Case in Point

Torsades de Pointes in Severe Alcohol Withdrawal and Cirrhosis: Implications for Risk Stratification and Management

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Close monitoring of the QT interval, timely and aggressive management of withdrawal, repletion of electrolytes, and telemetry monitoring may prevent life-threatening arrhythmias for patients being treated for acute alcohol withdrawal.

Torsades de pointes (TdP) is a life-threatening ventricular arrhythmia that is associated with both congenital and acquired QT interval prolongation. QT interval prolongation is commonly observed in acute alcohol withdrawal and cirrhotic cardiomyopathy.[1-3] In both conditions, there is a positive correlation between the degree of QT interval prolongation and disease severity.[4,5] The precise mechanisms of QT interval prolongation in these conditions are not well understood. One hypothesis is that autonomic hyperexcitability results in altered ventricular repolarization and QT interval prolongation. This mechanism of QT prolongation has been found in acute alcohol withdrawal independent of electrolyte abnormalities, use of QT-prolonging medications, and cirrhosis.[1,2,6]

The authors report the case of a veteran who was hospitalized for acute alcohol withdrawal and decompensated cirrhosis and was found to have a newly prolonged QT interval. On hospital day 3, the patient developed TdP, which required external defibrillation. Despite correction of electrolyte abnormalities, abstinence from alcohol, avoidance of QT-prolonging medications, and exclusion of cardiac ischemia, there was significant and persistent prolongation of the QT interval—ultimately attributed to cirrhotic cardiomyopathy. Acquired QT interval prolongation is common in both acute alcohol withdrawal and cirrhosis.

This case highlights the importance of close monitoring of the QT interval and TdP susceptibility in patients being treated for acute alcohol withdrawal, particularly those with cirrhosis.

CASE REPORT

A 66-year-old male veteran with a 35-year history of alcohol dependence presented for alcohol detoxification. He reported having drunk at least 32 ounces of vodka every day of the preceding 5 years and reported having unsuccessfully attempted self-detoxification several times. Prior detoxification efforts were unsuccessful because of intractable nausea and tremulousness. Additional presenting symptoms included lethargy, anorexia, and a fall with transient right-side hemiparesis (findings on magnetic resonance imaging of the head had been normal).

His medical history included type 2 diabetes, tobacco dependence, and macular degeneration. The only medication being taken was glargine 25 units daily. On admission, the patient was afebrile (98.1°F), normotensive (103/77 mm Hg), and oriented to person, place, and time. Examination also

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revealed a protuberant abdomen with caput medusae, and no shifting dullness or lower extremity edema. The neurologic examination was nonfocal.

Laboratory test results on admission were significant for elevated serum alcohol level (243.8 mg/dL); elevated levels of aspartate aminotransferase (144 units/L) alanine aminotransferase (25 units/L), and total bilirubin (4.2 mg/L); hypoalbuminemia; normocalemia; hypomagnesemia; normal corrected calcium level; and normal renal function (0.84 mg/dL)(Table). The patient's admission Child-Pugh score of 10 indicated class C liver disease. Admission electrocardiogram (EKG) revealed normal sinus rhythm, first-degree atrioventricular block, and prolongation of the QTc interval (519 ms). Six years earlier, the patient's QTc interval had been 409 ms (Figures 1 and 2). As QT interval depends on heart rate, it is most commonly expressed as corrected QT, or QTc, where QTc = QT/(√RR).

