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CASE REPORT

INTERMEDIATE

CLINICAL CASE SERIES

Class III Antiarrhythmics and Periprocedural Torsades de Pointes

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ABSTRACT

This case series describes 2 women on prolonged therapy with class III antiarrhythmics who developed torsades de pointes polymorphic ventricular tachycardia in the setting of catheter ablation for atrial fibrillation as a result of QTc prolonging factors. Clinicians must exercise increased vigilance in the perioperative period in patients on QTc-prolonging medications. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2023;23:101998)

Atrial fibrillation is the most common sustained arrhythmia and is associated with significant morbidity. In patients with significant symptoms, rhythm control with antiarrhythmic therapy is used to attempt to maintain sinus rhythm. Class III antiarrhythmics are commonly used but are associated with the development of torsades de pointes polymorphic ventricular tachycardia (TdP) because of the prolongation of the cardiac repolarization duration, manifested as a prolonged QTc interval on the electrocardiogram (ECG). Initiation of class III antiarrhythmics, sotalol and dofetilide, has traditionally been performed during in-hospitalization with monitoring for QTc prolongation. QTc prolongation and risk of TdP is highest early after initiation of class III antiarrhythmics. Risk of TdP in patients on QTc prolonging medications has been found increased with bradycardia, fluid shifts, and electrolyte imbalances.[1] This case series describes 2 women on prolonged sotalol or dofetilide therapy with normal QTc on prior ECGs and who developed TdP during or early after catheter ablation for atrial fibrillation.

LEARNING OBJECTIVES

- To understand the risk factors associated with torsades de pointes in patients taking QTc-prolonging medications.
- To emphasize the importance of increased vigilance in the perioperative period in patients on class III antiarrhythmics.

CASE 1

Case 1 describes a 68-year-old woman with persistent atrial fibrillation and on dofetilide for rhythm control. All ECGs during initial loading 8 months before her subsequent ablation procedure and during follow-up were <500 ms (range: 429-491 ms). The patient underwent catheter ablation for atrial fibrillation. ECGs at admission and discharge showed sinus rhythm and QTc of 437 ms and 426 ms. The patient presented to the emergency department with episodes of sudden-onset lightheadedness, chest pressure, and nausea 2 days after catheter ablation for atrial fibrillation.

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ABBREVIATIONS AND ACRONYMS

ECG = electrocardiogram

TdP = torsades de pointes

Initial ECG showed a heart rate of 86 beats/min and QTc of 426 ms. Temperature was noted to be 101.5 °F, and the patient was treated for presumed pneumonia with a single dose of piperacillin-tazobactam. The following day, ECG showed sinus bradycardia with a heart rate of 55 beats/min and a markedly prolonged QT interval of 577 ms, corrected with Bazett's formula (Figure 1). Her telemetry showed brief episodes of polymorphic nonsustained ventricular tachycardia consistent with TdP. Potassium level was 3.7 mEq/L, and magnesium level was 1.4 mEq/L. Dofetilide was discontinued, and intravenous magnesium and potassium were administered. The patient had no subsequent ventricular arrhythmias. QTc on ECGs normalized.

