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Rare Case of Second Recurrence of Takotsubo Cardiomyopathy With Variable Ballooning Pattern

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Patient: Female, 71-year-old
Final Diagnosis: Takotsubo cardiomyopathy
Symptoms: Chest pain
Clinical Procedure: —
Specialty: Cardiology

Objective: Unusual clinical course
Background: Takotsubo cardiomyopathy (TCM) is a transient form of myocardial dysfunction often precipitated by emotional or physical stress with characteristic apical ventricular ballooning pattern on echocardiogram with no acute coronary event. Recurrent TCM is rare, only occurring in approximately 1-6% of cases, with re-recurrences being even more unusual. We describe a rare case of a second recurrence of TCM in a patient with chronic anxiety but no clear inciting physical or emotional stressors.
Case Report: A 71-year-old woman with recurrent TCM episodes (2013, 2016) and chronic anxiety presented with chest pain, nausea, diaphoresis, and elevated troponins with a normal EKG and coronary angiography that revealed no signs of significant coronary disease. Transthoracic echocardiogram was notable for mildly reduced left ventricular ejection fraction associated with circumferential hypokinesis and mild left ventricular outflow tract (LVOT) gradient consistent with her second recurrence of TCM. The mid-ventricular ballooning pattern differed from her prior patterns of TCM.
Conclusions: This case highlights the importance of clinical suspicion of re-recurrent TCM despite its rarity, especially as it may occur in the absence of clear triggers. Recurrence risk is likely higher in patients with a history of psychiatric conditions, suggesting that optimizing psychiatric care, including psychotherapy and pharmacological management, could be key to preventing further episodes. Although beta-blockers are commonly used for recurrence prevention, their effectiveness may be limited in some patients, particularly those with hypotension or orthostasis. Further research is needed to better understand the mechanisms underlying TCM recurrence and to refine preventive strategies.

Keywords: Anxiety • Cardiovascular Diseases • Echocardiography • Recurrence • Takotsubo Cardiomyopathy

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Introduction

Takotsubo cardiomyopathy (TCM) is a disorder characterized by myocardial injury secondary to high catecholamine levels often due to a physical or emotional stressor in the absence of an acute coronary process. Women account for 90% of TCM cases, with an average age of 58-75 years and with only 3% of patients less than 50 years old. Postmenopausal women are more likely to be attacked due to estrogen deficiency and altered catecholamine hormonal receptor sensitivity [1]. However, approximately a third of patients do not recall any identifiable stressor [1]. Recurrence of the acute phase of TCM is rare, with a lifetime rate of 1-6% and yearly recurrence rate of 1-2% [2,3]. Due to its rarity, there is no universal rate of recurrence. Variable ventricular ballooning pattern is a unique echocardiography feature of recurrent cases and may shed insight on prognosis. Current understanding of the risks of TCM reoccurrence is limited, and further investigation into such cases is warranted to assist clinicians in being able to better identify associated clinical forewarning. The true pathophysiology of recurrent TCM is unknown; however, we do know that it is more common in postmenopausal women, women with psychiatric history, and patients with arterial hypertension. Our case demonstrates the uniqueness and clinical significance of multiple recurrences of TCM with variable ventricular ballooning patterns and explores possible predisposing factors to this unusual presentation, including chronic psychiatric diagnoses.

Case Report

The patient was a 71-year-old woman with a past medical history significant for hypertension, chronic anxiety on a stable dose of serotonin selective reuptake inhibitor (SSRI) therapy, and recurrent TCM in 2013 and 2016 who presented with acute chest pain, nausea, diaphoresis, and elevated troponins. Her chest pain was described as heavy, radiated to the top of her left chest, and began about 90 minutes before her presentation. The patient reported her pain was similar to prior episodes of TCM. She denied any vomiting, fevers, night sweats, or recent viral illness. The patient had recently been under increased stress due to her husband being recently diagnosed with pulmonary fibrosis. Her chronic anxiety has been reportedly otherwise well controlled on a stable dose of SSRI therapy for several years without any known psychiatric hospitalizations. She received an aspirin load in the acute period given clinical suspicion for acute coronary syndrome. The patient reported that her chest pain and nausea self-resolved several hours after initial presentation prior to obtaining left heart catheterization.

EKG on admission demonstrated a normal sinus rhythm with a heart rate of 77 beats-per-minute and was unremarkable for any significant ST abnormalities. Serial troponin levels trended

on admission to a peak of 0.278 ng/mL, which overall could be concerning for transient coronary vasospasm, acute coronary syndrome, and recurrent stress cardiomyopathy given the clinical history.

Left heart catheterization with coronary angiography was notable for very mild non-obstructive coronary artery disease and no evidence of an acute thrombotic rupture, which was essential to rule out non-ST-elevation myocardial infarction (NSTEMI) (type I event), which would require urgent percutaneous coronary intervention.

