Tako-tsubo cardiomyopathy precipitated by alcohol withdrawal

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Abstract
A 57 year-old woman with no history of cardiac disease presented to the emergency department with confusion and seizures secondary to alcohol withdrawal. Elevated troponin levels and an electrocardiogram demonstrating global T-wave inversions prompted coronary angiography, which revealed coronary vessels free of significant disease. An echocardiogram showed both hypokinesis of the left-ventricular mid-segments with apical involvement and a hyperkinetic base consistent with tako-tsubo cardiomyopathy (TCM). Several clinical conditions have been reported as triggers of TCM. We report a case of TCM in a post-menopausal woman that was precipitated by alcohol withdrawal. (Cardiol J 2012; 19, 1: 81–85)

Key words: tako-tsubo cardiomyopathy, transient apical ballooning, stress-induced cardiomyopathy, alcohol withdrawal

Introduction
Tako-tsubo cardiomyopathy (TCM) was formally described by Sato et al. [1] in 1990. Usually occurring after periods of emotional or physical stress, the abnormal myocardial contraction clinically and electrocardiographically mimics an acute myocardial infarction (AMI) without angiographic evidence of coronary obstruction. The characteristic apical ballooning seen on a ventriculogram is fully reversible (within a few weeks at most). An estimated 2% of suspected AMI may in fact be TCM, although this is likely to be an underestimation given the diagnostic requirement for percutaneous coronary intervention and relative lack of awareness.

Most cases of TCM occur in post-menopausal women. As normalization commonly occurs within a few weeks, TCM has a favorable prognosis; however, recurrence rates have been reported as high as 11.4% over four years [2]. Heart failure is a common complication; rare yet potentially fatal complications include left-ventricular thrombus, cardiac rupture, and arrhythmias such as complete heart block and long QT interval associated with torsade de pointes [3, 4]. Given its transient nature, the all-cause mortality due to TCM is difficult to accurately determine.

Several clinical conditions have been reported as triggers of TCM. We report a case of TCM in a post-menopausal woman that was precipitated by alcohol withdrawal.

Case report
Our patient is a 57 year-old woman with a 12 year history of alcohol abuse and a 40 pack-year smoker with chronic obstructive pulmonary disease; however, she had no known personal or family history of cardiovascular disease. She experienced alcohol-related seizures for ten years, recently achieving control with levetiracetam 1 g bid. She
was not taking any other medications. She presented to the emergency department (ED) after two episodes of seizures and confusion occurring the morning after a night of binge drinking. She did not report dyspnea, chest discomfort, or palpitations. While in the ED, she displayed the typical signs of alcohol withdrawal, including tachycardia, agitation, tremulousness, diaphoresis, and seizure activity. The alcohol withdrawal was treated using standard practices including benzodiazepines and thiamine. The seizures were described as complex partial, with an aura of confusion that lasted a few minutes followed by secondary generalization to tonic-clonic seizure activity. In addition, the patient was febrile and hypotensive, requiring admission to the intensive care unit for vasopressor and inotropic support for suspected sepsis or meningitis. Imaging of her head was unremarkable. Blood cultures were negative, and the cerebrospinal fluid was unremarkable. The patient was noted to be hypokalemic (2.7 mmol/L), with a normal renal function, and an elevated troponin I of 4.075 μg/L (normal 0–0.06 μg/L). Her electrocardiogram (ECG) showed new global T-wave inversions in leads V1–V6, I, and II, III and aVF (Fig. 1B) when compared to baseline (Fig. 1A); in addition, a prolonged QT interval (QTc = 558 ms) was noted (Fig. 1B). The echocardiogram was consistent with apical ballooning on systole and confirmed hypokinesis of the left-ventricular mid-segments and apex (Fig. 1C). Angiographically, the left ventriculogram revealed a characteristic pattern of apical ballooning (Fig. 1D) in the absence of coronary atherosclerosis (Fig. 1E). Within days of presentation, the clinical signs of heart failure were apparent, including peripheral edema and an elevated jugular venous pressure of 6 cm above the sternal angle. General supportive measures were instituted including ACE inhibitor, beta-blocker and diuretics. A repeat echocardiogram 12 days after admission revealed reversal of ventricular wall motion.

Figure 1. Studies demonstrating tako-tsubo cardiomyopathy; A. 12-lead ECG eight months prior to admission; B. 12-lead ECG on admission. Note the global T-wave inversions in V1–V6, I, and II, III and aVF. QTc interval prolongation; C. Echocardiogram (four-chamber view) confirming hypokinesis of mid-segments and apex of the left ventricle; D. Ventriculogram (systole) demonstrating ampule-shaped apical ballooning; E. Coronary angiogram showing no obstruction of left coronary arteries.
abnormalities and improvement in function. Her symptoms improved, and after counseling on smoking and alcohol cessation she was discharged home on aspirin, ramipril, metoprolol and furosemide. At the time of discharge, the QT interval had returned to normal (QTc = 434 ms).

Discussion

The presented report highlights a case of TCM secondary to alcohol withdrawal. The diagnosis of TCM was confirmed by the absence of coronary artery disease (CAD) in the presence of a characteristic, transient, left ventricular apical ballooning pattern which was in keeping with the recently revised Mayo criteria (Table 1) [5]. Although we did not record ST-elevations, the 12-lead ECG showed giant inverted T-waves globally (Fig. 1B), consistent with the ECG timeline of TCM. Evolutionary T-wave inversion in most leads is expected to occur following transient ST-segment elevation [6]. We also observed QT interval prolongation (Fig. 1B) that can lead to polymorphic ventricular arrhythmias. QT prolongation complicated with torsade de pointes has been associated with TCM [3]. It has been previously reported that prolonging the interval from the peak to the end of the T-wave and its dispersion has been associated with an increased risk of arrhythmic events [4]. Although our patient was not taking any medications with known effects on cardiac repolarization, the hypokalemia, chronic alcoholism and alcohol withdrawal may have contributed to the QT interval prolongation in this case [7].

