Takotsubo Cardiomyopathy in the Setting of Acute Alcohol Withdrawal

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Abstract

Takotsubo Cardiomyopathy (TCM), also known as stress-induced cardiomyopathy, is a cardiomyopathy characterized by acute reversible apical ventricular dysfunction and apical akinesis in the absence of obstructive coronary artery disease. Although the disease may be precipitated by an acute emotional or physical stressor, the pathophysiology, postulated to involve excess catecholamine release, remains unproven. In contrast, the role of catecholamine excess and hyperadrenergic physiology in acute alcohol withdrawal (AAW) is more established. TCM in the context of acute alcohol withdrawal has been only rarely described. The authors present a new case of TCM in the setting of AAW, along with a review of other reported cases. Current theories on the etiology of TCM and a possible pathophysiologic linkage between TCM and AAW are discussed.

Keywords

Takotsubo Cardiomyopathy; Alcohol Withdrawal; Stress-induced Cardiomyopathy; Stress Cardiomyopathy; Cardiac Complications of Alcohol Withdrawal

Introduction

Takotsubo Cardiomyopathy (TCM), also known as stress-induced cardiomyopathy, is a cardiomyopathy characterized by acute reversible apical ventricular dysfunction and apical akinesis in the absence of obstructive coronary artery disease. Although the disease may be precipitated by an acute emotional or physical stressor, the pathophysiology, postulated to involve excess catecholamine release, remains unproven. In contrast, the role of catecholamine excess and hyperadrenergic physiology in acute alcohol withdrawal (AAW) is more established.

"Takotsubo" means "octopus trap" in Japanese, a jar-shaped device with a similar appearance to the apical akinetic heart of TCM. Also known as apical ballooning syndrome, broken heart syndrome, and stress or stress-induced cardiomyopathy, TCM is recognized clinically by presenting signs and symptoms (chest pain, dyspnea, and occasional syncope, as well as abnormal EKG findings with elevated cardiac biochemical markers) that often mimic Acute Coronary Syndrome. Diagnosis is essentially one of exclusion, often following cardiac catheterization that reveals normal or nonobstructive coronary artery disease. Left ventricular dysfunction is common, demonstrated with echocardiogram or left ventriculogram. Common findings are depressed ejection fraction and left ventricular apical akinesis. Treatment for TCM is supportive, as there appears to be no definitive benefit to pharmacologic therapy, to include beta-blockade, calcium channel blockade, ace inhibitor, or aspirin therapy.[1] The long term prognosis in individuals with this condition is generally very good, with many patients experiencing full resolution of systolic dysfunction in 4-8 weeks. Complications are rare, and include heart failure, free-wall rupture, fatal ventricular arrhythmias, and mural thrombus formation.

Multiple etiologies for TCM have been proposed, and catecholamine toxicity is increasingly accepted as the likely explanation. Excessive adrenergic stimulus is known to cause a cardiotoxic effect in other conditions involving excessive catecholamine release. One example is myocardial damage as a result of hypertensive crisis in the setting of pheochromocytoma.[2] Three pathophysiologic mechanisms for catecholamine toxicity in TCM have been suggested, none of which is mutually exclusive. Catecholamine toxicity may lead to vasospasm of distal coronary arteries, causing apical wall akinesis.[3] Supraphysiologic levels of epinephrine may turn myocyte beta-receptors into a Gi-coupled receptor from a Gs-coupled receptor, thereby inhibiting cardiac contractility as a means for cardioprotection.[4] A severe intracardiac gradient secondary to basal hypercontractility with left ventricular output tract obstruction may result in apical wall stress and ischemia.[5] Nef, et al, summarized the concurrent effects of catecholamine overload as the development of general morphological alterations and disturbance of Ca2+ homeostasis.[6] It was postulated that the relatively rapid recovery of cardiomyocytes often seen in this disorder were possibly due to protective mechanisms of Pi3K–akt signaling pathways.

