

ECG Diagnosis: Ibutilide-induced Torsade de Pointes

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Perm J 2019;23:18-187

E-pub: 01/17/2019

<https://doi.org/10.7812/TPP/18-187>

INTRODUCTION

Ibutilide is recommended by professional society guidelines for the cardioversion of atrial fibrillation and flutter.^{1,2} Its rapid effect and minimal impact on hemodynamics make it well suited for use in the Emergency Department (ED).³ Ibutilide, however, prolongs the corrected QT (QTc) interval and increases risk for ventricular tachycardia (VT).⁴⁻⁶ The risk of VT can be greatly mitigated by careful selection of low-risk patients, the optimal dose of prophylactic magnesium sulfate, and at least 4 hours of postibutilide electrocardiographic monitoring.³ This case illustrates the dangers of overlooking ibutilide contraindications and provides practical lessons in ibutilide use and management of ibutilide-induced VT.

CASE PRESENTATION

A 61-year-old man with a medical history of hypertension, type 2 diabetes mellitus, paroxysmal atrial fibrillation, and a recent community-acquired pneumonia, presented to the ED complaining of several hours of a rapid, irregular heart rate. He denied chest pain and shortness of breath. His initial vital signs were: Temperature, 37.1°C; systolic blood pressure, 107 mmHg; pulse, 139 beats/min; respiration rate, 16 breaths/min; and oxygen saturation, 95% on room air. His mental status and lung examination were normal, and his cardiovascular examination revealed a rapid, irregularly irregular pulse without murmurs. The initial 12-lead electrocardiogram (ECG; Figure 1) demonstrated atrial fibrillation with a ventricular rate of 118 beats/min, and a prolonged QTc interval of 488 msec (normal range 360-440 msec). He had a history of minimally prolonged QTc interval, measured, for example, at 452 msec while in sinus bradycardia 7 years earlier. See Figure 2 for the endpoints of the QT interval. We used Bazett's formula to correct the QT interval for heart rate: $QT_c = \frac{QT}{\sqrt{RR}}$. His outpatient medications at the time of presentation included the following: Atenolol, warfarin, amlodipine, lisinopril-hydrochlorothiazide, glipizide, terbinafine, atorvastatin, allopurinol, and a 7-day course of cefpodoxime and doxycycline. None of these are known to directly prolong the QTc interval.

The patient received 3 serial 5-mg bolus injections of intravenous metoprolol for ventricular rate control, resulting in a ventricular rate of 85 beats/min. During the reduction in heart rate, he underwent another 12-lead ECG (not shown), which revealed a ventricular rate of 95 beats/min and a QTc interval of 478 msec. Laboratory tests were significant for a serum potassium of 3.1 mEq/L (normal range 3.5-5.3 mEq/L), a serum magnesium of 1.8 mEq/L (normal range 1.6-2.3 mEq/L), and an international normalized ratio of 1.2 (therapeutic target 2.0-3.0). The patient received 1 g intravenous magnesium sulfate over 30 minutes, followed by 2 intravenous infusions of

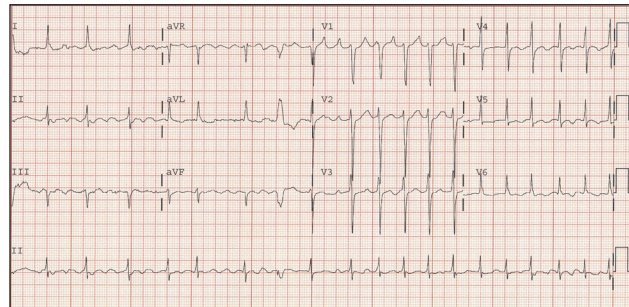


Figure 1. 12-lead electrocardiogram from a 61-year-old man with palpitations. Demonstrates atrial fibrillation with a ventricular response of 118 beats/min, and a prolonged QTc interval of 488 msec.

