Case Report

Clostridium Difficile Infection and Takotsubo Cardiomyopathy: Is There a Relation?

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Abstract

Context: Takotsubo cardiomyopathy (TCM) mimics acute coronary syndrome and is accompanied by reversible left ventricular apical ballooning in the absence of angiographically significant coronary artery stenosis. It is a transient condition that typically precedes physical or emotional triggers. **Case Report:** We describe the case of a 65-year-old woman who presented to our institution with symptomatic *Clostridium difficile* infection. 24 hours after admission, the patient complained of severe, retrosternal chest pain. Electrocardiogram showed diffuse elevation of ST-segment in the chest leads; however, coronary angiography demonstrated normal coronary arteries. Therein, an echocardiography was performed, which revealed apical ballooning and hypercontractile base with global left ventricular hypokinesis. These features were consistent with TCM. The patient was managed conservatively. Repeat echocardiogram 2 weeks later showed resolution of heart failure. **Conclusion:** To our research, this is the first report of TCM caused by *C. difficile* infection. Clinicians involved in the care of patients with *C. difficile* infection must be aware of this complication and should consider TCM in those who develop atypical chest pain.

Keywords: Apical ballooning, *Clostridium difficile*, coronary artery disease, takotsubo cardiomyopathy

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Introduction

Takotsubo cardiomyopathy (TCM) is characterized by transient left ventricular dysfunction without any evidence of coronary artery obstruction. In literature, there are reports of TCM caused by emotional or physical stress, drug use, hormone imbalance, or medical conditions such as pulmonary disease, sepsis, and trauma; however, a relationship between TCM and *Clostridium difficile* infection has not previously been described. The present report brings to light the risk of TCM in patients with *C. difficile* infection.

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Case Report

A 65-year-old female, who was recently treated with amoxicillin for bacterial sinusitis in outpatient for 7 days, presented to the Mount Sinai St. Luke's Emergency Department with severe abdominal pain, fever, and diarrhea. Her vital signs were notable for temperature 39°C, heart rate 112 beats/min, and blood pressure 99/65 mmHg. Abdominal examination revealed hyperactive bowel sounds and diffuse abdominal tenderness with rebound. There was no abdominal rigidity or guarding. She was non-alcoholic, non-smoker, and drug-free. Initial laboratory

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evaluation was remarkable for white cell count 17,000/μL (4–11000/μL) and creatinine 1.7 mg/dl. Enzyme immunoassay was positive for toxigenic strain of *C. difficile*. The patient was resuscitated with intravenous fluids, and oral metronidazole therapy was initiated.

On the night of her admission, she started having retrosternal chest pain of severe intensity with moderate distress in breathing. Electrocardiogram (EKG) showed ST-segment elevation in the chest leads V1–V5, consistent with left main coronary artery or left anterior descending artery occlusion [Figure 1]. Aspirin 325 mg was administered. Cardiac biomarkers, troponin-I and b-type natriuretic peptide, were elevated at 2.16 ng/mL and 447 pg/mL, respectively. Serial troponin-I was trended with a peak level of 9.8 ng/mL. Chest radiography and hepatobiliary ultrasound were unremarkable. Initial transthoracic echocardiogram showed apical ballooning and global left ventricular hypokinesis with a left ventricle ejection fraction (LVEF) of ~ 20–25% [Figure 2].

ST-segment elevation myocardial (STEMI) infarction code was activated. Emergent coronary angiogram demonstrated normal coronary arteries with no coronary disease but consistent with global hypokinesia. Left ventriculogram showed hypokinetic left ventricular apex consistent with TCM [Figure 3]. After supportive treatment, the patient's condition improved along with resolution of fever and diarrhea. On day 5 of her admission, EKG showed normalization of ST-segment elevation, and she was discharged from the hospital. A repeat echocardiogram 2 weeks later demonstrated an improved LVEF of ~60% indicating the transient nature of the disease, essential for diagnosis [Figure 4].

