Case Reports

Three Episodes of Takotsubo Cardiomyopathy

with Variant Ballooning Patterns in 2 Elderly Women

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Takotsubo cardiomyopathy can present with transient apical, midventricular, or basal left ventricular ballooning patterns. Reported recurrences of this cardiomyopathy are few. We present the cases of 2 elderly women who each had 3 episodes of takotsubo cardiomyopathy in various ballooning patterns. We explore the potential pathophysiologic mechanisms, and we discuss the best treatment approach for this disease, which carries a substantial risk of in-hospital complications. ***(Tex Heart Inst J 2018;45(4):247-51)***

Variants of takotsubo cardiomyopathy (TC), including its midventricular and basal forms, have been defined but are less prevalent than the classic apical ballooning shape. Single recurrences of TC are infrequent, and multiple recurrences are even rarer. We describe the cases of 2 patients who each had 3 episodes of TC, and we discuss the ballooning patterns.

Key words: *Aged; female; heart ventricles/diagnostic imaging/physiopathology; recurrence; stress, physiological; takotsubo cardiomyopathy/diagnostic imaging/diagnosis/epidemiology/physiopathology/therapy; time factors; treatment outcome; ventricular dysfunction, left/etiology*

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Case Summaries

Patient 1

In March 2015, a 67-year-old white woman was admitted to the hospital because of severe dyspnea. She was being treated for chronic obstructive pulmonary disease exacerbation. Her electrocardiographic (ECG) results were abnormal, and her serum cardiac biomarker levels were elevated; however, cardiac catheterization revealed only mild-to-moderate nonobstructive coronary artery disease (CAD). A left ventriculogram showed akinesis of the mid walls but preserved contractility of the basal and apical wall segments, a pattern consistent with the midventricular variant of TC (Fig. 1). We supplemented her current β-blocker with an angiotensin receptor blocker. Four months later, an echocardiogram showed normal left ventricular (LV) contractility of all wall segments.

In March 2016, the patient presented with gastrointestinal symptoms and was diagnosed with gastritis. Although her serum cardiac biomarker levels were elevated again, cardiac catheterization revealed stable CAD. A left ventriculogram showed a recurrent midventricular TC pattern despite her angiotensin receptor and β-blocker therapy (Fig. 2A). These medications were continued, and the LV wall-motion abnormalities resolved one month later.

The patient's third episode of midventricular TC occurred in the presence of colitis 26 months after the initial event (Fig. 2B). Normal LV systolic function was noted one month later (Table I).

Patient 2

In March 2016, a 75-year-old white woman, hospitalized for treatment of severe gastritis, reported chest discomfort and dyspnea. An ECG showed ischemic changes, and the patient's serum cardiac biomarker levels were elevated. Cardiac catheterization revealed only mild CAD; however, a left ventriculogram showed a large area of apical and mid wall akinesis and ballooning, consistent with classic TC (Fig. 3). The patient's borderline-low blood pressures precluded heart failure therapy. Two months later, an echocardiogram showed normal LV wall motion.

Five months later, the patient had respiratory failure during treatment for cholecystitis. Transthoracic echocardiograms revealed depressed LV systolic function with a

