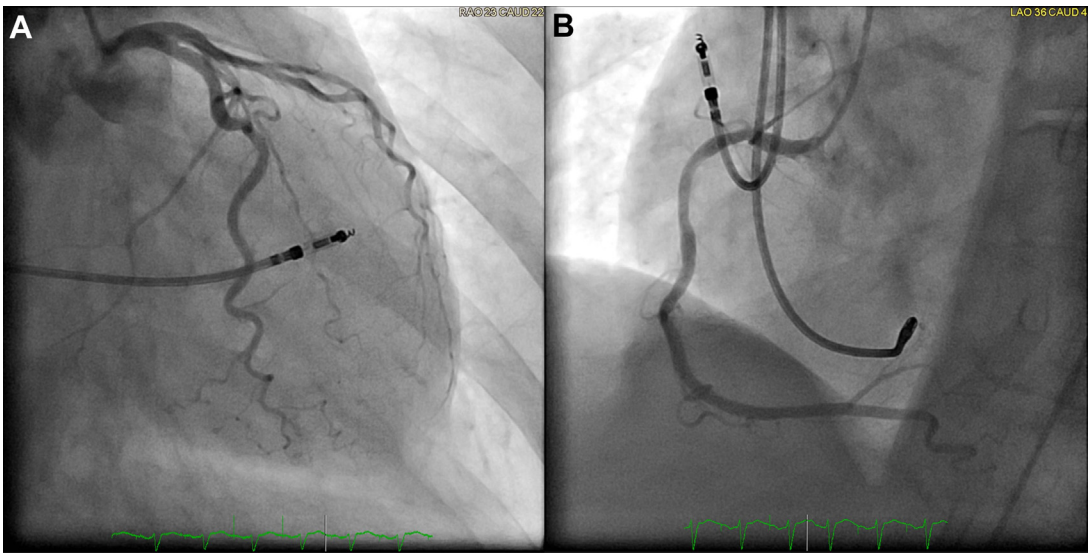
FIGURE 3 Left Heart Catheterization Fluoroscopy Imaging



Left heart catheterization of the (A) left coronary system and (B) right coronary system showing absence of any cardiac lesions.

subsequent supportive care and flecainide clearance, her clinical status improved.

DISCUSSION

Flecainide toxicity is a rare occurrence. Electrophysiological manifestations include increased QRS duration and PR interval, QTc prolongation, atrioventricular block, tachyarrhythmias, and severe bradycardia.[1,2] However, there is no association between flecainide levels and electrographic changes (eg, QRS abnormalities).[3] Symptoms of toxicity include acute encephalopathy, hypotension, and seizures. Therapeutic levels are 0.2 to 1.0 μg/mL; however, some reports suggest toxicity occurring as low as 0.7 μg/mL.[2] Administration of sodium bicarbonate and timing of the flecainide level draw could have affected the flecainide levels observed here.

In one published report, flecainide toxicity was seen at normal flecainide levels, with hyponatremia determined to have predisposed the patient.[4] Another case occurred in a patient while on a chronically therapeutic dose. Their course was complicated by lactic acidosis, renal dysfunction, and hyponatremia, with ECG showing complete atrioventricular block and wide QRS escape rhythm. Flecainide toxicity was treated with bicarbonate and temporary pacing, ultimately resulting in clinical improvement. Although no flecainide levels were drawn, the authors suspect that the toxicity was precipitated by renal dysfunction despite a chronically stable dose.[5]

Uptitration of flecainide[6] and accidental ingestions[3] have also been implicated in flecainide toxicity. In one case, a patient took 600 mg of additional flecainide due to palpitations concerning for known paroxysmal atrial fibrillation.[7] Flecainide toxicity can also result in loss of pacemaker capture.[6]

Other known causes of VT were either ruled out or highly unlikely here. The patient had no history of cardiac ischemia, with ECG, troponin trend, and left heart catheterization nonsuggestive of acute coronary syndrome. Echocardiography did not identify dilated hypertrophic cardiomyopathy or moderate to severe valvular heart disease. There were no electrolyte abnormalities or renal dysfunction on admission. There was no history of cardiac tumors or evidence of active myocarditis. Thyroid stimulating hormone was normal.[8]

Acute COVID-19 has been associated with VT and cardiomyopathy. VT may cause direct myocyte injury, whereas stress cardiomyopathy may be mediated by cytokine storm and catecholamine response.[9] In this case, we suspect that COVID-19 illness resulted in stress cardiomyopathy and

predisposed the patient to proarrhythmogenic effects from flecainide irrespective of dose.

Flecainide toxicity may be treated with sodium bicarbonate, pacing, and intralipid.[2] In this case, the patient was found to have profound lactic acidosis and showed significant electrographic improvement after administration of sodium bicarbonate.

FOLLOW-UP

The patient was discharged to inpatient rehabilitation after her hospital course. She denied any chest pain, dyspnea, or palpitations since discharge. For long-term rhythm control of atrial fibrillation, she was placed on amiodarone after a flecainide washout and normalization of electrographic abnormalities of the QTc and QRS intervals. Flecainide was noted as an allergy on the patient's electronic medical record. She followed-up in the cardiology clinic, and a referral to electrophysiology was placed for consideration of catheter ablation to further treat atrial fibrillation.

CONCLUSIONS

We present the third reported case of flecainide toxicity with therapeutic flecainide levels in the setting of COVID-19–induced stress cardiomyopathy. Electrocardiographic findings were consistent with flecainide toxicity which improved with supportive care. No other source of ventricular arrhythmia was identified. Physicians should consider flecainide toxicity in instances where presenting ECG changes and history are consistent with toxicity, even if levels are within typical therapeutic range.

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