A transthoracic echocardiogram (TTE) was significant for normal left ventricular size with mildly reduced systolic function (LVEF 48%). There was circumferential hypokinesis seen at the mid to apical wall segments consistent with a final diagnosis of stress-induced cardiomyopathy. A mild left ventricular outflow track (LVOT) gradient of 12 mmHg was appreciated at rest, increasing to 16 mmHg with Valsalva maneuver (**Figure 1**). The TTE from her previous episode of TCM in 2016 demonstrated normal left ventricular diastolic dimension, an ejection fraction of 50%, and akinetic mid and distal anterolateral wall and apex (**Figure 2**). Her first TTE, from 2013, was consistent with TCM and was significant for normal LV diastolic dimension with mildly reduced EF (40%), type I diastolic dysfunction, and mid-distal anteroapical and mid-lateral wall hypokinesis (**Figure 3**).

Once a diagnosis of TCM was established, the patient was increased to maximally tolerated metoprolol tartrate therapy to prevent catecholamine surge and reduce risk of LVOT obstruction. Recommended long-term therapy was discussed with the patient, including frequent psychiatric follow-up, provision of therapy resources, and ongoing sertraline medical therapy in addition to classic beta blocker prophylaxis.

Discussion

A diagnosis of TCM is often elusive given its clinical resemblance to ACS. Classic symptoms of TCM include chest pain, dyspnea, and syncope. Appropriate systematic workup to suspected TCM includes assessment of EKG, which shows diverse ST changes in about 95% of TCM cases. Cases of ST elevation in the augmented vector right (AVR) and the anteroapical leads has been shown to be 100% specific to TCM vs ACS. Evaluation of the cardiac biomarkers, TTE, and cardiac catheterization are often all warranted to rule out an acute thrombotic event or vasospasm. Cardiac MRI is indicated when ruling out suspected myocarditis and can also be utilized to distinguish TCM from apical myocardial infarction. [4]. Accurate diagnosis is crucial given the potentially dangerous complications of TCM including pulmonary edema, cardiogenic shock, and cardiac arrest [5]. While cardiac catheterization is the only definitive method to

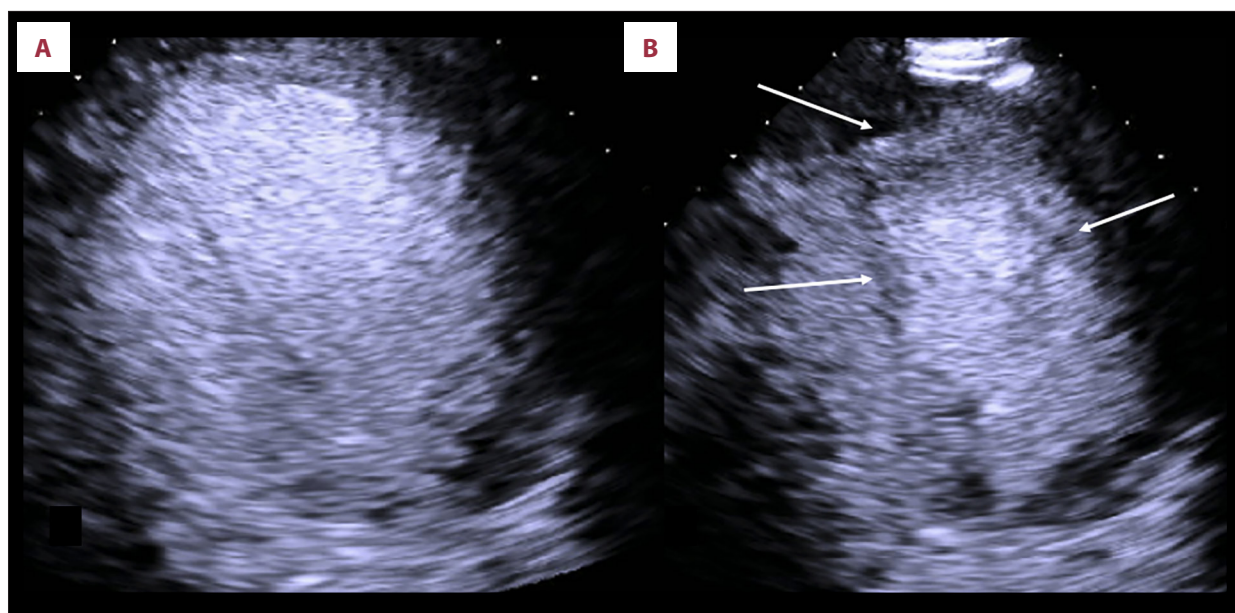


Figure 1. Takotsubo cardiomyopathy event in 2023: transthoracic echocardiogram with apical 4-chamber view; diastole (A), systole (B). Circumferential, mid-distal hypokinesis is shown, excluding the apical segment. Arrows demonstrate akinetic anterolateral and inferoseptal walls with a contractile apex.