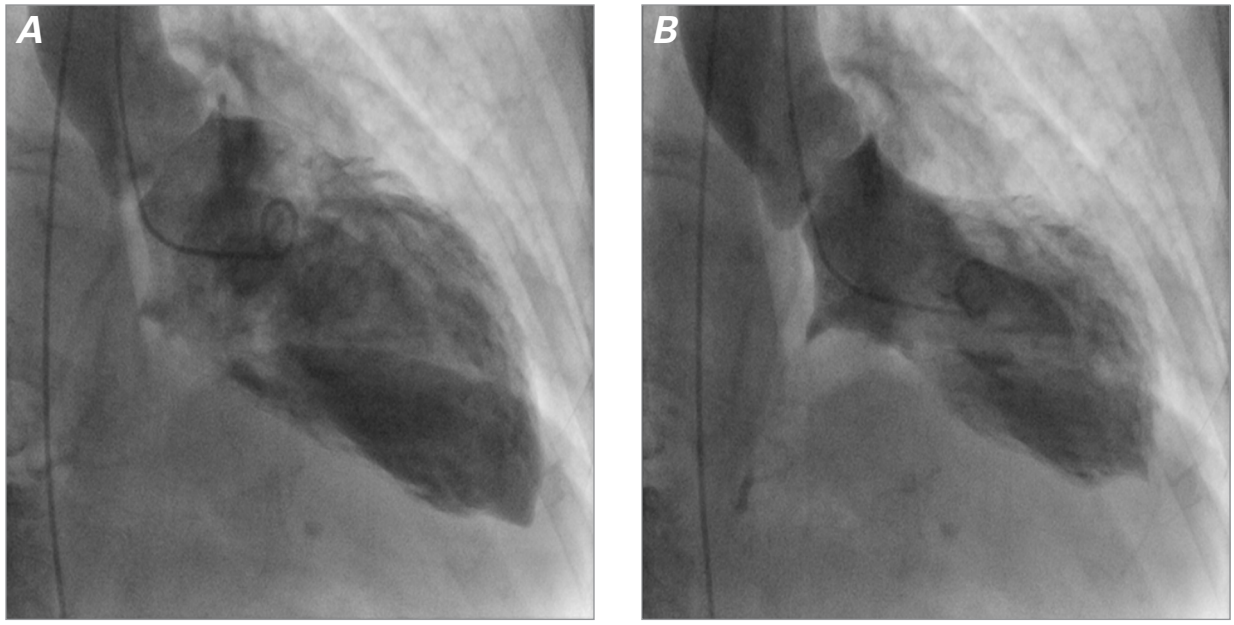


Fig. 1 *Patient 1. On first presentation, left ventriculograms (right anterior oblique views) during* ***A****) diastole and* ***B****) systole show regional wall-motion abnormalities of a midventricular variant of takotsubo cardiomyopathy, consisting of akinetic mid wall segments and hyperkinetic basal and apical wall segments.*

Supplemental motion image is available for Figure 1.

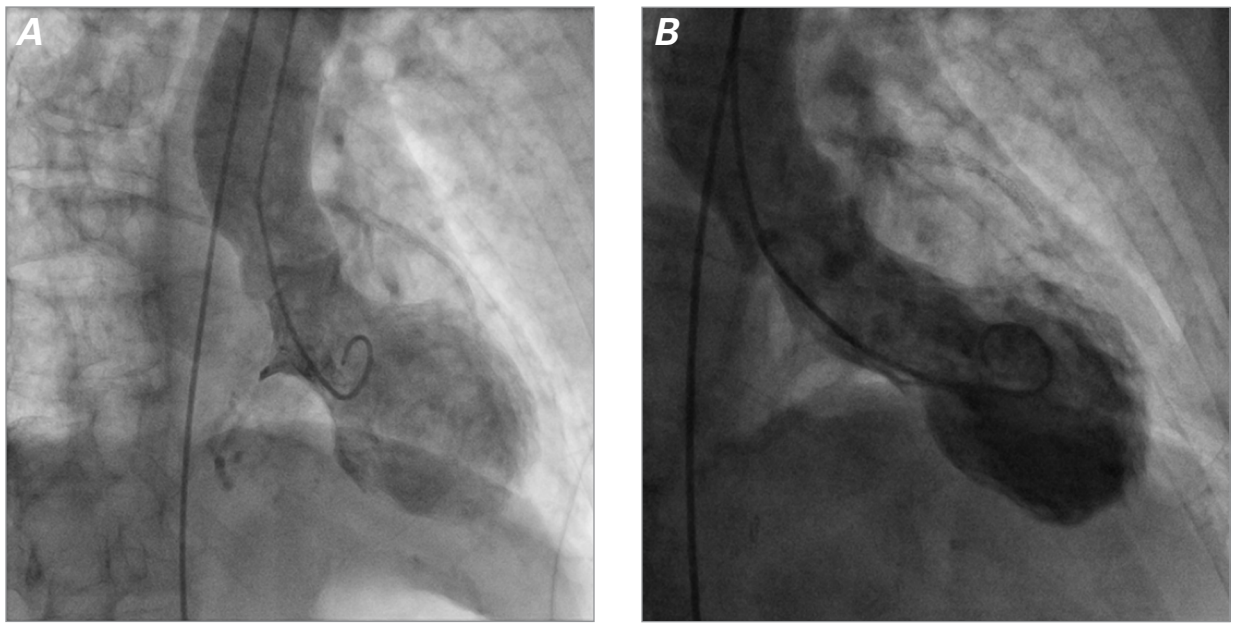


Fig. 2 *Patient 1. On* ***A****) second and* ***B****) third presentation, left ventriculograms (right anterior oblique views) during systole show regional wall-motion abnormalities consistent with a midventricular variant of takotsubo cardiomyopathy.*

