Case Report

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Reverse takotsubo syndrome heralding as ventricular fibrillation: a case report

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Introduction and importance: Reverse takotsubo syndrome, a variant of takotsubo cardiomyopathy, is an acute left ventricular failure characterized by the basal akinesis/hypokinesis associated with apical hyperkinesis. Its presentation is similar to that of the acute coronary syndrome.

Case presentation: The authors present a case of a 49-year-old woman, a vice principal at a local school with a history of hypertension, who was brought to our center after she collapsed while giving a graduation speech. Reverse takotsubo was a presumed diagnosis after we ruled out other differentials.

Clinical discussion: The pathophysiology of reverse takotsubo syndrome is poorly understood. It might be due to a different pattern of catecholamine-mediated myocardial dysfunction than classic takotsubo cardiomyopathy. It is often associated with physical and/or emotional stressors.

Conclusion: Supportive treatment and identification and prevention of triggers can reduce the recurrence of reverse takotsubo cardiomyopathy. Physicians should be aware of various triggers for this condition.

Keywords: heart failure, reverse takotsubo syndrome, takotsubo cardiomyopathy

Introduction

Takotsubo cardiomyopathy (TTC), initially discovered in Japan and described in 1990, is characterized by a takotsubo-like shape observed during left ventriculography at the end-systolic stage[1]. The term 'takotsubo' was derived from the vase-like contraption utilized in octopus fishing, featuring a narrow entry and wider body area. This typical angiographic finding in TC represents excessive compensatory contraction at the heart's base to offset reduced contraction at the left ventricular apex. Takotsubo cardiomyopathy (TTC) is an acute, often reversible left ventricular dysfunction mainly triggered by emotional or physical stress. Around 1–23% of TTC are reverse takotsubo syndrome (rTTS)[2]. It is known by the basal akinesis/hypokinesis associated with apical hyperkinesis and often resolves spontaneously[3]. The presentation of rTTS is similar to an acute coronary syndrome (ACS), so initially, they are treated as per ACS treatment protocol[4,5]. Unlike TTC, where there is often a nonidentifiable trigger, rTTS is often associated with emotional and physical stressors[6,7].

We present a rare case of reverse takotsubo in a 49-year-old female who collapsed while giving a graduation speech.

HIGHLIGHTS

- Reverse takotsubo syndrome, which accounts for around 1–23% of takotsubo cardiomyopathy, is known by the basal akinesis/hypokinesis associated with apical hyperkinesis.
- Catecholamine-mediated myocardial dysfunction, a sudden increase in vagal tone leading to a transient increase in left ventricular outflow tract obstruction, and coronary microcirculation impairment are some of the purposed pathophysiologies of reverse takotsubo.
- Symptomatic treatment and avoiding trigger factors are crucial for preventing this reversible condition's reoccurrence.

Case presentation

A 49-year-old woman, a vice principal at a local school with a history of hypertension, was brought by Emergency Medical Services after she collapsed and lost consciousness while giving a graduation speech. Upon Emergency Medical Services arrival, she was found to be in ventricular fibrillation. Cardiopulmonary resuscitation was initiated; she was intubated and was shocked for the underlying rhythm with return of spontaneous circulation. However, she continued to have ventricular fibrillation en route to the hospital and had to be defibrillated eight times with a return of spontaneous circulation each time. The patient has no

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documented medical history of palpitations, dyspnea, syncope, or related cardiac conditions. She has no history of alcohol consumption or smoking and denies using any medications or drugs. Furthermore, there is no reported family history of cardiac pathology or sudden cardiac death.

At the presentation, her vitals were stable, and her physical examination was unremarkable. Chest radiograph was negative for acute cardiopulmonary pathology as shown in Figure 1. Electrocardiogram revealed sinus rhythm with nonspecific ST-segment changes, unchanged from baseline as presented in Figure 2. Lab studies showed troponin of 0.03 ng/ml (reference range 0–0.04 ng/ml). Urine toxicology was negative. Computed tomography scan of the head was negative for acute intracranial pathology. A Transthoracic Echocardiogram (TTE) was performed, which showed mild left ventricular dilation, ejection fraction (EF) of 31%, and hypokinesis of the basal and mid-ventricular segments compared to apical segments, suggestive of an rTTS as shown in Figure 3. Her electrolytes, including serum magnesium, potassium and sodium levels, were normal. Her thyroid function test was also normal. She was treated as per ACS protocol with emergency percutaneous coronary intervention. Emergent cardiac catheterization revealed clean coronary arteries. She was transferred to a cardiac ICU and was treated with targeted temperature management for cardiac arrest. She was extubated after a successful extubation trial. Repeat TTE was performed two days later that showed EF of 41–45% with persistent basal hypokinesis. Given cardiac arrest without coronary artery disease, Implantable cardioverter defibrillator was placed, and she was discharged home on guideline-directed medical therapy including metoprolol and valsartan-sacubitril with outpatient cardiology follow-up.