Ingestion of ethanol results in well described effects on adrenergic activity. While initial or periodic ingestion can result in transiently increased levels of adrenergic activity, chronic or repeated exposure to ethanol results in global inhibition of catecholamine release and increased GABA pathway activation in the brain.[7,8] Acute alcohol withdrawal, which can be precipitated by discontinuation or marked reduction in ethanol intake, may result in a 48-96 hour period of unopposed catecholamine activation and decreased central inhibition.[8] The manifestations of this relatively unopposed adrenergic activity are stereotypic, and include tremulousness, anxiety, nausea, vomiting, diarrhea, tachycardia, and hypertension.[9] While not demonstrated definitively in human subjects, the cardiomyotoxic effect of a hyperadrenergic state due to alcohol withdrawal has been demonstrated in animals.[10] TCM occurring in the presence of AAW has rarely been described.

Case Report

A 45-year-old woman with a history of depression, anxiety, alcoholism, and recurrent Stage IIB left lower lobe pulmonary adenocarcinoma presented with epigastric pain, nausea, and emesis for 72 hours. These symptoms arose 24-48 hours after abrupt discontinuation of alcohol, with estimated prior daily consumption of 6-10 beers for 10 years. She also reported simultaneously discontinuing her antidepressant and anxiolytic medications. Physical exam showed tachycardia and tremulousness, but was otherwise unremarkable. An electrocardiogram revealed sinus tachycardia, right axis deviation, and T-wave inversion in the inferolateral leads. Troponin I marker was elevated and peaked to 0.974 ng/ml. TIMI risk score was 2.

Clinical Institute Withdrawal Assessment (CIWA) score was 9, with intermittent vomiting, mild anxiety, and moderate tremor. Transthoracic echocardiogram showed hyperkinesis of mid- to distal left ventricular walls with akinetic apical walls, and an ejection fraction of 30%-35%. Cardiac catheterization revealed minimal luminal irregularities of the main coronaries and no significant obstruction. A left ventriculogram was not performed. The patient received appropriate therapy for her AAW and supportive therapy for TCM with excellent clinical response.

Discussion

Four other cases of TCM occurring in the setting of AAW were identified. The initial case of TCM reported in the setting of AAW involved a 64-year-old man with alcohol dependence admitted with hypokalemia-related cardiomyopathy.[11] The patient had a cardiopulmonary arrest on hospital day five, and developed ST-elevations and T-wave inversions on ECG, with elevated CK-MB. Cardiac catheterization was normal, and left ventriculogram showed anterior left ventricular akinesis consistent with TCM.

A second case involved a 49-year-old woman who was admitted to a hospital with altered mental status.[12] She was started on an alcohol withdrawal protocol, but later became unstable, with ST elevations, T-wave inversions on ECG, and elevated cardiac biomarkers. Transthoracic echocardiogram showed apical wall akinesis of the left ventricle consistent with TCM.

The third case of TCM reported involved a 61 year old man who presented in acute withdrawal and with typical anginal symptoms.[13] The patient had elevated troponins and T-wave inversions on EKG evolving to ST elevations in leads V3-V5. Ultimately, cardiac catheterization revealed normal coronary arteries with additional findings of ventriculomegally and left ventricular apical ballooning.

A more recent case occurred in a 56-year-old man admitted for alcohol withdrawal, presented findings consistent with acute congestive heart failure, an EKG remarkable for pathologic Q waves in the precordial leads, and a mildly elevated troponin I and brain natriuretic peptide (BNP).[14] Transthoracic echocardiogram revealed left ventricular apical ballooning, hyperkinesis of base segments, and an LVEF of 20%. Cardiac catheterization revealed no significant obstructive coronary disease, evidence of plaque rupture, or vasospasm.

Conclusion

The central role of excess catecholamines in the development of TCM is increasingly accepted. AAW is a well-described state of excessive adrenergic activity. Whereas TCM reported in the context of acute alcohol withdrawal remains rarely reported, this may reflect the possibility that cardiac function testing and an ischemic evaluation are not routinely undertaken as part of the evaluation and treatment of AAW. Clinicians should be aware of TCM as a possible complication of AAW and providers should consider the possibility of TCM in patients with signs and symptoms of chest pain or left ventricular dysfunction in patients with AAW.

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Conflict of Interest

None of the authors identify any conflict of interest.

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