Case Report

Drink, Drugs, and the QT Interval

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ABSTRACT

The effects of several prescription and illicitly-used drugs on electrocardiographic repolarization are well documented, most frequently manifested as prolongation of the corrected QT (QTc) interval. The combination of multiple repolarization-modulating drugs taken in high dosage can occasionally lead to extreme abnormalities of the QTc interval and ST-segment on the surface ECG, which can lead to the erroneous diagnosis of underlying myocardial ischemia and inappropriate treatment. We report on one such case in which the acute management of a syncopal patient was detrimentally influenced by misinterpretation of a very unusual ECG.

A 30-year-old female with a long history of illicit drug use was found by paramedics following a collapse in the street. There were no witnesses to the event. The patient had no cardiac or significant medicosurgical history. She had been injecting heroin daily for 3 years, and regularly used benzodiazepines, cannabis, cocaine, codeine, and amphetamines. Her regular daily prescription medications were citalopram (20 mg) and methadone (80 mg). She also consumed approximately 1 liter of alcoholic cider each day.

Clinical examination revealed a drowsy, but easily rousable patient, with a Glasgow Coma Scale of 14. Her blood pressure was 95/60 mm Hg with a heart rate of 80 beats per minute (bpm). Cardiovascular, respiratory, abdominal, and neurological systemic examinations were normal. Laboratory tests showed modest hypokalemia (serum potassium 3.4 mmol/L) and elevation of hepatic transaminases (alanine aminotransferase 123 IU/L, aspartate aminotransferase 104 IU/L) and gamma-glutamyltransferase (309 IU/L). The rest of the serum biochemistry, including magnesium (1.01 mmol/L) and corrected calcium (2.43 mmol/L) concentration, was within normal limits. Thyroid function tests were normal and serum troponin I (TnI) was <0.04 mg/L.

A 12 lead electrocardiogram (ECG) was recorded on admission to the hospital. It revealed a sinus rhythm of 76 bpm with gross repolarization abnormalities (Figure). The corrected QT (QTc) interval was markedly prolonged at 742 ms (Bazett's formula).[1] The ST-segments were abnormal across all leads, with a bifid morphology; deep delayed inversion of the ST-segments was seen in leads II, III, and aVF. An echocardiogram displayed a structurally normal heart with left ventricular ejection fraction 68% (Simpson's biplane rule).

The admitting general physician treated the patient for an acute coronary syndrome, citing inferior T-wave inversion as a possible manifestation of underlying coronary artery disease. This diagnosis was subsequently revoked following cardiology referral, with the ECG changes deemed to be nonischemic in etiology.

Both of the patient's regular prescription medications—citalopram and methadone—are documented QTc-prolonging agents, as were several of the illicit drugs she used including cocaine and amphetamines, which she admitted to having consumed "in large quantities" the previous day. The mechanism of the syncopal episode that precipitated her hospital admission was difficult to ascertain, but an arrhythmic etiology could not be excluded.

The patient was admitted to the cardiac intensive care unit for continuous ECG monitoring. Having initially been labeled as an acute coronary syndrome, she was treated with aspirin (300 mg), clopidogrel (300 mg orally), and unfractionated heparin. Potassium chloride was infused intravenously to correct the hypokalemia. A urine toxicology screen confirmed recent ingestion of large concentrations of benzodiazepines, cocaine, and opiates. Her clinical recovery over the ensuing 24 hours was uncomplicated, with no arrhythmias recorded. Repeat 12 lead ECG the following morning (15 h after the ECG in Figure) showed normalization of QTc interval duration (420 ms) and ST-segment morphology across all leads. Repeat serum potassium concentration was 4.6 mmol/L. Aspirin, clopidogrel, and heparin were discontinued.

