

Takotsubo Cardiomyopathy Due to Iatrogenic Methadone Withdrawal

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Takotsubo cardiomyopathy is a syndrome characterized by transient apical ballooning or reversible midventricular systolic dysfunction. Most cases occur in postmenopausal women and are typically triggered by an acute medical illness or emotional or physical stress. Its presentation is highly suggestive of myocardial ischemia, but there is little or no evidence of epicardial coronary artery disease. To our knowledge there are only three reported cases in the literature of Takotsubo cardiomyopathy induced by opioid agonist withdrawal in adults; ours is the first reported case of iatrogenic methadone withdrawal leading to Takotsubo cardiomyopathy.

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A 60-year-old man with a past medical history of chronic obstructive pulmonary disease, hepatitis C, and intravenous drug abuse who was on a high-dose methadone maintenance program was brought to the emergency room (ER). In the ER he was lethargic with labored breathing. He was diagnosed with methadone intoxication by the ER team and was started on a naloxone infusion. The patient's mental status improved markedly. He stated that he had accidentally ingested double the prescribed dosage of methadone earlier in the day and denied using any form of narcotics or other illicit substances. However, he soon became agitated, tachycardic, and hypertensive.

He began complaining of severe retrosternal chest pressure. Electrocardiograph (ECG) showed ST-segment elevation in the precordial leads with T-wave inversions in the anterolateral leads, and a normal QT interval

(Figure 1). Laboratory investigations revealed a troponin level of 1.68 ng/mL and creatine kinase MB of 30.4 IU/L. Emergent coronary angiography did not reveal any significant coronary artery disease (Figure 2). Contrast

ventriculography revealed an ejection fraction (EF) of 25%. A post-catheterization echocardiogram revealed anteroapical and inferoapical ballooning, distal septal hypokinesis, and an EF of 35% (Figure 3). A diagnosis of stress-induced, or Takotsubo, cardiomyopathy resulting from acute methadone withdrawal was made. The patient was discharged home on hospital day 5 in stable condition. He followed up with his cardiologist 1 month later. Repeat echocardiogram revealed an EF of 55% and no residual hypokinesis of any of the walls. Repeat ECG revealed normalization of the ST-segment elevation and T-wave inversion (Figure 4).

Discussion

Takotsubo cardiomyopathy, also known as stress-induced cardiomyopathy, is characterized by transient apical or midventricular systolic dysfunction. It is usually reversible, and its name is derived from the appearance of the ventriculogram, which resembles a Japanese octopus fishing pot called *takotsubo*.^{1,2} Clinically, patients present with symptoms highly suggestive of myocardial ischemia, such as chest pain and dyspnea. ECG findings often include ST elevations, T-wave inversion, and Q-wave formation, which are indistinguishable from an acute coronary syndrome, but there is an absence of significant coronary artery disease.^{1,2} It is most common in postmenopausal women and is typically triggered by an acute medical illness or emotional or physical stress.¹⁻³ Pathophysiology is still controversial, although several etiological mechanisms have been proposed, including coronary spasm, coronary microvascular impairment, transient coronary occlusion, neurogenic stunning, and catecholamine toxicity.¹ There is no validated benchmark for the diagnosis of this

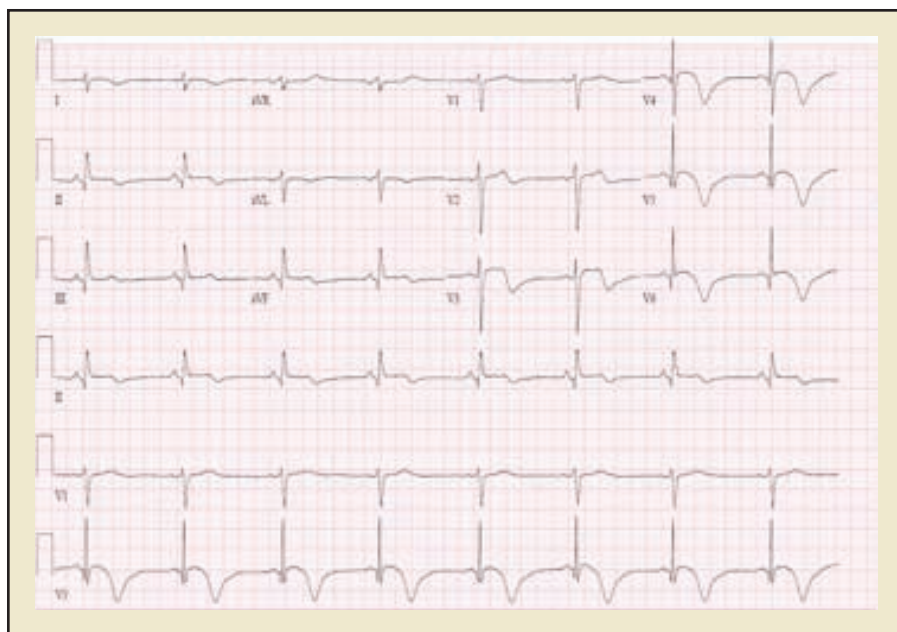


Figure 1. Initial electrocardiograph with ST elevation in lead V₃ and T-wave inversions in the anterolateral precordial leads.

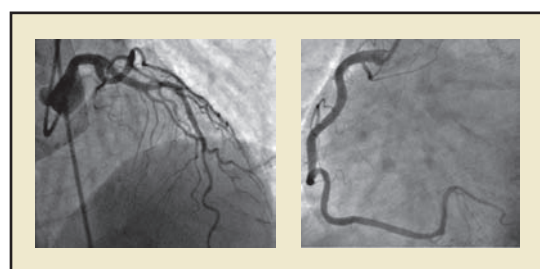


Figure 2. Angiography showing a nonobstructive lesion of the mid left anterior descending artery (left) and a clean right circumflex artery (right).