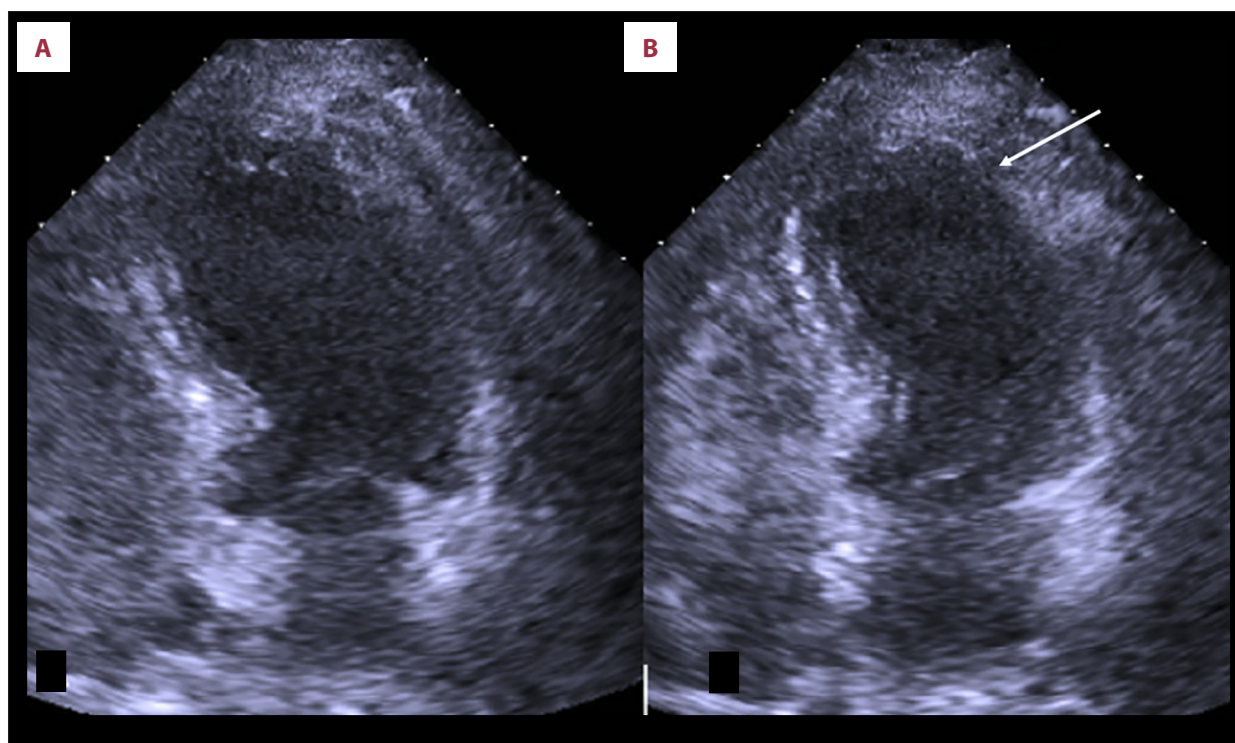


Figure 2. Takotsubo cardiomyopathy event in 2016: transthoracic echocardiogram with apical 4-chamber view; diastole (A), systole (B). The arrow in B indicates akinetic mid-distal anterolateral wall and apex during systole.