A repeat TTE was performed 6 weeks postdischarge during a follow-up, which showed a normal left ventricular size, wall thickness, and systolic function with an EF of 56–60% and a review of the system was negative for chest pain, shortness of breath, palpitation, and dizziness.

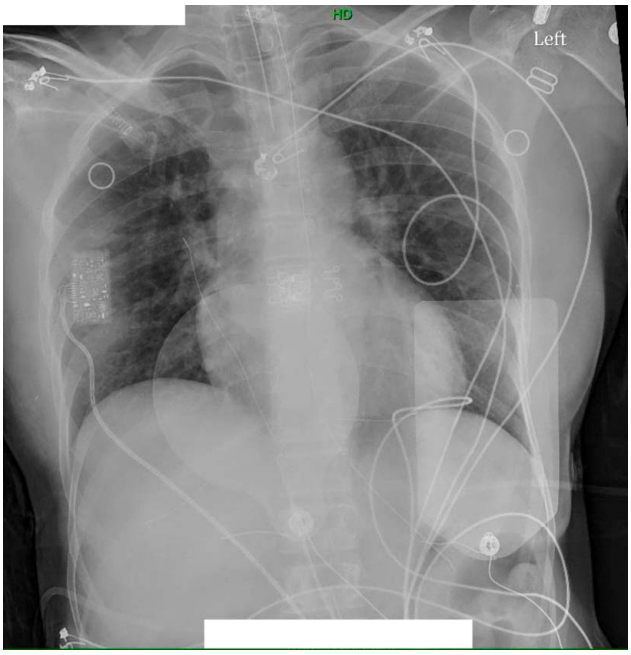

Figure 1. Chest radiograph showing no acute cardiopulmonary pathology.

Discussion

rTTS is a variant of takotsubo syndrome (TTS) that affects the basal segments of the left ventricle, with apical sparing or hyperkinesia. rTTS accounts for ~1–23% of all TTS cases and predominantly affects males[2]. Although rTTS typically follows a benign course, it can rarely result in life-threatening ventricular arrhythmias. Syed *et al.* reported a prevalence of ventricular fibrillation of 1.8% (15 out of 816 cases) in their study investigating arrhythmia occurrence with rTTS. In comparison, another study reported a rate of 4.2% (4 out of 105 cases)[8,9]. The pathophysiology of rTTS is poorly understood, but it is believed to involve a different pattern of catecholamine-mediated myocardial dysfunction than classic TTS[10–12]. Multiple direct and indirect mechanisms have been proposed to elucidate the cardiotoxic effects of catecholamines. One such mechanism involves the surge in adrenergic receptor stimulation, leading to heightened heart rate and cardiac contractility. This, in turn, disrupts the balance between oxygen supply and demand, ultimately causing areas of myocellular hypoxia[12]. Another proposed mechanism is a relative sympathetic nervous system withdrawal or parasympathetic overactivation leading to myocardial relaxation and subsequent dysfunction[13]. Another theory suggests that a sudden increase in vagal tone may lead to a transient increase in left ventricular outflow tract obstruction, resulting in rTTS[12,13]. Also, coronary microcirculation impairment leading to abnormal wall motion abnormalities in a different segment of the myocardium had been linked to rTTS[14]. Although emotional and physical stress is the most commonly recognized triggers for TTC, around 30% of all patients with TTC have no identifiable triggers[15]. rTTS has also been reported in patients with multiple types of life-threatening intracranial hemorrhages, during various surgical procedures, due to exogenous amphetamine and methamphetamine use, eating disorders, and rarely by consumption of energy drinks[2,4,16,17].

