

Amphetamine Induced Reverse Takotsubo Cardiomyopathy: Case Report and Review of Literature

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1. Abstract

Takotsubo cardiomyopathy is a clinical syndrome characterized by an acute and transient left ventricular dysfunction usually triggered by an emotional or physical stressful event. The hallmark of Takotsubo cardiomyopathy is a presentation similar to acute coronary syndrome but with no evidence of obstructive coronary artery disease. The most common symptoms are acute chest pain and/or shortness of breath. Reverse Takotsubo cardiomyopathy is a rare anatomical variant (1-23%) characterized by basal hypokinesia/akinesia with apical hyperkinesis. Reverse Takotsubo cardiomyopathy is more frequent among young females and is associated with less LV dysfunction and more neurological disease. Takotsubo cardiomyopathy is proposed to develop following sympathetic activation with circulating catecholamine surges. It has been associated with exposure to adrenergic drugs in 20% of reported Takotsubo cardiomyopathy cases. We describe below a rare case of a young female who presented with chest discomfort and shortness of breath after an unknown recreational drug use and was found to have reverse Takotsubo cardiomyopathy on bedside echocardiogram with a positive urine toxicology screen for amphetamine.

2. Introduction

Takotsubo cardiomyopathy, first described in 1980, is defined as a stress induced left ventricular dysfunction that is reversible in most of the cases. It is typically seen in the setting of an acute medical illness or during physical/emotional stress, thus its other name: Broken heart syndrome [1]. Clinical presentation is similar to that of acute coronary syndrome, and it is associated with

EKG changes, elevated troponin and abnormal wall motion abnormalities on echocardiography; however, there is no evidence of obstructive pericardial coronary artery disease [2]. The incidence of stress cardiomyopathy ranges from 1.0% to 2.0% in patients presenting with a picture of acute myocardial infarction [3], with a significant rise in incidence to almost 8% during the Covid 19 pandemic [4]. Several phenotypic variants of Takotsubo cardiomyopathy have been reported, with the reverse form making <25% of all cases.

Reverse Takotsubo demonstrates apical hyperkinesis with basal and midventricular hypo- or akinesia [5]. The exact underlying pathophysiology is still being investigated; hypothesized mechanisms include catecholamine cardiotoxicity, coronary artery spasm, coronary microvasculature impairment, and estrogen deficiency [2].

We present a case of a reverse cardiomyopathy in a young healthy woman after illicit drug use.

3. Case Presentation

A previously healthy 19-year-old female presented to the emergency department with chest pain, palpitations and facial paresthesia. Her symptoms started 3 hours after she took a pill at a party. She also reported progressive shortness of breath, nausea and few episode of non-bloody vomiting. She reports having energy drinks as well as Tetrahydrocannabinol (THC). Review of systems was otherwise negative.

Upon presentation, she was tachycardic with a HR of 137 BPM. She was anxious, complaining of difficulty breathing as well as

some diaphoresis. Her pupils were dilated and reactive. The rest of her exam was otherwise negative.

ECG showed sinus tachycardia with ST segment elevation in I and aVL (Figure 1).

Chest X-ray was normal. Her troponin level was 1.048 ng/mL (Normal <0.030 ng/mL). The urine drug screen was positive for Amphetamines and THC. Bedside transthoracic echocardiography showed moderately impaired left ventricular systolic function with an estimated LVEF of 35-39%. Hypokinesia of basal and mid left ventricular segments with hyperkinesia of the apical segments

suggestive of reverse Takotsubo cardiomyopathy (Videos 1, 2).

Her palpitations and chest pain improved after giving a dose of Diazepam IV 2mg and her rate went from 130 to 90 bpm.

Cardiac catheterization was not done given the patient's age and the improvement in her symptoms after her rate dropped.

She was then started on Ivabradine 5 mg twice daily. She was admitted to the cardiac care unit for observation and discharged 48 hours after complete resolution of her symptoms. A transthoracic echocardiography was repeated 1 week later showing complete recovery of her LV systolic function (Video 3).