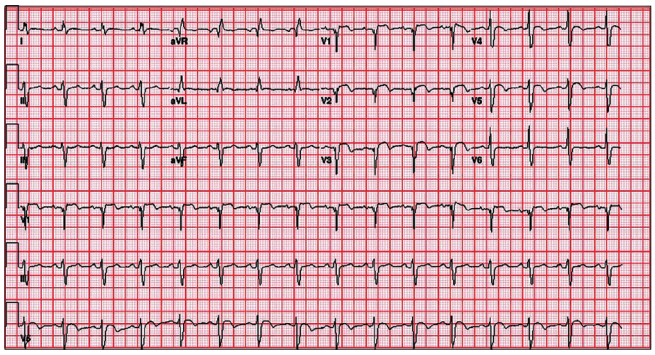

Figure 1: Electrocardiogram showing diffuse elevation of ST segment in the chest leads

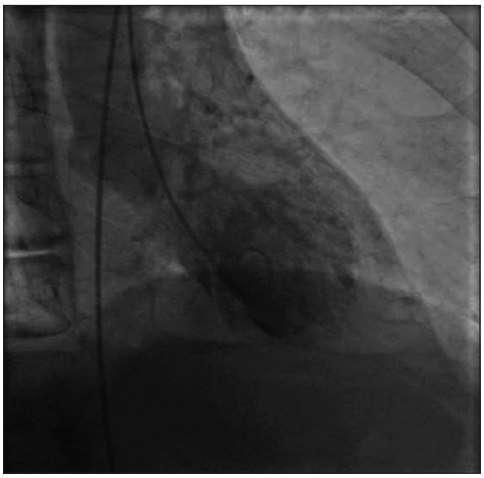

Figure 3: Left ventriculography demonstrating reduced left ventricle ejection fraction and apical ballooning consistent with Takotsubo cardiomyopathy

Discussion

TCM was first described in 1990 in Japan.[1] Since then, it has been a topic of numerous studies; however, current knowledge on TCM remains limited. It has an estimated prevalence of 2.2% of cases presenting with suspected acute coronary syndrome.[2] TCM predominantly involves elderly women and frequently present with acute substernal chest pain, dyspnea, nausea, and vomiting.[3]

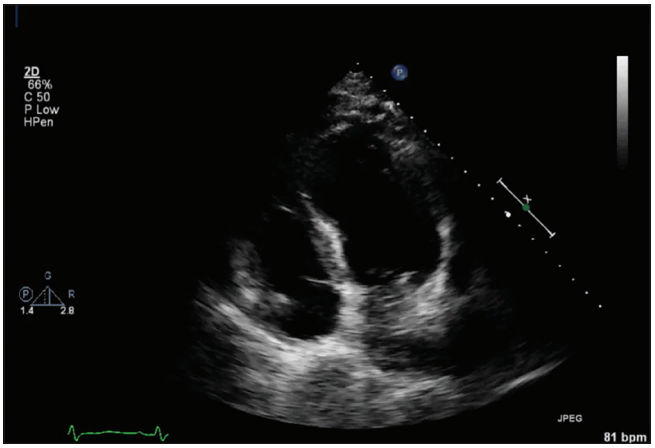

Figure 2: Transthoracic echocardiogram demonstrating apical ballooning and hypercontractile base

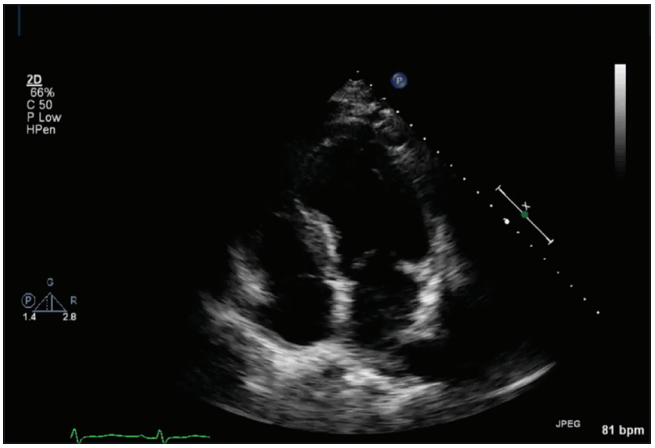

Figure 4: Transthoracic echocardiogram 2 weeks after discharge demonstrating normal left ventricle ejection fraction with no wall motion abnormalities