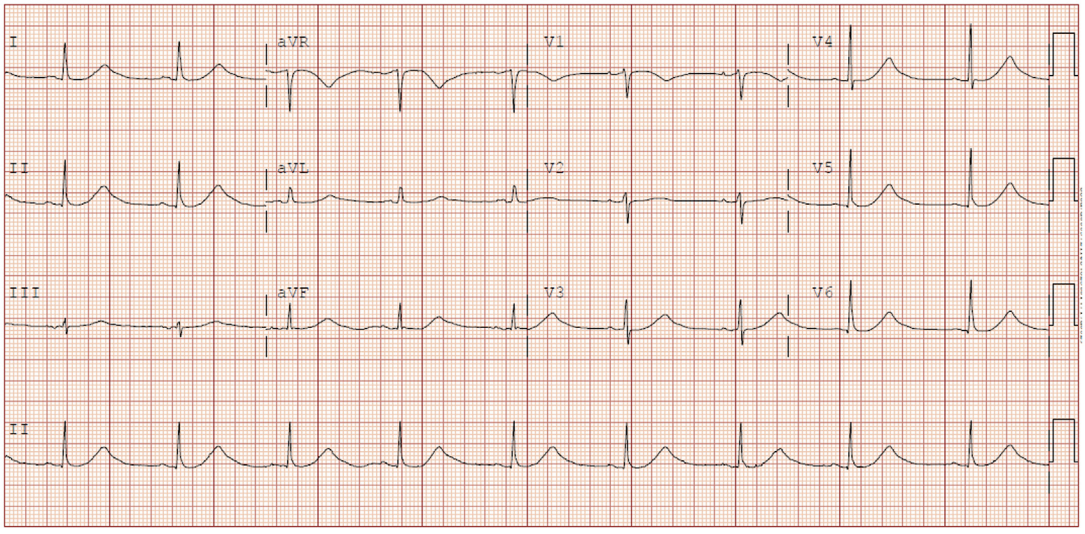
CASE 2

Case 2 describes a 68-year-old woman with a history of paroxysmal atrial fibrillation on sotalol for more than 6 years. ECG during follow-up had shown QTc of <500 ms (range: 399-473 ms). The patient presented for catheter ablation for her atrial fibrillation. ECG at presentation showed sinus bradycardia with heart rate of 54 beats/min and QTc of 467 ms (Figure 2). After induction of anesthesia, the patient developed sinus bradycardia at a heart rate of 40 beats/min. Shortly afterward, the patient's heart rate further decreased to 34 beats/min, and the QTc interval was measured to be 640 ms. She subsequently developed TdP (Figure 3). Defibrillation at 200 J was successful. However, she had an additional run of polymorphic ventricular tachycardia, which was self-limited. Pacing from the coronary sinus was performed to prevent bradycardia, and the patient underwent successful ablation for atrial fibrillation. Sotalol was discontinued, and the patient was monitored for 2 days without recurrence of ventricular arrhythmias.

DISCUSSION

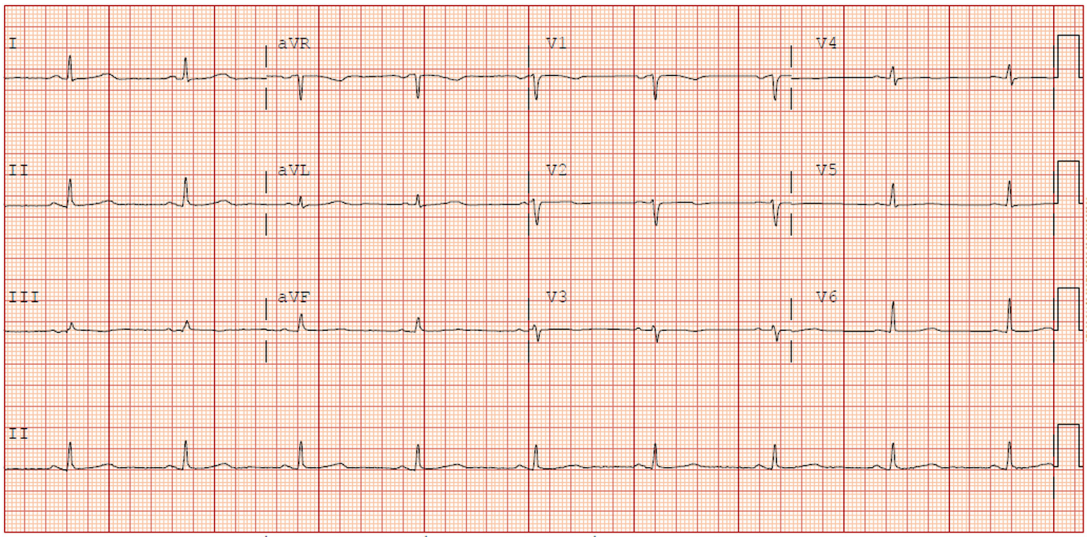
The reported cases demonstrate precipitation of TdP in patients on class III antiarrhythmics with previously acceptable QTc of <500 ms and no prior arrhythmia and who developed acute QTc prolongation during or shortly after catheter ablation for atrial fibrillation. Acute fluid and electrolyte shifts and bradycardia likely contributed to precipitating acutely prolonged QTc and development of TdP, despite normal electrolyte levels and no administration of other QTc-prolonging medications, which may include certain psychotropic medications, antibiotics, and antiemetics.[1] The QT-prolonging effect of class III antiarrhythmics is caused by inhibition of the rapid

FIGURE 1 Case 1 Electrocardiogram



Electrocardiogram demonstrates sinus bradycardia with a rate of 55 beats/min and a prolonged QT interval of 577 ms, corrected with Bazett's formula.