rTTS differs from classic TTS in several ways. The main differentiating feature is the pattern of left ventricular dysfunction. In classic TTS, the apical segments of the left ventricle are typically affected, while the basal segments are spared. In contrast, rTTS is characterized by acute left ventricular systolic dysfunction affecting the basal segments of the left ventricle, with apical sparing or hyperkinesia[2,3]. Other features that may help differentiate rTTS from classic TTS include patient demographics and comorbidities. Patients with rTTS are more likely to be male, older, and have a higher prevalence of comorbidities such as hypertension, diabetes, and chronic kidney disease than patients with classic TTS. Additionally, patients with rTTS have a lower incidence of emotional triggers and a higher incidence of neurological disorders than classic TTS[15,17].

The clinical presentation of TTC is similar to that of an ACS, with chest pain and dyspnea being common[2,18]. Rarely syncope and pulmonary edema had been noted. Some individuals at the presentation had arrhythmias, cardiogenic shock, or cardiac arrest[12].

TTS is diagnosed through a comprehensive clinical, electrocardiographic, biochemical (cardiac troponin and B-type Natriuretic Peptide), evaluation and imaging[5]. Echocardiography and cardiac MRI are the main diagnostic tools for identifying left ventricular dysfunction and differentiating rTTS from classic TTS.

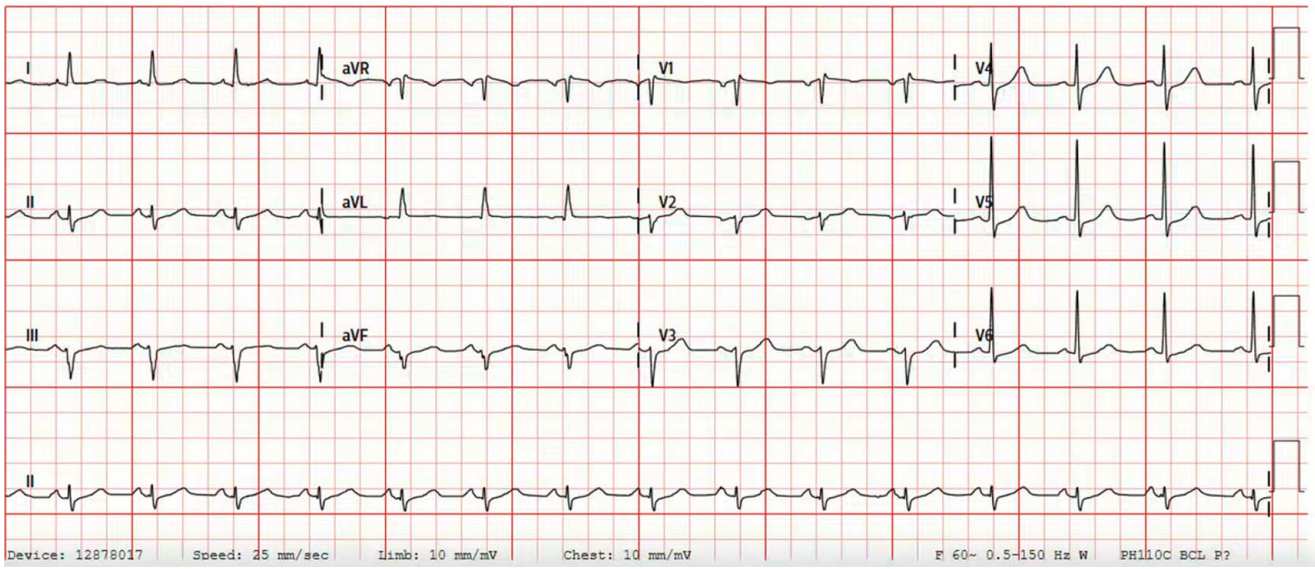

Figure 2. EKG showing normal sinus rhythm with nonspecific ST-T changes.

Cardiac biomarkers, such as troponin and brain natriuretic peptide, are often elevated in TTS and may be useful in evaluating patients with suspected rTTS[14]. ECG may show ST-segment elevation or T-wave inversion, common in TTS but not specific to rTTS. Cardiac MRI is often used to quantify right ventricular function and visualize wall motion abnormalities. It also helps us rule out other differentials like myocardial infarction, fibrosis, myocarditis, and the presence of thrombus in the ventricles[2].