Current Mayo Clinic Criteria is the gold standard for the diagnosis of TCM.[4,5] It is defined as: (1) Transient hypokinesia, akinesia, or dyskinesia in the left ventricle mid-segments with/without apical involvement; regional wall motion abnormalities that usually extend beyond a single epicardial vascular distribution; and frequently, but not always, a stressful trigger; (2) absence of obstructive coronary disease or angiographic evidence of acute plaque rupture; (3) new EKG abnormalities (ST-segment elevations or T-wave inversion) or modest elevation in cardiac troponin; and (4) absence of pheochromocytoma and myocarditis. The ECG and transthoracic echocardiogram changes in this 65-year-old woman were consistent with these criteria for differentiating TCM from an acute myocardial infarction. Accurate and prompt diagnosis has substantial prognostic implications in view of the evidence that in TCM patients, the underlying critical illness is the main driver of the mortality rates.[6] Previously, studies demonstrated numerous emotional or physical triggers preceding TCM.[7] Reports are available on possible associations of acute pancreatitis, subarachnoid hemorrhage, epilepsy, electroconvulsive therapy, head injury, stroke, and anxiety or depression.[8,9]

Infectious diseases and sepsis can derange the ventricular function, systolic blood pressure, ventricular extension, circulating volume, and vessel tone by intracellular and extracellular mechanisms.[10,11] Therefore, they are regarded as important etiological factors for TCM. Case reports are available in the medical literature implicating methicillin-resistant *Staphylococcus aureus*, *Klebsiella pneumonia*, methicillin-resistant *Staphylococcus saprophyticus*, *Streptococcus pneumonia*, *Klebsiella oxytoca*, *Escherichia coli*, *Streptococcus* Group B, *Aeromonas hydrophila*, *Clostridium tetani*, *Staphylococcus gallinarum*, *Staphylococcus aureus* as culprits behind TCM.[12] Furthermore, TCM cases by viral agents have been presented with cytomegalovirus and herpesvirus 6 infections.[12] There are also various reports on relationship between sepsis and TCM.[13,14] However, to our knowledge, TCM in the setting of *C. difficile* infection has never been reported. *C. difficile* is the causative organism of mild to life-threatening antibiotic-related colitis. The incidence and severity of nosocomial *C. difficile* infection have tremendously increased in recent years, particularly in elderly patients.[15]

The most widely accepted hypotheses for TCM pathogenesis are catecholamine-toxicity and microvascular dysfunction. *C. difficile* as a classic anaerobic bacterium has been associated with the sympathetic overdrive. Toxigenic strains of *C. difficile* release two large molecular weight proteinaceous exotoxins identified as toxins A and B. Xia *et al*.[16] demonstrated in their bench research that *C. difficile* toxin A causes prevention of sympathetic inactivation of the enteric microcircuits that generate intestinal motor activity and other intestinal behaviors during *C. difficile* enteritis.[16] Patients with predisposition to TCM have high endogenous levels of catecholamines along with differential distribution of adrenergic receptors on the myocardial surface.[17] This hypothesis is further strengthened by highlighting the role of other sympathetic overdrive states such as acute pancreatitis, pheochromocytoma, stroke, and subarachnoid hemorrhage in the causation of TCM.[8,9] In addition, the distributive shock that develops with *C. difficile* infection may result in transient myocardial dysfunction and microvascular hypoperfusion. The pathophysiologic mechanism of TCM development in our patient may be designated as the catecholamine surge in the setting of *C. difficile* and hypovolemia. However, the exact pathogenesis of induced-TCM remains to be determined and merits further investigation.

Conclusion

The present case highlights the first report of *C. difficile* infection-related TCM. Albeit rare, further clinical studies are warranted to broaden the scope of our knowledge on this association and to frame guidelines to standardize the care of these patients.

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Conflicts of interest

There are no conflicts of interest.

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