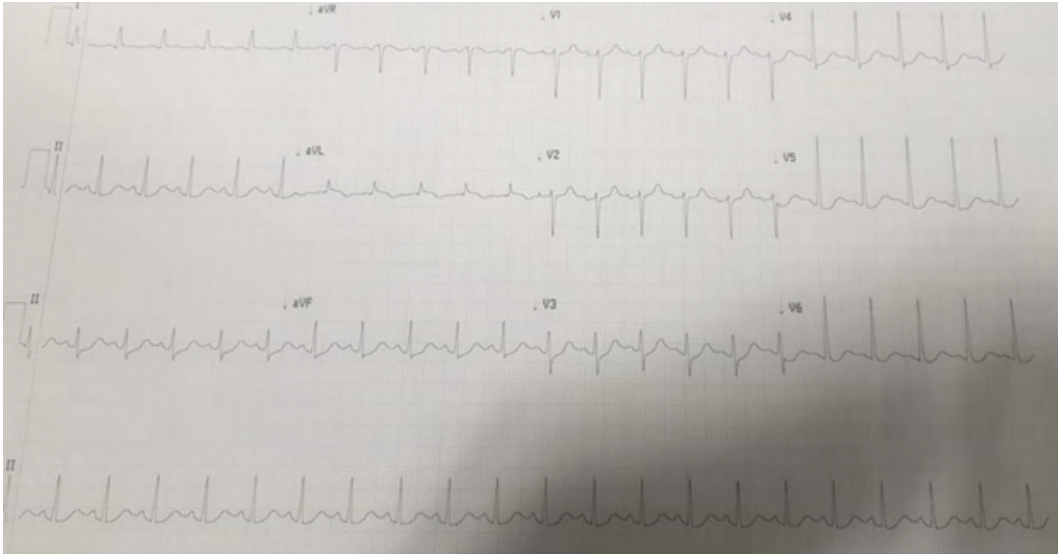


Figure 1: ECG showing sinus tachycardia with ST elevations in I and aVL.

4. Discussion

Takotsubo cardiomyopathy, also known as stress induced cardiomyopathy, is an acute but often reversible form of left ventricular dysfunction that mimics the presentation of an acute myocardial infarction. The disease concept was first noted by Dote and colleagues in 1990 after coming across several cases that exhibited apical ballooning on ventriculography that mimicked a takotsubo-shape, a Japanese pot used to fish octopus [6]. The disease is thought to be triggered by physical and emotional stress, but the absence of any triggers has also been reported [7]. The incidence is reported to be around 15-30 cases per 100,000 per year in the United States, but this may be underestimated due to confusion with acute coronary syndrome and subclinical cases that do not require any medical attention [8]. It is more common in females, and specifically post-menopausal women [7].

Several variants of Takotsubo cardiomyopathy have been described based on the location of ventricular wall motion (akinesis or hypokinesia). The most common type is the apical one forming 81.7 % of the cases, followed by midventricular type forming 14.6 % of cases, and finally the basal and focal forms forming respectively 2.2 and 1.5 % of cases respectively [7]. Reverse Takotsubo cardiomyopathy, refers to the basal type of TTC where there is

akinesis/severe hypokinesia of the basis with sparing of the apex. Contrary to the apical type, reverse Takotsubo cardiomyopathy is more commonly seen in young rather than post-menopausal women [8-10]. It has also been reported to be associated with Amphetamine type stimulants [10].

The exact pathophysiology of Takotsubo cardiomyopathy remains unclear. The most commonly accepted theory is catecholamine induced cardiotoxicity, where a surge of catecholamines and other stress hormones results in direct cardiotoxic effect and microvascular dysfunction [11,12]. Neuro cardiac dysfunction has been described before in several cases of acute stroke whether hemorrhagic or ischemic and in patients with electroconvulsive therapy and seizures. With the introduction of neuroimaging technology, it has been shown that patients in early phases of Takotsubo cardiomyopathy have increased cerebral blood flow in the hippocampus, basal ganglia and brain stem compared to control subjects which returns to normal with resolution of cardiac dysfunction [11]. The systems are connected via the central autonomic nervous system which has a cardiovascular regulatory role in response to stress. Coronary microvascular impairment is another proposed mechanism where an imbalance between coronary vasodilation and excessive constriction may lead to myocardial ischemia and injury

[12]. Estrogen deficiency is another proposed theory for Takotsubo cardiomyopathy. Estrogen receptors are expressed on cardiac myocytes and are thought to modulate contractility and regulate calcium uptake [12].

Patients with Takotsubo cardiomyopathy, in its different forms, often present with similar symptoms to acute coronary syndrome. The most common symptoms reported are angina like chest pain, dyspnea, syncope, nausea, diaphoresis, and epigastric pain [9,12]. Patients may also present in cardiogenic shock or dysrhythmias. ECG often shows ST segment elevations mimicking an ST elevation myocardial infarction. These changes are transient and often resolve within a few days. Other findings include ST segment depression, T wave inversion, QT prolongation and a new bundle branch block [9]. Patients with reverse Takotsubo cardiomyopathy often present with ST depression and QT prolongation [12]. Troponin and BNP levels are often elevated reflecting both myocardial insult and high LV pressure respectively. Echocardiography can often distinguish between acute myocardial infarction and Takotsubo cardiomyopathy. Cardiac catheterization with ventriculography remains the gold standard for diagnosis. The most commonly diagnostic criteria used is the revised Mayo clinic criteria which includes: 1) Transient hypokinesis, akinesis, or dyskinesis of the left ventricular midsegments with or without apical involvement with regional wall motion abnormalities extending beyond a single epicardial vascular distribution; 2) Absence of obstructive

coronary disease or angiographic evidence of acute plaque rupture; 3) New ECG abnormalities (ST segment elevation or T wave inversion) or modest elevation in cardiac troponin; 4) Absence of significant stressful event including pheochromocytoma, myocarditis, intracranial bleed or recent significant head trauma [11]. Other diagnostic criteria exist including the Heart failure association-European Society of Cardiology Criteria and International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria). Management of Takotsubo cardiomyopathy is focused of supportive care and management of complications including cardiogenic shock and arrhythmias. According to the European Society of Cardiology, patients with Takotsubo syndrome should be admitted to a monitored unit and risk stratified into high or low risk. Risk stratification is based on several criteria as shown in Table 1. Low-risk patients are often managed conservatively with consideration of beta blocker therapy and ACE inhibitors in patients with LVEF <45%. In high-risk patients, observation is recommended in a monitored unit for at least 72 hours to assess for complications including cardiogenic shock, pulmonary edema, thrombus formation, and arrhythmias. Beta blockers can be used for management of arrhythmias, left ventricular outflow tract obstruction (with a gradient >40 mmHg) and when LVEF <45%. ACE inhibitors are also recommended if LVEF is < 45 %. Serial imaging is helpful to reassess for improvement in regional wall motion with follow up in 3 to 6 months [13].

