Stress-Induced Cardiomyopathy: Not Always Apical Ballooning

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Apical ballooning (takotsubo syndrome) mimics acute myocardial infarction with transient apical dyskinesia and normal coronary arteries. It is often precipitated by emotional or physical stress. The prevalence of this syndrome has been increasing, probably because it is now more frequently recognized. Multiple theoretical hypotheses have been developed to explain its genesis, but the mechanism remains unclear. Rarely, cases of apical sparing and other wall motion involvement have been cited. We collected data on 12 patients who had acute myocardial infarction and normal coronary arteries with abnormal wall motion that had completely healed on repeat studies. Five patients had typical apical ballooning, and the other 7 had wall motion abnormalities in other segments. We determined that stress-induced cardiomyopathy can involve any wall of the myocardium and is not always apical ballooning.
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Key words: Apical ballooning • Takotsubo syndrome • Wall motion abnormalities • Midventricular ballooning • Global hypokinesis

Takotsubo syndrome was initially described in Japan; the term means "octopus catcher" in Japanese. This condition is characterized by chest discomfort and acute myocardial infarction that is induced by emotional or physical stress. It typically has been described in women, and is manifested by evidence of apical ballooning and normal coronaries.[1] The exact etiology remains unclear, but potentially it could be explained by microvascular coronary spasm induced by excess catecholamine production, myocarditis, or aborted myocardial infarction due to spontaneous thrombolysis and stunned

myocardium.[2] Recently, a case series of 4 white patients was described in which transient midventricular ballooning occurred with sparing of the apex.[3]

In this report, we describe 12 patients with various wall motion abnormalities, normal coronaries, and complete recovery of left ventricular (LV) function. Five of the patients demonstrated typical apical ballooning, 3 had midventricular ballooning, 2 had exclusively posterobasal ballooning, 1 had exclusive anterolateral wall ballooning, and 1 had global hypokinesis.

Methods

From March 2004 through March 2006, clinical, echocardiographic, and angiographic data from our hospital were reviewed to identify the patients (Table 1). The age of the patients ranged from 31 to 80 years, with a mean of 57 years. Ten patients were white, 1 was Hispanic, and 1 was eastern Indian. Transthoracic echocardiography had been performed in all patients within 4 weeks of the event.

Results

Five patients (42%) had typical apical ballooning (Figure 1). The remaining 7 patients had other wall motion abnormalities as follows: 2 had localized ballooning of the posterobasal wall only (Figure 2), 3 had midventricular ballooning with sparing of the apex and base (Figure 3), 1 had global hypokinesis (Figure 4), and 1 had exclusive ballooning of the anterolateral wall (Figure 5).

Eight patients in the study had a triggering stressor identified. For 5 patients, it was emotional stress, and for 3 it was physical stress. Eleven patients presented with chest pain, and 5 of these patients had associated shortness of breath. The twelfth patient presented with syncope. One of the patients who presented with

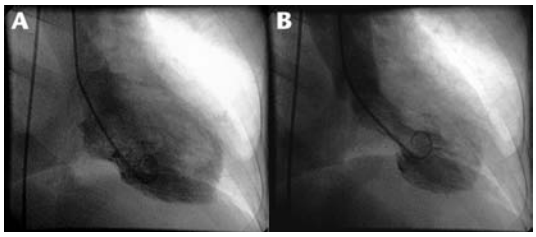

Figure 1. *Left ventriculograms in diastole* **(A)** *and systole* **(B).** *Note the apical ballooning in B. Both images are of Patient 1.* www.medreviews.com

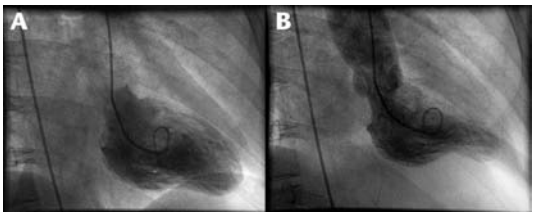

Figure 2. *Left ventriculograms in diastole* **(A)** *and systole* **(B).** *Note the posterobasal ballooning in B. Both images are of Patient 3.* www.medreviews.com

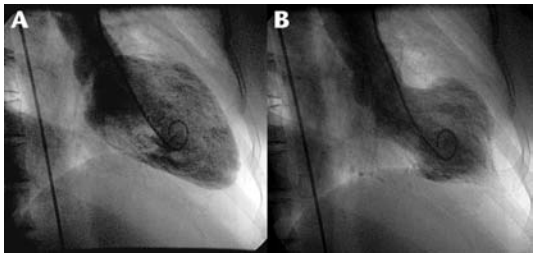

Figure 3. *Left ventriculograms in diastole* **(A)** *and systole* **(B).** *Note the midventricular ballooning in B. Both images are of Patient 2.* www.medreviews.com

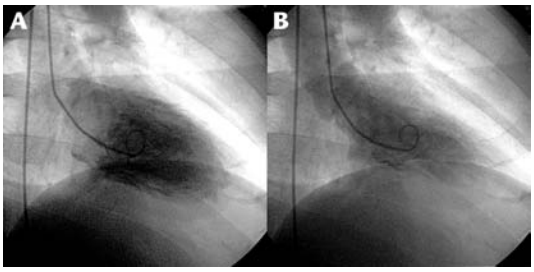

Figure 4. *Left ventriculograms in diastole* **(A)** *and systole* **(B).** *Note the global hypokinesia in B. Both images are of Patient 8.* www.medreviews.com

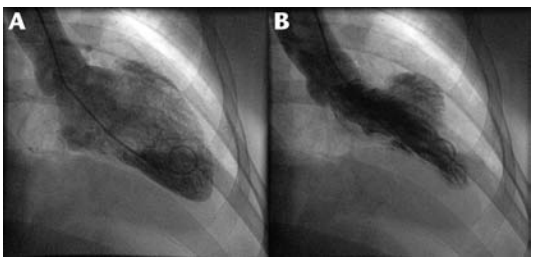

Figure 5. *Left ventriculograms in diastole* **(A)** *and systole* **(B).** *Note the anterolateral ballooning in B. Both images are of Patient 10.* www.medreviews.com

chest pain had ventricular fibrillation on admission.