Table. Laboratory Results, QTc Interval, and Lorazepam Use

Laboratory Test	Reference Range	Hospital Day 0	Hospital Day 3
Blood urea nitrogen, mg/dL	7-25	6	7
Creatinine, mg/dL	0.5-1.5	0.84	0.69
Sodium, mmol/L	135-145	137	134
Potassium, mmol/L	3.5-5.0	3.9	3.9
Calcium, mmol/L	8.5-10.5	8.4	7.5
Corrected calcium, mg/dL	8.5-10.5	9.52	8.86
Ionized calcium, mmol/L	1.16-1.32	NP	1.01
Magnesium, mmol/L	1.6-2.6	1.4	2.3
Albumin, g/dL	3.2-5.0	2.6	2.3
Lorazepam, total mg	—	2	6 in prior 24 h
Heart rate, bpm	—	100-110	60-80
Troponin, ng/mL	—	> 0.03	> 0.03
QTc interval, ms	< 440	519	549

Abbreviation: NP, not performed.

Symptom-triggered therapy for alcohol withdrawal was instituted, and the patient's electrolyte abnormalities were corrected. Telemetry monitoring demonstrated polymorphic ventricular ectopy, including a 6.8-s run of polymorphic ventricular tachycardia and several shorter runs (4-10 beats) of nonsustained ventricular tachycardia, prompting initiation of a low-dose beta blocker. Based on elevated scores on the symptom-triggered scale for alcohol withdrawal, the Clinical Institute Withdrawal Assessement for Alcohol Withdrawal (CIWA), several doses of oral lorazepam were given for withdrawal symptoms.

The patient became increasingly confused, and new-onset nystagmus was noted. These findings raised concern for Wernicke encephalopathy, so the patient was empirically started on IV high-dose thiamine supplementation. The CIWA scores remained high, and there were frequent episodes of ventricular ectopy during the first 2 hospital days. Interval EKG revealed further prolongation of the QTc interval (549 ms) without evidence of cardiac ischemia (Figure 3). Cardiac enzymes were negative, and electrolyte levels were within normal limits.

On hospital day 3, the patient had a TdP cardiac arrest. Treatment for the arrest consisted of cardiopulmonary resuscitation, administration of epinephrine and amiodarone, and 2 uses of external defibrillation (Table). Rhythm returned to sinus with these measures, and spontaneous circulation was regained. The patient was intubated, placed on the hypothermia protocol, and transferred to the intensive care unit. Transthoracic echocardiogram revealed preserved left ventricular ejection fraction of 65%, mild concentric left ventricular hypertrophy, mild bi-atrial dilatation, and severe aortic stenosis. After rewarming, the patient was encephalopathic (result of hypoxic brain injury), and he was extubated on hospital day 7.

The month-long hospitalization was notable for development of significant ascites, continual electrolyte repletion in the setting of diuresis, formal diagnosis of alcoholic cirrhoisis, cognitive and physical rehabilitation. During the hospitalization, QTc interval remained prolonged (range, 460-500 ms), despite

Figure 1. 2009 Electrocardiogram (QTC 409 ms)

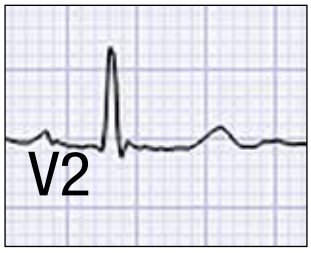


Figure 2. Hospital Day 0 Electrocardiogram (QTC 519 ms)

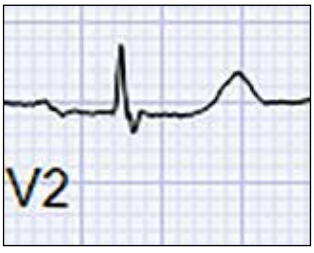


Figure 3. Hospital Day 3 Electrocardiogram (QTC 549 ms)

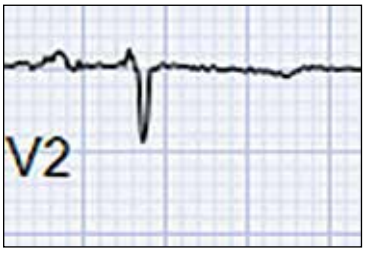
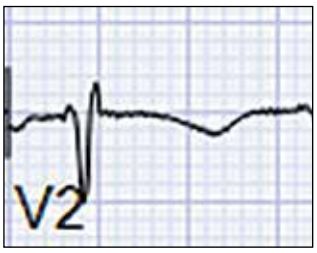