Supplemental motion images are available for Figure 2A and 2B.

different wall-motion abnormality: mid and basal wall akinesis with preserved apical wall contractility, consistent with the basal variant of TC (Fig. 4A). No cardiac catheterization was performed, and again the patient's low blood pressures precluded heart failure therapy. Normal LV wall motion was noted one month later.

The patient had a third episode of cardiomyopathy with a repeat basal variant of TC, 12 months after her

TABLE I. Clinical Characteristics of Patient 1

Variable	Episode 1	Episode 2	Episode 3
Time after first episode (mo)	—	12	26
Age at each episode (yr)	67	68	69
Physical trigger	COPD exacerbation	Gastritis	Colitis
Hemodynamic values			
Systolic BP (mmHg)	108	140	132
Diastolic BP (mmHg)	74	94	96
Heart rate (beats/min)	109	108	120
Laboratory values			
Brain natriuretic peptide (pg/mL)	NA	254	261
Troponin I (ng/mL)	2.07	1.52	1.68
Creatine kinase (U/L)	142	56	77
ECG findings	Deep T-wave inversions	—	—
QTc prolongation (ms)	573	543	522
Takotsubo variant	Midventricular	Midventricular	Midventricular
Initial LVEF	0.40–0.45	0.35–0.40	0.40–0.45
Coronary artery disease	Mild to moderate	Stable	Stable
Chest radiographic findings	Pulmonary edema	Pulmonary edema	Left pleural effusion
Heart failure medications before recurrence	β-blocker	Angiotensin-receptor blocker and β-blocker	Angiotensin-receptor blocker and β-blocker
Time to recovery (mo)	4	1	1
Follow-up LVEF	0.65–0.70	0.60–0.65	0.65–0.70

BP = blood pressure; COPD = chronic obstructive pulmonary disease; ECG = electrocardiographic; LVEF = left ventricular ejection fraction; NA = not applicable

first event, in the presence of gastritis (Fig. 4B). We observed normal LV wall motion 3 months later (Table II).

Discussion

A syndrome of transient LV systolic dysfunction in the absence of obstructive CAD, TC is diagnosed in 1.7% to 3.5% of patients who present with suspected acute coronary syndrome.[1,2] The classic apical ballooning shape predominates; however, the midventricular and basal variants occur in 16.8% to 40% of patients.[3-5] Although investigators in observational studies have compared the respective clinical profiles of classic and