FIGURE 2 **Case 2 Electrocardiogram**



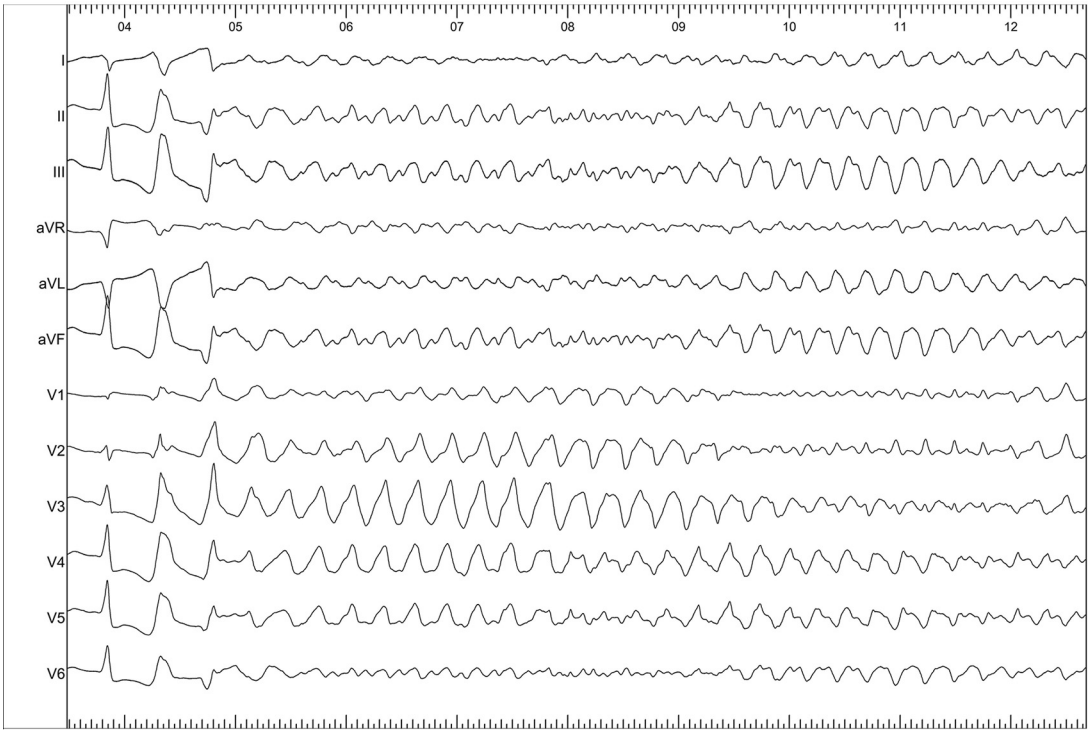
Electrocardiogram demonstrates sinus bradycardia with a rate of 54 beats/min and a slightly prolonged corrected QT interval of 467 s.

component of the delayed rectifier potassium current (I_{Kr}) mediated by the potassium channel encoded by the *KCHN2* gene.[1] This results in prolongation of the action potential duration and increased susceptibility to afterdepolarizations that can trigger TdP.[1] Women are more prone to drug-induced TdP for unclear reasons, but it is postulated that hormonal differences may play a role.[2] Bradycardia is a major risk factor for drug-induced TdP because of the reverse-use dependency of inhibition of I_{Kr}.[3]

Initiation of sotalol conventionally requires at least a 3-day hospital stay while up-titrating the medication dose, because the incidence of developing adverse QT prolongation and subsequent TdP in patients on sotalol is as high as 1% to 4%,[4] and this has been shown to occur in a dose-dependent fashion.[4] Risk factors for TdP in patients on sotalol include doses above 320 mg/d, creatinine clearance of <40 mL/min, history of sustained ventricular arrhythmias, history of heart failure or coronary artery disease, and female sex.[4] Similarly, dofetilide initiation requires a 3-day hospital stay and has a dose-dependent risk of TdP,[5] and incidence is estimated at 2.4%.[6] Risk factors for TdP in patients taking dofetilide have been identified to be older age, female sex, electrolyte disorders, renal or hepatic dysfunction, and concomitant use of other QT-prolonging medications.[6]

During and after procedural interventions, there are often electrolyte shifts and anesthesia-related changes in heart rate that can trigger TdP. There is a lack of evidence regarding perioperative TdP, and most events are likely unreported. Existing case reports of TdP occurring in close temporal relationship to surgical procedures were described in a systemic analysis that reported that almost all of the episodes of TdP were preceded by significant QTc interval prolongation >100 ms.[7] Most of these cases were triggered by other factors such as medications, hypokalemia, or bradycardia.[7] Our patients' episodes of TdP were preceded by marked QTc interval prolongation only in very close temporal relation to the arrhythmia event, whereas other ECGs showed QTc within the normal range. This was likely the result of QTc-prolonging factors such as electrolyte abnormalities with potentially superimposed transient potassium shifts[8] and bradycardia in the setting of class III antiarrhythmic use.

FIGURE 3 Case 2 Telemetry Strip



Telemetry strip demonstrates initiation of polymorphic ventricular tachycardia consistent with torsades de pointes.

CONCLUSIONS

These 2 cases illustrate the importance of carefully monitoring patients with risk factors for QTc prolongation, particularly those taking class III antiarrhythmics, during and after surgical procedures, because they are at risk for developing TdP precipitated by electrolyte shifts and bradycardia. Clinicians must exercise increased vigilance in the perioperative period in patients who are taking QTc-prolonging medications.

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