

Electrocardiogram Challenge Syncope in a Woman With Nausea and Diarrhea

ECG CHALLENGE

A 71-year-old woman was sent referred to the emergency department from a rehabilitation facility after suffering her first episode of syncope. She was recovering from a recent episode of diarrhea and had been receiving intravenous vancomycin, piperacillin-tazobactam, and fluconazole. Her oral medications included 8 mg ondansetron every 8 hours, cholecalciferol, clonazepam, and esomeprazole. A 12-lead ECG was recorded in the emergency department (Figure 1).

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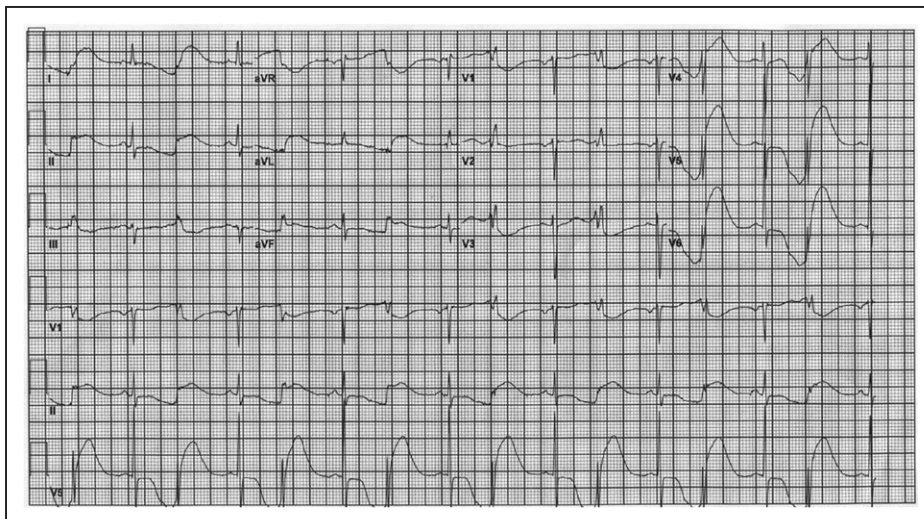


Figure 1. 12-lead ECG recorded on admission to the emergency department.

Please turn the page to read the diagnosis.

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RESPONSE TO ECG CHALLENGE

This ECG demonstrates sinus bradycardia with premature ventricular contractions in a bigeminal pattern. The conducted QRS duration is 84 ms with a normal PR interval of 135 ms. Marked QT interval prolongation occurs with premature QRS complexes at a coupling interval of 500 ms (Figure 2). The premature QRS complexes have a relatively narrow RBBB morphology (QRS duration 115 ms), suggesting a site of origin within the Purkinje system of the left ventricle. The occurrence of these premature beats near the end of a markedly prolonged QT interval suggests that they are the result of early afterdepolarizations (EADs) within the Purkinje cells of the left ventricle. Note that the T-wave axis after the premature beats is opposite in polarity to that of the sinus beats. The QTc was markedly prolonged and challenging to accurately measure because of the premature beats. The serum potassium was 3.2 mmol/L, and the serum magnesium was 2.1 mm/L on presentation. The patient was given a single intravenous bolus of calcium chloride with resolution of the premature beats within minutes (Figure 3) but continued to have marked QT prolongation (QTc 666 ms), and intravenous KCl 40 mEq was infused.

L-type Ca^{2+} current plays a key role in both action potential (AP) prolongation and EAD formation. The late component of the L-type Ca^{2+} current may be especially

relevant to EADs.¹ EADs are oscillations of the cell membrane and require inward calcium and outward potassium currents to be properly matched in amplitude and timing. L-type calcium channels are a promising therapeutic target to normalize AP duration (APD) and suppress EADs. L-type calcium channels are modulated by both voltage- and calcium-dependent inactivation gating mechanisms.¹ Although the mechanism by which intravenous calcium appeared to suppress EADs in this case is unclear, calcium could lead to a slightly higher plateau of the AP, leaving only a prolonged APD but attenuating EADs. Intravenous calcium might also attenuate EADs by increased calcium-dependent inactivation of the late component of L-type calcium channels.¹ Intravenous calcium chloride shortens the APD and may promote delayed afterdepolarizations.