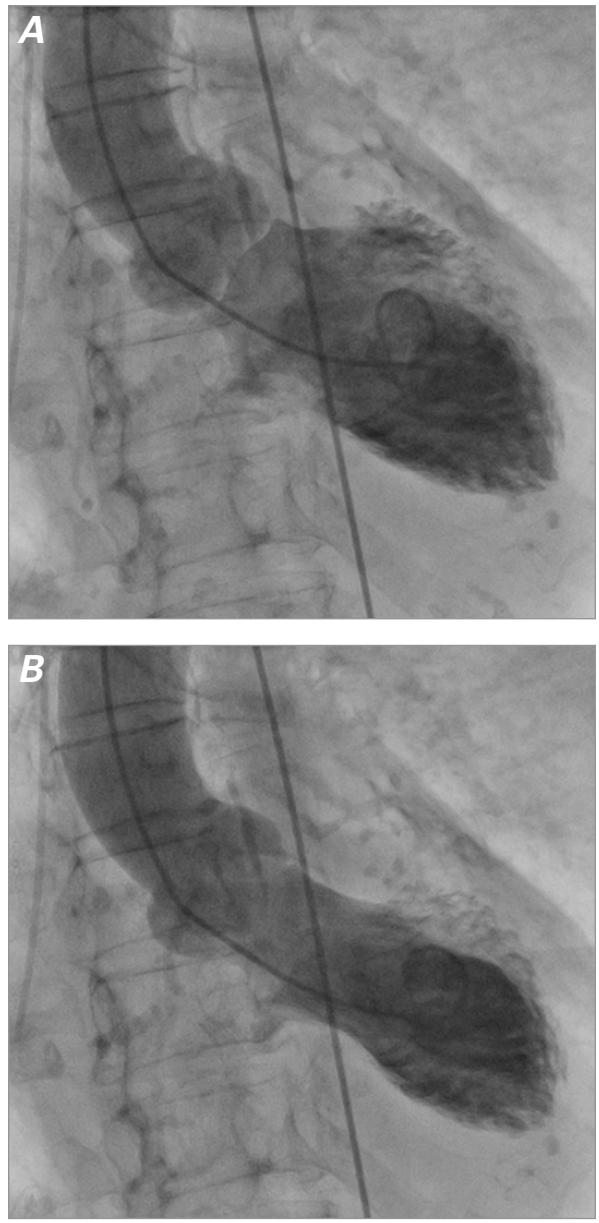
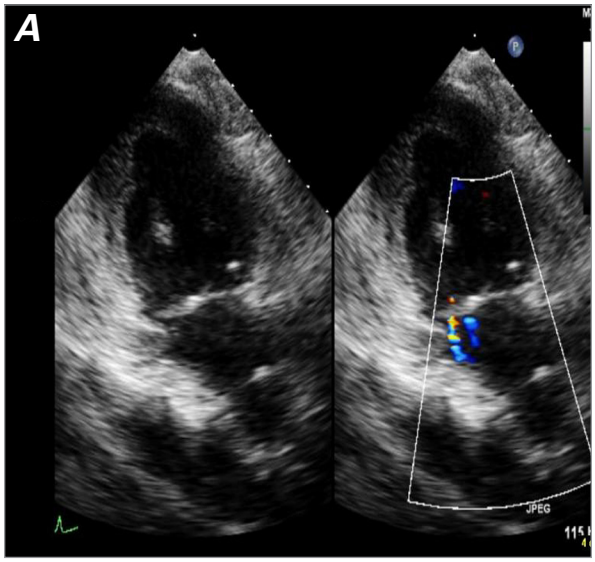


Fig. 3 *Patient 2. On first presentation, left ventriculograms (right anterior oblique views) during **A**) diastole and **B**) systole show regional wall-motion abnormalities consistent with classic apical ballooning takotsubo cardiomyopathy.*

Supplemental motion image is available for Figure 3.

variant TC, information about recurrent TC is sparse because only a few events have been reported. In one observational study of patients with only apical ballooning, the annual recurrence rate after initial presentation was 2.9% in the first 4 years and 1.3% thereafter.[6] In a mixed population of TC patients who had classic and variant forms, the annual recurrence rate was also low (1%–1.5%).[7,8] These series described primarily single recurrences of TC, and only a handful of reports have been about patients whose recurrent TC had variant ballooning patterns.[9,10]



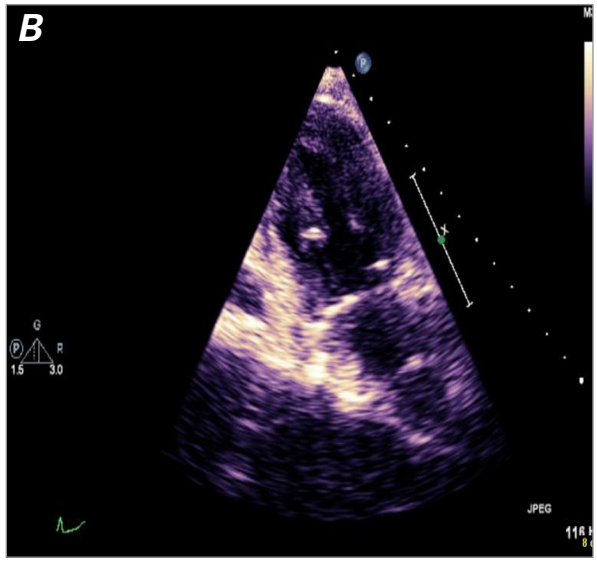


Fig. 4 *Patient 2.* ***A****) On second presentation, a transthoracic echocardiogram during systole shows a basal variant of takotsubo cardiomyopathy. Apical wall contractility is preserved, whereas the mid and basal left ventricular wall segments are akinetic.* ***B****) On third presentation, a transthoracic echocardiogram during systole shows a second episode of the basal variant of takotsubo cardiomyopathy.*

Supplemental motion images are available for Figure 4A and 4B.