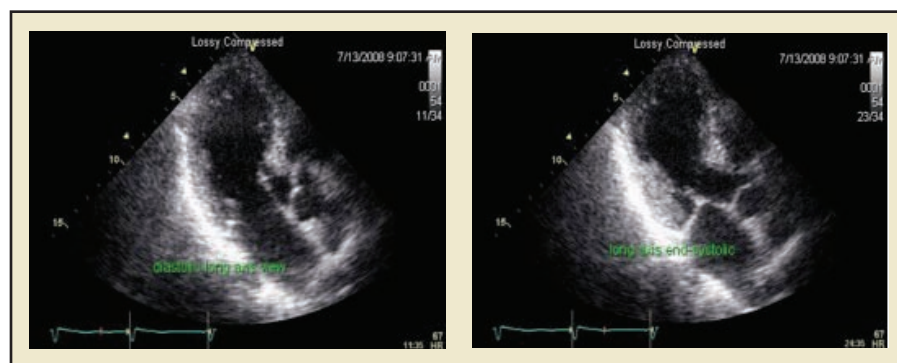


Figure 3. Long-axis view of diastole and systole with apical akinesis and ballooning of the left ventricle.

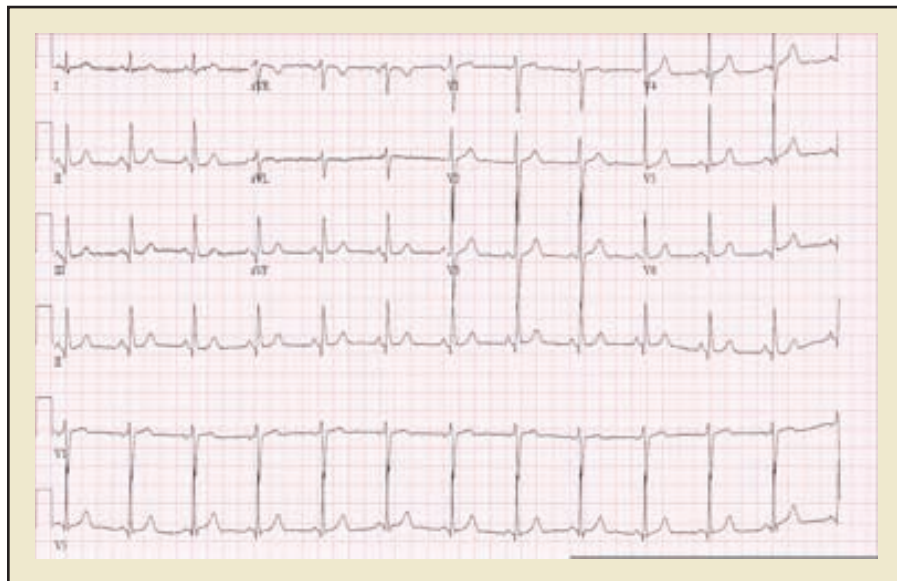


Figure 4. Repeat electrocardiograph at follow-up visit showing resolution of ST elevation and T-wave inversion.

phenomenon. Bybee and colleagues⁴ and Prasad and associates⁵ proposed a set of guidelines in 2004, known as the Mayo Criteria, that have been updated recently for the diagnosis of Takotsubo cardiomyopathy (Table 1). In order for the diagnosis to be made, a patient must meet all four criteria. Acute and long-term management of patients with Takotsubo cardiomyopathy has not been clearly defined, and more research in this area is needed. The prognosis of patients with Takotsubo cardiomyopathy is generally favorable with

supportive treatment; however, some fatal complications have been reported, such as cardiogenic shock, left ventricular free wall rupture, heart failure, left ventricle thrombus formation, ventricular fibrillation, pneumothorax, and stroke.⁶ Most

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patients who survive the acute episode show improved or normal left ventricular function within 1 to

Table 1
Proposed Mayo Criteria for the Diagnosis of Takotsubo Cardiomyopathy

1. Transient hypokinesis, akinesis, or dyskinesis in the left ventricular mid segments with or without apical involvement; regional wall motion abnormalities that 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 electrocardiographic abnormalities (ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin.
4. Absence of pheochromocytoma or myocarditis.

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4 weeks. We present a case of Takotsubo cardiomyopathy due to iatrogenic reversal of an opioid agonist, which had been adminis-

tered to treat a life-threatening opioid overdose. Opioid withdrawal likely induces a plasma catecholamine

Main Points

- Takotsubo cardiomyopathy is a reversible cardiomyopathy, typically triggered by an acute medical illness or emotional or physical stress.
- Opioid withdrawal likely induces a plasma catecholamine surge, contributing to development of Takotsubo cardiomyopathy.
- ECG findings often include ST elevations, T-wave inversion, and Q-wave formation, which are indistinguishable from an acute coronary syndrome, but there is an absence of significant coronary artery disease.
- Given the significant population of drug abusers that are on high-dose methadone maintenance, clinicians (especially emergency clinicians) should be aware of this serious complication in those coming to the emergency room presenting with an overdose.

surge, contributing to development of Takotsubo cardiomyopathy.⁷ There have been only three reported cases in the literature of Takotsubo cardiomyopathy in adults being induced by an opioid agonist withdrawal.⁸⁻¹⁰ To our knowledge this is the first report case of Takotsubo cardiomyopathy due to iatrogenic methadone withdrawal. Given the significant population of drug abusers that are on high-dose methadone maintenance, clinicians (especially ER clinicians) should be aware of this serious complication in those coming to ER clinic presenting with an overdose. ■

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