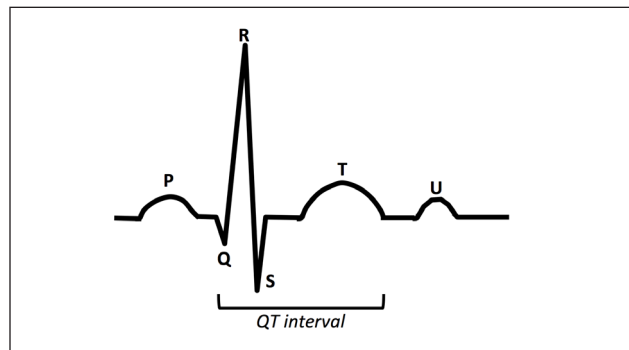


Figure 2. How to measure the QT interval on an electrocardiogram.

ibutilide (10 mg each, separated by 30 minutes) for pharmacologic conversion to sinus rhythm. Shortly after completion of the ibutilide infusions, his atrial fibrillation resolved, and he developed ventricular bigeminy with intermittent episodes of sustained polymorphic VT (Figure 3). The patient remained hemodynamically stable throughout these VT episodes (systolic blood pressure approximately 135 mmHg). Intravenous

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Keywords: atrial fibrillation, atrial flutter, cardioversion, ECG diagnosis, ibutilide, polymorphic VT, prolonged QTc interval, torsade de pointes

amiodarone (150 mg) and magnesium sulfate (4 g) were then administered. His cardiac rhythm converted to sinus bradycardia with a prolonged QTc interval of 600 msec and inverted T waves (as a result of repolarization changes following pharmacologic cardioversion?; Figure 4). The patient began oral potassium replacement in the ED and was admitted to the Intensive Care Unit overnight for close monitoring. He had no further episodes of ventricular dysrhythmia and was discharged the following day in sinus rhythm with a corrected serum potassium, a heart rate of 43 beats/min, and a QTc interval of 572 msec.

DISCUSSION

The ED management of the stable patient with primary nonvalvular paroxysmal atrial fibrillation or flutter and recent-onset symptoms may include attempts at pharmacologic or electrical cardioversion.^{1,8} The choice to pursue the restoration of sinus rhythm in the ED is influenced by many variables and is well suited for shared decision making.^{9,10} An ED rhythm-control strategy was a viable option for our patient, although the selection of ibutilide was not ideal because he had 2 notable contraindications: A prolonged QTc interval and hypokalemia. Both of these are known to increase the risk for polymorphic VT, which is a dangerous rhythm that can degenerate into ventricular fibrillation and cause cardiac arrest.^{3,11,12}

Barring contraindications, ibutilide is a good selection for the pharmacologic cardioversion of recent-onset (< 48 hours) atrial fibrillation. In a multicenter retrospective cohort study in a real-world, community-based ED setting, ibutilide was found to be comparable to procainamide in the cardioversion of recent-onset atrial fibrillation at 90 minutes (40% vs 46% effective, respectively) and superior to intravenous amiodarone (40% vs 18% effective, respectively).^{3,13,14} Among pharmacologic agents for the cardioversion of recent-onset atrial flutter, however, ibutilide is unrivaled (eg, ibutilide had a 64% cardioversion rate at 90 minutes vs 22% for procainamide).^{3,13,14}

Polymorphic VT is the most serious side effect of ibutilide. The multiple ventricular foci of polymorphic VT are evident in QRS complexes of varying amplitude, axis, and duration. When associated with acquired or congenital QTc interval prolongation, polymorphic VT is called torsade de pointes (TdP). This French term has 2 complementary meanings: 1) “twisting of points,” referring to the ribbon-like twisting of the rhythm around the ECG isoelectric line; and 2) “fringe of pointed tips,” another apt description of the ECG image (Figure 3). TdP is uncommonly captured on a 12-lead ECG because of the brevity and paroxysmal nature of the dysrhythmia and the gravity of the clinical situation.

Risk factors for drug-induced TdP include hypokalemia, female sex, drug-drug interactions, advancing age, genetic predisposition, hypomagnesemia, heart failure, bradycardia, and QTc interval prolongation.¹⁵⁻¹⁷ Numerous medications are known to prolong the QTc interval, including levofloxacin, erythromycin (and other macrolides), haloperidol, and methadone, as well as Class III antiarrhythmics such as ibutilide.¹⁵ These medications induce TdP by inhibiting positive ion channels, making