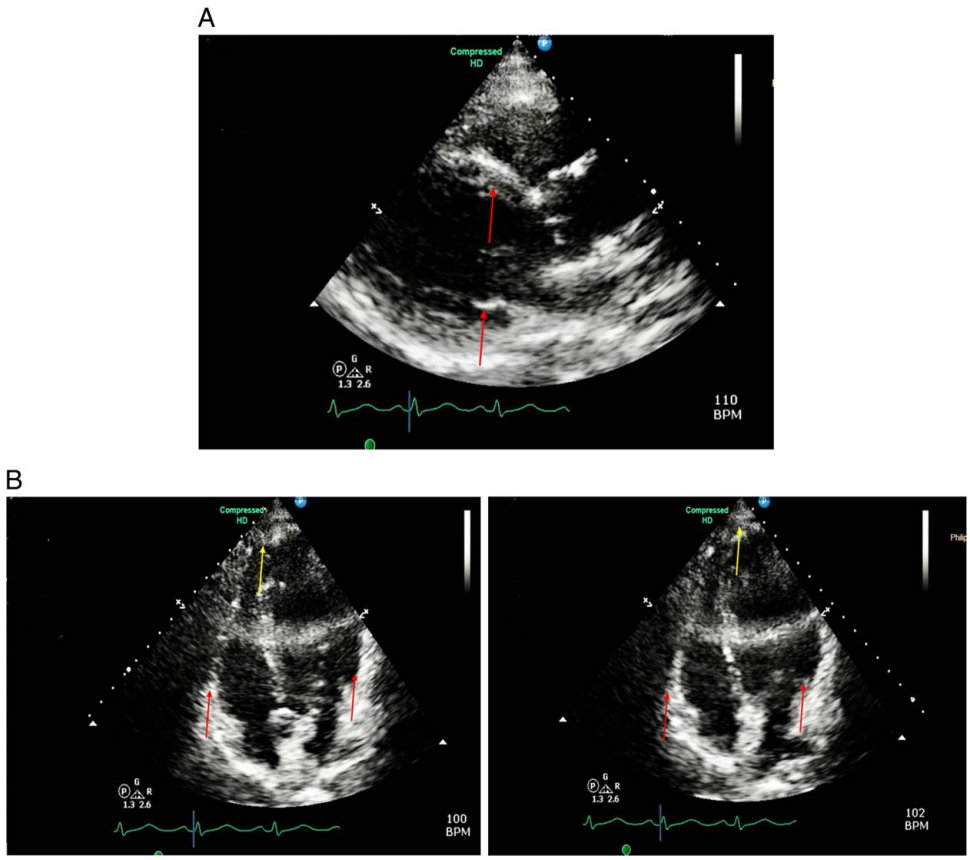

Figure 3. Transthoracic echocardiogram. (A) Para-sternal long axis view showing hypokinetic bases (red arrows). (B) Apical four-chamber view showing hyper-kinetic apex (yellow arrows) and hypokinetic bases (red arrows).

According to the European Society of Cardiology and the American College of Cardiology, aggressive and immediate symptomatic treatment of rTTC can improve survival by reversing left ventricular function. Due to an initial presentation that mimics ACS, patients are generally acutely treated according to the guidelines of ACS management[2,3]. For rTTC patients with dynamic LV obstruction, beta-blockers can be cautiously given to reduce the contractility of the myocardial segment affected. Long-term therapy with beta-blockers has been hypothesized to reduce the likelihood of recurrence[15]. However, more research needs to be done to support this theory. Symptomatic treatment for low blood pressure includes vasopressors and/or intra-aortic balloon counter-pulsation as required. Prophylactic anticoagulant with warfarin may be considered irrespective of heart rhythm. Pulmonary edema is treated with an upright position, oxygen, and diuretics. Managing ventricular fibrillation in the context of rTTS requires immediate defibrillation and initiation of CPR, which are vital for saving the patient's life. Magnesium sulfate can be given for ventricular tachycardia with prolonged QT interval. Overall, the management of rTTS should be individualized based on the patient's clinical presentation, underlying triggers or stressors, and associated comorbidities.