Figure 4. 30-Day Follow-Up Electrocardiogram (QTC 499 ms)



electrolyte repletion, and he was discharged with a wearable cardioverter defibrillator. A month after discharge, QTc interval was still significantly prolonged (497 ms), despite the patient's continued abstinence from alcohol and normal electrolyte levels (Figure 4). He ultimately fully recovered from the cardiac arrest, and with alcohol cessation, his Child-Pugh score improved to 4. The patient later underwent aortic valve replacement and received an internal cardiac defibrillator without complications.

DISCUSSION

Alcohol dependence is a common chronic and relapsing disease that often requires controlled detoxification. Investigators have found a high incidence of QT interval prolongation in alcohol withdrawal and hepatic disease.[3,6] Common causes of QT interval prolongation in this setting are poor nutrition, electrolyte abnormalities (particularly hypocalcemia and hypomagnesemia), and use of certain medications.[1-3,7,8] In addition, alcohol is directly toxic to the renal tubules, resulting in renal wasting of divalent cations, which may persist up to 30 days after the most recent alcohol exposure.[9,10]

The patient in this case report was initially thought to have hypomagnesemia-induced long QT syndrome (leading to TdP cardiac arrest), but the authors' review of laboratory test results revealed the QT interval remained markedly prolonged, despite adequate correction of hypomagnesemia implicating the hyperadrenergic state of acute alcohol withdrawal in QT interval prolongation and TdP cardiac arrest. Interestingly, the QT interval remained prolonged 2 months after TdP arrest, despite sustained normalization of electrolyte levels and the absence of active ischemia or use of QT-prolonging medications.

Given the exclusion of other causes of QT interval prolongation, the authors hypothesized that autonomic hyperactivity of acute alcohol withdrawal and resultant QT interval prolongation were potentiated by underlying cirrhotic cardiomyopathy, a well described cause of QT interval prolongation. Cirrhotic cardiomyopathy is thought to cause QT interval prolongation by delayed repolarization of cardiomyocytes and promotion of sympatho-adrenergic hyperactivity.[6] In other case series, TdP development has been associated with severe withdrawal symptoms, particularly delirium tremens.[2] In cirrhosis, QT interval prolongation often is described as an early manifestation of cirrhotic cardiomyopathy, irrespective of the underlying etiology, and precedes systolic and diastolic dysfunction.[6]

The magnitude of QT prolongation has been associated with severity of liver disease as expressed by Child-Pugh score, with reports of QT normalization after liver transplantation.[4,5] Patients with higher Child-Pugh scores should be considered to be at elevated risk for malignant ventricular arrhythmias. The authors recommend checking an EKG on admission of any patient who has liver disease or has presented for alcohol withdrawal. Patients with a prolonged QTc interval should be monitored on telemetry. The authors also recommend aggressive repletion of electrolytes, particularly potassium and magnesium, in patients who present with cirrhosis and alcohol withdrawal.

Avoidance of QT-prolonging medications is advisable for all patients with a long QT interval. Beta blockers shorten the QT interval in cirrhotic patients, but the role of beta blockers in preventing malignant arrhythmias in this group of patients is not yet clear.[11] The present patient's QT interval had been normal before he developed cirrhotic liver disease. His presentation was suggestive of acquired long QT syndrome, likely caused by cirrhotic cardiomyopathy given

the exhaustive exclusion of other causes of QT interval prolongation.

CONCLUSION

This case highlights the importance of close monitoring of the QT interval in patients being treated for acute alcohol withdrawal, particularly those with cirrhosis, and suggests that timely and aggressive management of withdrawal, repletion of electrolytes, and telemetry monitoring may prevent life-threatening arrhythmia. ●

Author disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

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