Table 1:

Risk Stratification in Takotsubo Cardiomyopathy			
Risk Factor	Major	Risk Factor	Minor Criteria
Age	≥ 75 years	Age	<70-75 years
Blood pressure	< 110 mmHg	Physical stressor	+
LV function	< 35%	LV function	35-45%
Pulmonary edema	+	Biventricular involvement	+
Arrhythmias/ Syncope	+	Concomitant obstructive CAD	+
LVOTO	≥ 40 mmHg	NT- proBNP	≥2000 pg/ml
Moderate to severe Mitral regurgitation	+	BNP	≥ 600 pg/ml
Apical Thrombus	+	QTC ≥ 500 ms	+
New/contained VSD	+	Pathological Q waves	+
		Persistent ST elevation	+
High risk: at least 1 major + 2 minor criteria			

Adopted from the European Society of Cardiology Guidelines.

5. Conclusion

In conclusion, this case emphasizes the importance of recognizing amphetamine-induced reverse takotsubo cardiomyopathy in patients with acute cardiac symptoms, especially in young individuals with stimulant abuse history. Prompt diagnosis through

comprehensive evaluation is essential to differentiate it from acute coronary syndrome. Effective management of substance abuse is crucial to prevent recurrence. Further research is needed to understand its mechanisms and develop targeted therapies. Increased awareness and collaboration among clinicians can lead to better outcomes for affected individuals.

References

1. Patankar GR, Choi JW, Schussler JM. Reverse takotsubo cardiomyopathy: two case reports and review of the literature. *J Med Case Reports*. 2013; 7: 84.
2. Awad HH, McNeal AR, Goyal H. Reverse Takotsubo cardiomyopathy: a comprehensive review. *Ann Transl Med*. 2018; 6(23): 460.
3. Akashi YJ, Goldstein DS, Barbaro G, Ueyama T. Takotsubo cardiomyopathy: a new form of acute, reversible heart failure. *Circulation*. 2008; 118(25): 2754-62.
4. Jabri A, Kalra A, Kumar A, Alameh A, Adroja S, Bashir H, et al. Incidence of Stress Cardiomyopathy During the Coronavirus Disease 2019 Pandemic. *JAMA Netw Open*. 2020; 3(7): e2014780.
5. Takafuji H, Arai J, Saigusa K, Obunai K. Reverse takotsubo cardiomyopathy caused by patent foramen ovale-related cryptogenic stroke: a case report, *European Heart Journal - Case Reports*. 2020; 4(6): 1-6.
6. Aizawa K, Suzuki T. Takotsubo cardiomyopathy: Japanese perspective. *Heart Fail Clin*. 2013; 9(2): 243-7.
7. Templin C, Ghadri JR, Diekmann J, Napp LC, Bataiosu DR, Jaguszewski M, et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. *N Engl J Med*. 2015; 373(10): 929-38.
8. Ramaraj R, Movahed MR. Reverse or Inverted Takotsubo Cardiomyopathy (Reverse Left Ventricular Apical Ballooning Syndrome) Presents at a Younger Age Compared With the Mid or Apical Variant and Is Always Associated With Triggering. 2010.
9. Ghadri JR, Cammann VL, Napp LC, Jurisic S, Diekmann J, Bataiosu DR, et al. Differences in the Clinical Profile and Outcomes of Typical and Atypical Takotsubo Syndrome: Data From the International Takotsubo Registry. *JAMA Cardiol*. 2016; 1(3): 335-340.
10. Jafari Giv M. Exposure to Amphetamines Leads to Development of Amphetamine Type Stimulants Associated Cardiomyopathy (AT-SAC). *Cardiovasc Toxicol*. 2017; 17: 13-24.
11. Medina de Chazal H, Del Buono MG, Keyser-Marcus L, Ma L, Moeller FG, Berrocal D, et al. Stress Cardiomyopathy Diagnosis and Treatment: JACC State-of-the-Art Review. *J Am Coll Cardiol*. 2018; 72(16): 1955-71.
12. Awad HH, McNeal AR, Goyal H. Reverse Takotsubo cardiomyopathy: a comprehensive review. *Ann Transl Med*. 2018; 6(23): 460.
13. Lyon AR, Bossone E, Schneider B, Sechtem U, Citro R, Underwood SR, et al. Current state of knowledge on Takotsubo syndrome: a Position Statement from the Taskforce on Takotsubo Syndrome of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2016; 18: 8-27.