The patient's episode of syncope was most likely caused by an episode of torsades de pointes ventricular tachycardia because of the combined effects of ondansetron, fluconazole, hypokalemia, and sinus bradycardia. After discontinuation of ondansetron and fluconazole and the replenishment of her serum potassium, the corrected QT interval remained prolonged at 490 ms, suggesting previously unrecognized congenital long QT syndrome, which predisposed her to drug-induced QT prolongation (Figure 4).



Figure 2. Initial 12-lead electrocardiogram.

The underlying rhythm is sinus with a conducted QRS duration of 84 ms and marked QT prolongation with relatively narrow premature ventricular depolarizations (arrows) having RBBB morphology and QRS duration of 115 ms, suggesting a site of origin within the Purkinje system of the left ventricle. The premature beats occur near the end of the T-wave as it begins to return toward the baseline. These features suggest that the underlying mechanism of these premature beats is most likely early afterdepolarizations within Purkinje cells. It is important to note that the T-wave axis after the premature beats is opposite in polarity to the sinus beats.

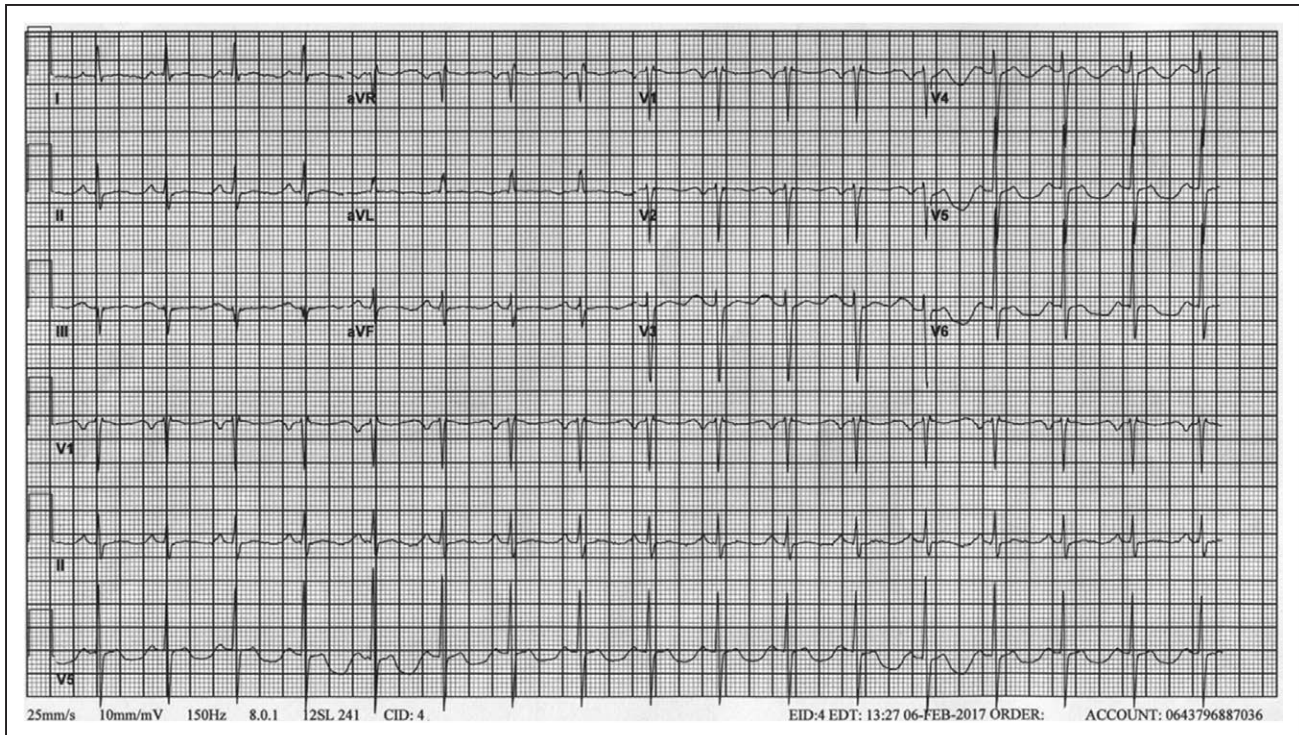


Figure 3. 12-lead ECG taken 9 minutes after the initial ECG after intravenous bolus of calcium chloride.

The QTc is markedly prolonged with fusion of the T- and U-waves, with complete suppression of the premature ventricular beats.