TABLE II. Clinical Characteristics of Patient 2

Variable	Episode 1	Episode 2	Episode 3
Time after first episode (mo)	—	5	12
Age at each episode (yr)	75	76	76
Physical trigger	Gastritis	Cholecystitis	Gastritis
Hemodynamic values			
Systolic BP (mmHg)	114	118	106
Diastolic BP (mmHg)	65	58	65
Heart rate (beats/min)	116	109	119
Laboratory values			
Brain natriuretic peptide (pg/mL)	3,012	NA	4,904
Troponin I (ng/mL)	1.92	0.45	0.45
Creatine kinase (U/L)	244	177	83
ECG findings	Deep T-wave inversions	Slight ST-segment depressions	Slight ST-segment depressions
QTc prolongation (ms)	503	472	472
Takotsubo variant	Apical	Basal	Basal
Initial LVEF	0.35–0.40	0.40–0.45	0.30–0.35
Coronary artery disease	Mild	NA	NA
Chest radiographic findings	Pulmonary edema	Pulmonary edema and pleural effusions	Pleural effusions
Heart failure medications before recurrence	None	None	None
Time to recovery (mo)	2	1	3
Follow-up LVEF	0.60–0.65	0.55–0.60	0.65–0.70

BP = blood pressure; COPD = chronic obstructive pulmonary disease; ECG = electrocardiographic; LVEF = left ventricular ejection fraction; NA = not applicable

Our patients each had 3 episodes of TC within a relatively short period of 1 to 2 years. Each episode was triggered by stress, and all 6 resultant cardiomyopathies were uncovered during the management of noncardiac illness. Patient 1 had only midventricular TC, whereas Patient 2 initially had classic apical ballooning and then the basal variant. We detected no pathologic findings associated with transient LV ballooning patterns, such as pheochromocytoma, Doppler echocardiographic evidence of mid-LV or LV outflow tract obstruction, or left anterior descending coronary artery wraparound or myocardial bridging.[11,12] Consistent with previous reports in which individuals with recurrent versus isolated TC were compared, we found no obvious demographic or clinical features that distinguished our patients from those in whom TC occurred once. Both were postmenopausal women who had elevated serum biomarker levels and variable ST-segment ECG changes with or without QTc prolongation.[4,7,13]

The recognition of recurrent TC, especially with transient ballooning of different LV wall segments in the same individual, challenges some current theories on TC pathophysiology. The impact of a catechol-

amine surge on LV myocardial wall segments with varying β-receptor densities is frequently used to explain focal ballooning; however, this theory is not supported by the different recurrent ballooning patterns in Patient 2. In addition, the idea that one episode of stress-induced cardiomyopathy is protective in terms of precluding same-wall-segment recurrence[14] is not supported by our findings in Patient 1, in whom the recurrent LV ballooning shapes were identical. Nevertheless, sympathetic overflow is accepted as the prerequisite to pathophysiology. The roles of hormonal influences and innate susceptibility remain elusive.

Even though no prognostic differences are apparent among the variants,[15] TC is not benign and carries substantial risk. Despite the transience of cardiomyopathy, our patients were both at risk of in-hospital complications and long-term major adverse cardiac and cerebrovascular events, like those in patients whose acute coronary syndrome is due to obstructive CAD.[3] Therefore, preventing recurrent TC is crucial; however, the approach to the problem is unknown. Of note, ongoing heart failure therapy did not prevent recurrences in our first patient, a finding corroborated by data that support the neutrality of β-blockade in preventing recurrence.[3,4] Nevertheless, it appears clear that long-term survival prospects are improved in TC patients who are given a renin-angiotensin system inhibitor, so this class of medications should always be incorporated into the acute treatment algorithm depending on the patient's tolerance.[3]

Our report adds to the sparse body of literature on recurrent TC and the spectrum of transient focal ballooning. Multiple recurrence in the same individual is rarely reported and is most likely a result of underrecognition. Clinicians must familiarize themselves with TC in its variant forms and respond appropriately to patients who present with the characteristic profiles. More frequent identification of this complex syndrome will enable scrutiny of its natural course and reveal insights into more effective prevention.

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