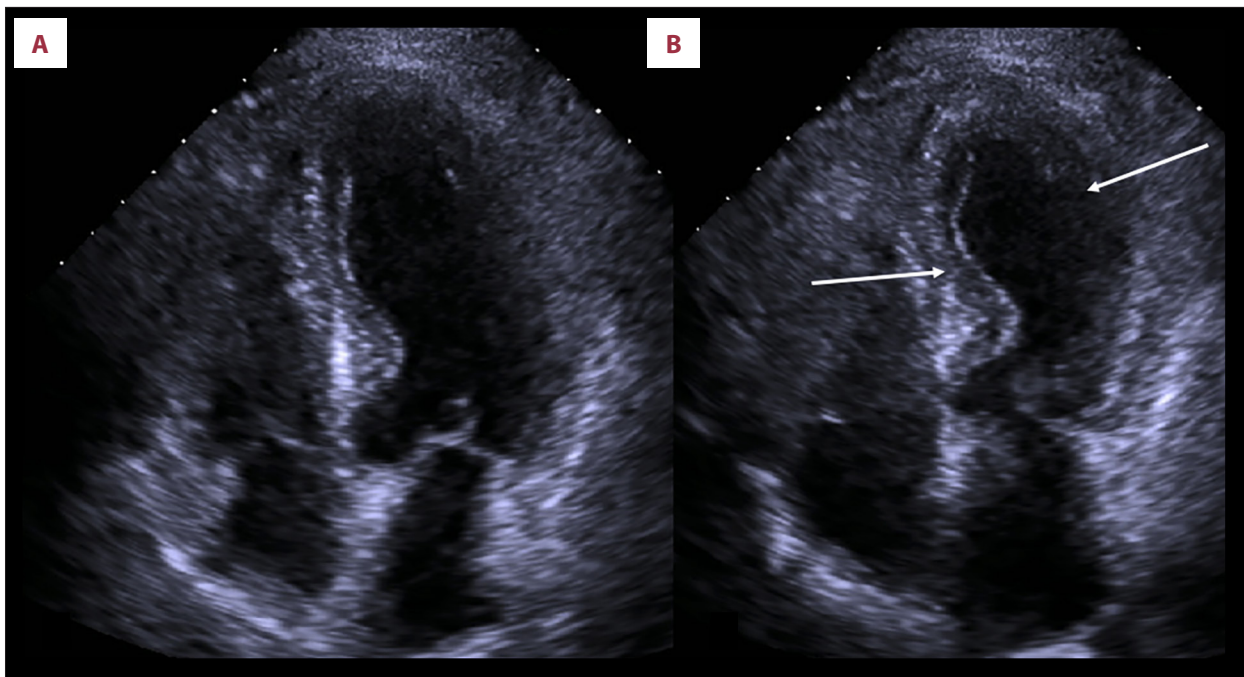


Figure 3. Takotsubo cardiomyopathy event in 2013: transthoracic echocardiogram with apical 4-chamber view; diastole (A), and systole (B). The arrows indicate akinetic inferoseptal and mid-distal anterolateral walls during systole.

rule out ACS, the InterTAK diagnostic score has been proposed as a non-invasive method to guide initial workup [6].

Our patient interestingly presented with a mid-ventricular ballooning pattern on TTE which was different from her 2 prior TCM episodes, which were characterized by classical apical akinesis. A study utilizing the international, multicenter German Italian Stress-Induced Cardiomyopathy (GEIST) registry found that approximately 20% of recurrence cases demonstrate a variable ventricle ballooning pattern. Variable akinesis patterns underscore that comprehensive imaging is necessitated during each episode, as recurrence may not present with the same wall motion abnormality as the initial event. While variability in ballooning pattern reflects the dynamic underlying pathophysiology of TCM, there are no observed prognosis differences among the possible ventricular akinesis patterns. However, meta-analyses suggest that recurrent atypical, non-apical ballooning patterns have fewer severe adverse effects including cardiogenic shock and pulmonary edema [7]. Of recurrent cases, arterial hypertension was determined to be of higher prevalence when compared with nonrecurrent cases [8]. Furthermore, patients with 2 or more recurrences are generally described as younger, experience more frequent emotional triggers, have more psychiatric diagnoses, have higher peaks of troponin, and lower ejection fractions [9]. Poor clinical outcomes have been associated with older age, male sex, history of diabetes, pulmonary disease, and kidney disease [10].

While risk factor identification and medical therapy are often not reliable for preventing a recurrence of TCM, it is important

to note that approximately 90% of patients with recurrence have a history of depression or anxiety, likely due to higher susceptibility to catecholamine surges [9]. The optimization of psychiatric treatment, such as appropriate utilization of psychotherapy and medical management in hospital discharge planning, would serve as an effective means of prophylaxis for future acute episodes of TCM. Furthermore, treatment of psychiatric conditions may become of heightened importance when up-titration of beta-blockers is not possible due to hypotension or orthostasis, as seen in our patient. Future longitudinal studies are needed to clarify the relationship between preexisting psychiatric conditions and TCM recurrence after optimal psychiatric treatment.

Conclusions

Patients with a history of TCM may present with re-recurrence and variable ventricular ballooning patterns in the absence of clear emotional or physical triggers. Initial evaluation should consist of cardiac catheterization and TTE to rule out the possibility of ACS. Recurrent TCM cases of a non-apical ballooning pattern may suggest a more favorable prognosis, as appreciated in our patient. While beta-blockers have been shown to reduce the risk of reoccurrence and event-free survival, they are not always reliable for prophylaxis. Most patients with a history of TCM have a longstanding history of anxiety and/or depression, and it could be of greater importance to ensure that optimal psychotherapy and medical psychiatric therapy are achieved.

Institution Where Work Was Done

Penn State College of Medicine, Lancaster, PA, and Penn State Milton S. Hershey Medical Center, Hershey, PA, USA.

Patient Consent

Written consent to publish case with anonymous data was obtained.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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