Two of this patient's medications, ondansetron and fluconazole, have been demonstrated in animal models to result in QT prolongation. Ondansetron may result in QT pro-

longation, prolong ventricular APD, increase dispersion of repolarization between the endocardium and epicardium, induce EADs in monophasic AP recordings, and produce

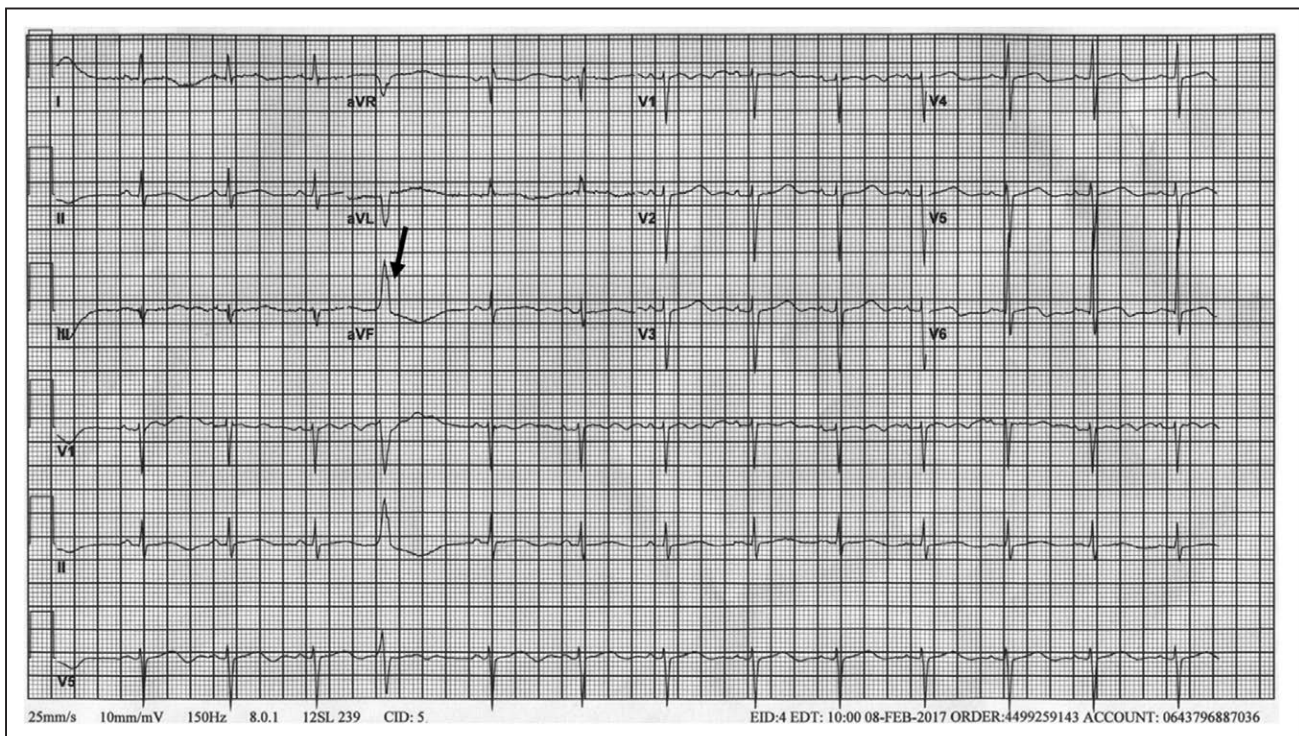


Figure 4. 12-lead ECG recorded 2 days after discontinuation of ondansetron and fluconazole.

Significant QT prolongation is present with QTc of 490 ms, suggesting an underlying abnormality in ventricular repolarization. There is a single PVC (arrow) with a significantly prolonged QT interval afterward.

torsades de pointes in a rabbit model.² The clinical safety of ondansetron has suggested that torsades de pointes is rare when administered orally. In addition, fluconazole may prolong the QT interval and prolong the endocardial ventricular APD, increase transmural dispersion of repolarization, and induce EADs in the rabbit model.³ The mechanism may be the result of decreased human ether-a-go-go-related gene protein trafficking.³ This case demonstrates that drugs producing mild effects on ventricular repolarization may precipitate marked repolarization delay when given to patients with impaired repolarization reserve.

FOOTNOTES

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