Prolonged ambulatory ECG monitoring was planned, but the patient took her own discharge against medical advice on day 2, and failed to attend a follow-up appointment. Whether ventricular (or other) arrhythmia was implicated in the syncopal event that precipitated admission remains unknown. The grossly abnormal ECG repolarization abnormalities, and their prompt resolution,

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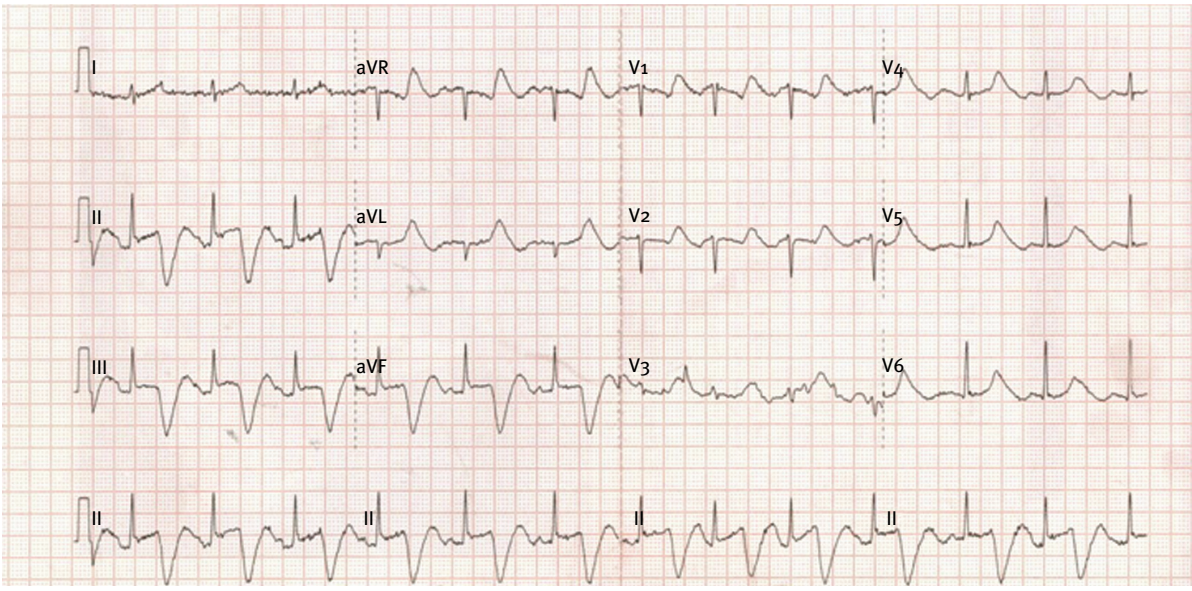

Figure 1. ECG on admission to hospital displaying sinus rhythm with grossly abnormal ST-segment morphology and QTc prolongation (742 ms).

were presumed to represent extreme toxic effects of ingestion of large concentrations of opiates, cocaine, and amphetamines, exacerbated by alcohol excess and modest hypokalemia. It is possible that the additive effects of the ingested drugs and metabolic disturbance had unmasked an underlying channelopathy such as Brugada syndrome, but unfortunately the patient took irregular discharge prior to consent for genetic analysis and screening, which would have been advised.

While prolongation of the QTc interval is well recognized in the context of marked electrolyte disturbances,[2,3] the relatively minor biochemical abnormalities in this case are insufficient to explain the extensive ECG changes. A multitude of pharmacologic agents promote QTc prolongation in healthy individuals, including methadone, cocaine, and amphetamines.[4–6] The mechanism of the QTc prolongation differs, however, between these drug classes. Cocaine and methadone bind to and inhibit the human ether-a-go-go related gene (hERG) voltage-gated potassium channels, and methadone may also induce bradycardia via calcium channel blockade on cardiomyocyte cell membranes, while amphetamines promote lengthening of the QTc interval through non-hERG-mediated pathways.[4,7] In as many as 15% of patients who acquire QTc interval prolongation in response to such agents, a genetic predisposition is supposed.[8] Silent, previously subclinical mutations in certain genes implicated in congenital long QT syndrome, including *KCNQ1*, have been demonstrated to predispose affected individuals to more dramatic QT-prolongation and also extensive T-wave changes.[9] Such patients may have a reduced "repolarization reserve" thus rendering them more susceptible to QT-prolonging agents.[10] Whether they are at greater risk of torsades de pointes and malignant ventricular arrhythmias than those without a genetic predisposition remains unclear.

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