The etiology of TCM remains controversial. Ibanez et al. [8] proposed that TCM may be due to MI abortion secondary to spontaneous thrombus autolysis that may lead to the transient akinesis of stunned myocardium. This was motivated by the demonstration of disrupted eccentric atherosclerotic plaques on intravascular ultrasound images of the left anterior descending coronary artery.

Most cases of TCM, however, occur during periods of stress. In fact, it was determined that catecholamine levels were two to three times higher in TCM patients as compared to AMI patients [9]. This fact may support the hypothesis of a mechanism of transient ventricular dysfunction not necessarily associated with epicardial CAD. The precise role that catecholamines may play in TCM to exert cardiotoxic effects has not yet been elucidated. Consistent with catecholamine toxicity are histological changes and findings of myocyte calcium overload that may lead to contractile dysfunction [10]. The stress hypothesis of TCM is consistent with our case of alcohol withdrawal.

Alcohol withdrawal syndrome is a serious and common complication of chronic alcoholism that occurs six to 48 hours after last alcohol consumption. Symptoms and signs include anxiety, agitation, tremulousness, tachycardia, and diaphoresis, potentially leading to profound confusion, hallucinations, and seizures. Sympathetic hyperactivity is responsible for the majority of these events, and has been well documented. Experiments on murine models during ethanol withdrawal in the 1970s demonstrated increased beta-adrenergic sensitivity in the brain and heart [11]. Moreover, it is well known that plasma levels of catecholamines increase during alcohol withdrawal, commensurate with symptoms, and fall with resolution [12]. These findings are paralleled with cerebrospinal fluid norepinephrine, as well as its turnover metabolite, 3-methoxy-4-hydroxyphenylethylene glycol, in cerebrospinal fluid and urine [13]. Finally, propranolol, a non-selective beta-adrenergic blocker, reduces urine norepinephrine [14] and alters cardiovascular responses [15] during alcohol withdrawal, further establishing a link with increased sympathetic tone. Thus, our case of TCM during alcohol withdrawal is consistent with the aforementioned stress hypothesis.

To our knowledge, there have been three cases thus far that have associated TCM with alcohol withdrawal. The presented report highlights a case of TCM secondary to alcohol withdrawal. The diagnosis of TCM was confirmed by the absence of coronary artery disease (CAD) in the presence of a characteristic, transient, left ventricular apical ballooning pattern which was in keeping with the recently revised Mayo criteria (Table 1) [5]. Although we did not record ST-elevations, the 12-lead ECG showed giant inverted T-waves globally (Fig. 1B), consistent with the ECG timeline of TCM. Evolutionary T-wave inversion in most leads is expected to occur following transient ST-segment elevation [6]. We also observed QT interval prolongation (Fig. 1B) that can lead to polymorphic ventricular arrhythmias. QT prolongation complicated with torsade de pointes has been associated with TCM [3]. It has been previously reported that prolonging the interval from the peak to the end of the T-wave and its dispersion has been associated with an increased risk of arrhythmic events [4]. Although our patient was not taking any medications with known effects on cardiac repolarization, the hypokalemia, chronic alcoholism and alcohol withdrawal may have contributed to the QT interval prolongation in this case [7].

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withdrawal (Table 2). In 2004, Suzuki et al. [16] described a case of suspected TCM during alcohol withdrawal; however, that case was atypical in that the akinesis was limited to the anterior left ventricle and septum with no apical ballooning. Furthermore, additional and significant stresses occurred with this patient, including a cardiac arrest preceding the suspected TCM. Moreover, his case was complicated by a diagnosis of hypokalemia-related myopathy, and his chief complaint did not center on the symptoms of alcohol withdrawal. Another case was discussed by Mitchell et al. [17]; however, the evidence of alcohol withdrawal potentially causing TCM was limited. Finally, a recent report by Kalra et al. [18] described a 25 year-old woman with alcoholic seizures and torsade de pointes leading to ventricular fibrillation. She presented with globally deep inverted T-waves on ECG in addition to a prolonged QTc interval and characteristic echocardiographic findings consistent with TCM, similar to our patient. However, this clinical picture was confounded by reported cocaine use in the days prior to hospitalization. It is unclear whether the arrhythmia was induced by cocaine and alcohol triggering the TCM, or whether it was the sympathetic effects of the alcohol withdrawal per se.

Indeed, there are many etiologies of stress, and it has been shown that hospitalization and intensive care admission may result in TCM [19]. Therefore, a universal limitation of the aforementioned cases, in addition to ours, is the difficulty of establishing a direct causal link between alcohol withdrawal and TCM in the face of the inherent stress associated with hospitalization.

Conclusions

Alcohol withdrawal is associated with significant sympathetic hyperactivity. This sudden increased sympathetic tone can result in the development of TCM. The potential prolongation of the QT interval and associated risk of ventricular arrhythmias in this setting warrants extended electrocardiographic monitoring. Establishing the timing of events during the course of alcohol withdrawal leading to TCM is of the utmost importance in managing reversible, but life-threatening, conditions.

Conflict of interest: none declared
References