Conclusion

As the presentation of takotsubo syndrome is often similar to the ACS, patients should be managed as per the guideline of ACS. Once the diagnosis of rTTS is confirmed, immediate supportive treatment can improve the outcome. Avoiding various triggers and stressors is also essential to prevent the recurrence of rTTS. Treating physicians should be aware of the triggers and associated complications of this rare entity. Further research and studies are needed for the definitive treatment and screening tools of rTTS.

Ethical approval

Not required.

Consent

Written informed consent was obtained from the patient. A copy of written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

A.B., S.L., N.R.S. were involved in writing original draft. K.T., J.V., S.K., and S.G. were involved in conceptualization, design and preparation of manuscript. S.L., N.R.S., and S.G. were involved in finalization of manuscript.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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References

[1] Sato H, Tateishi H, Uchida T, *et al*. Takotsubo type cardiomyopathy due to multivessel spasm In: Kodama K, Haze K, Hon M, editors. Clinical aspect of myocardial injury: from ischemia to heart failure. Kagaku Hyoronsha; Tokyo: 1990:56–64.
[2] Awad HH, McNeal AR, Goyal H. Reverse takotsubo cardiomyopathy: a comprehensive review. Ann Transl Med 2018;6:460.
[3] Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J 2008;155:408–17.
[4] Kaoukis A, Panagopoulou V, Mojibian HR, *et al*. Reverse takotsubo cardiomyopathy associated with the consumption of an energy drink. Circulation 2012;125:1584–5.
[5] Ghadri JR, Wittstein IS, Prasad A, *et al*. International expert consensus document on takotsubo syndrome (part i): clinical characteristics, diagnostic criteria, and pathophysiology. Eur Heart J 2018;39:2032–46.
[6] Khera R, Light-McGroary K, Zahr F, *et al*. Trends in hospitalization for takotsubo cardiomyopathy in the United States. Am Heart J 2016;172:53–63.
[7] Sharkey SW, Windenburg DC, Lesser JR, *et al*. Natural history and expansive clinical profile of stress (Tako-Tsubo) cardiomyopathy. J Am Coll Cardiol 2010;55:333–41.
[8] Syed FF, Asirvatham SJ, Francis J. Arrhythmia occurrence with takotsubo cardiomyopathy: a literature review. Europace 2011;13:780–8.
[9] Song BG, Chung SM, Kim SH, *et al*. The QT prolongation and clinical features in patients with takotsubo cardiomyopathy: experiences of two tertiary cardiovascular centers. Anadolu Kardiyoloji Dergisi/Anatol J Cardiol 2014;14:162–9.
[10] Ramphul K, Mejias SG, Sombans S, *et al*. Cardiac arrhythmias associated with Takotsubo cardiomyopathy and ST- segment Elevation Myocardial Infarction (STEMI). Am J Cardiol 2020;127:195.
[11] Williams R, Arri S, Prasad A. Current concepts in the pathogenesis of takotsubo syndrome. Heart Fail Clin 2016;12:473–84.
[12] Pelliccia F, Kaski JC, Crea F, *et al*. Pathophysiology of takotsubo syndrome. Circulation 2017;135:2426–41.
[13] Pelliccia F, Greco C, Vitale C, *et al*. Takotsubo syndrome (stress cardiomyopathy): an intriguing clinical condition in search of its identity. Am J Med 2014;127:699–704.
[14] Akashi YJ, Goldstein DS, Barbaro G, *et al*. Takotsubo cardiomyopathy. Circulation 2008;118:2754–62.
[15] Barbaryan A, Bailuc SL, Patel K, *et al*. An emotional stress as a trigger for reverse takotsubo cardiomyopathy: a case report and literature review. Am J Case Rep 2016;17:137–42.
[16] Tagami T, Mertens A, Rothschild D, *et al*. A case of reverse takotsubo cardiomyopathy caused by an eating disorder. J Cardiol Cases 2017;15:77–9.
[17] Kumai T, Inamasu J, Watanabe E, *et al*. Differences between Takotsubo cardiomyopathy and reverse Takotsubo cardiomyopathy associated with subarachnoid hemorrhage. IJC Heart & Vasculature 2016;11:99–103.
[18] Templin C, Ghadri JR, Diekmann J, *et al*. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. New Eng J Med 2015;373:929–38.