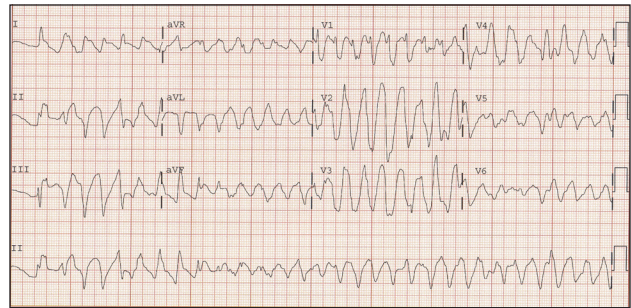


Figure 3. 12-lead electrocardiogram from the same patient as Figure 1, obtained 3 hours later, following the second ibutilide infusion. Demonstrates rapid polymorphic ventricular tachycardia (torsade de pointes).

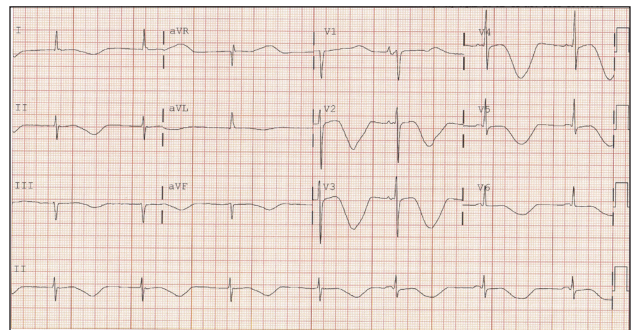


Figure 4. 12-lead electrocardiogram from the same patient as Figures 1 and 3, obtained 4 minutes later, following administration of magnesium sulfate and amiodarone. Demonstrates sinus bradycardia with a ventricular rate of 40 beats/min, and a prolonged QTc interval of 600 msec.

individuals with preexisting hypokalemia particularly susceptible to TdP.^{3,11,12} Because the QTc interval is generally more prolonged as the heart rate slows, polymorphic VT develops more commonly in bradycardic hearts, after ibutilide has resolved atrial fibrillation or flutter (as in our patient).

The most common and effective treatments for TdP include defibrillation and intravenous magnesium sulfate for unstable patients and magnesium sulfate alone for stable patients, regardless of baseline serum magnesium levels.^{18,19} Intravenous lidocaine (a Class Ib antiarrhythmic agent), which shortens the QTc interval, can also be useful. If TdP persists or recurs despite initial interventions, temporary overdrive pacing or intravenous isoproterenol can be used because these increase the heart rate and thereby shorten the QTc interval. Class Ia (eg, procainamide) and class III antiarrhythmics (eg, amiodarone, ibutilide, sotalol) should be avoided because they prolong the QTc interval and can aggravate TdP. Although amiodarone has been occasionally successful in the treatment of TdP, its use is discouraged given the unfavorable risk-benefit profile in this population and the availability of safer, more reliable TdP treatments.²⁰⁻²² In addition to treatments aimed at terminating TdP, causative medications should be discontinued and electrolyte deficiencies corrected.

CONCLUSION

This case teaches us several important clinical lessons. First, ibutilide should be avoided in patients with hypokalemia or prolonged QTc interval.¹⁵ Defibrillation would have been a safer choice than pharmacologic options for restoring sinus rhythm in this patient. Second, the 1-g dose of prophylactic magnesium that was administered as an adjunct to ibutilide was insufficient to either facilitate cardioversion or reduce the incidence of ibutilide-induced TdP. The dose of magnesium needed to enhance ibutilide effectiveness, even in patients with normal serum magnesium levels, is 2-4 g. The dose of magnesium required to minimize TdP is 5 g during the 1 hour preceding ibutilide administration and then 5 g during the 2 hours following the ibutilide infusion.^{3,23} (Ibutilide is contraindicated in patients with low magnesium levels.) Third, amiodarone is not ideal for TdP treatment, as noted above.^{19,20,24,25} When used properly, ibutilide can be an effective—and relatively safe—medication for the cardioversion of recent-onset atrial fibrillation and flutter.³ ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

How to Cite this Article

Le DD, Levis JT, Lugovskaya N, Vinson DR. ECG diagnosis: Ibutilide-induced torsade de pointes. *Perm J* 2019;23:18-187. DOI: <https://doi.org/10.7812/TPP/18-187>

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