Four patients presented with varying degrees of ST elevation in the inferior leads (II, III, and AVL); 2 had apical ballooning, and the other 2 had posterobasal wall hypokinesis. One patient of the 4 had new-onset atrial fibrillation.

The other patients had different electrocardiogram presentations as follows. One patient had a 1 mm ST depression in leads II, III, and AVF, and an inverted T wave in leads I and AVL. One patient had diffuse broad inverted T waves. One patient had hyperacute T waves in leads V3 to V6, and inverted T waves in leads II, III, and AVF. Two patients had normal sinus rhythm with no ST-T changes (1 had global hypokinesis, and the other had anterolateral wall hypokinesis). One patient had a 1.5 mm ST elevation in leads I, AVL, V5, and V6. One patient had a 1 mm ST elevation in leads V2, V3, and V4. One patient had an ST depression in leads V3 to V6, and an inverted T wave in leads I and AVL.

Troponin levels varied, with 10 patients having elevated levels. The highest level was 14.31 ng/mL and the lowest was 0.11 ng/mL. The mean was 3.945 ng/mL. (The normal troponin range is up to 0.1 ng/mL.) All patients were taken immediately for cardiac catheterization.

Ten patients had normal coronaries without significant stenosis. The other 2 patients had coronary disease that was not consistent with their wall motion abnormalities (the reason they were included in the study). One patient had a 99% very distal circumflex stenosis (in a nondominant vessel), but had apical ballooning. The other patient had a chronic 60% right coronary artery stenosis present on a previous angiogram, with collaterals from the normal left anterior descending and circumflex arteries. This patient had apical ballooning as well. The ejection fraction on ventriculograms ranged between 15% and 60%, with a mean of 31%. The patients had a mean LV end-diastolic pressure level of 25 mm Hg.

All patients underwent repeated transthoracic studies between 24 hours and 4 weeks after the event. All had complete recovery of LV function and no evidence of wall motion abnormalities on the follow-up echocardiogram.

Discussion

Stress-induced cardiomyopathy has generally been associated with apical ballooning. We report here the first case series of stress-induced cardiomyopathy with wall motion abnormalities including apical ballooning but also midventricular ballooning. Six patients with midventricular ballooning have been described in the literature, 4 of them recently described,[3] and the other 2 described earlier in Japanese literature.[4] We also described localized exclusive posterobasal, anterolateral ballooning and global hypokinesis. Regional wall motion abnormality in patients with subarachnoidal hemorrhage has been associated with normal myocardial perfusion, but with abnormal sympathetic innervation due to a surge of norepinephrine release.[5] The distribution of LV wall motion abnormality in such patients (with apical ballooning, global hypokinesis, or midventricular ballooning) does not correlate with the specific coronary distribution. For the localized posterobasal and anterolateral wall, it should correlate. However, no coronary lesion was identified and the LV dysfunction was transient. This variability adds to the mystery of the underlying pathophysiology behind stress-induced cardiomyopathy.

A variety of hypotheses have been proposed to date. One suggested mechanism is ischemia due to coronary spasm, with increased sympathetic tone causing diffuse or localized coronary spasm in patients with normal coronaries.[6] None of our patients had evidence of a coronary spasm, not even those with a localized wall motion abnormality that could correspond to a single coronary distribution.

Another proposed mechanism is microvascular spasm,[6] which has been described in a patient with stress-induced cardiomyopathy.[7] Other possible mechanisms include direct myocyte injury caused by high levels of catecholamines,[5,8] and paroxysmal or new-onset atrial fibrillation causing acute coronary emboli that spontaneously resolves. The variability of wall motion abnormalities in our study may be attributable to variations in the patients' LV wall sensitivity and response to catecholamines. Spontaneously aborted myocardial infarction with autothrombolysis or medication-induced thrombolysis may also be a factor, particularly in patients with a single-wall motion abnormality.[2]

Previously reported cases, as well as our review, suggest that women are more susceptible than men to stress-induced cardiomyopathy, for reasons that remain unclear. This preponderance may be a reflection of gender-related differences in the sympathetic neurohormonal axis that are still poorly understood.[9]

Conclusion

We believe that stress-induced cardiomyopathy can involve any wall of the left ventricle or can even cause global hypokinesis. Three of our patients had localized wall motion abnormalities occurring after an emotional stress, with normal coronaries and complete recovery. Multiple variants appear to exist, including apical ballooning, midventricular

Table 1
Patient Characteristics

Patient Number	Age/Sex/ Ethnicity	Stressor	Troponin	Electrocardiogram	Angiogram/LV End-Diastolic Pressure	Ventriculogram	Follow-Up Echocardiogram
1	55 Female White	None	0.11	3 mm ST elevation in leads II, III, AVF, and V3-V6, with 2 mm ST depression in leads V1-V2	Normal coronaries, slow-filling LAD artery, but no stenosis 18 mm Hg	Severe hypokinesis of distal anteroseptal, apical, and inferoapical walls (apical ballooning)	1 month later, no WMA, EF 65%
2	71 Female White	Argument with son	3.13	ST elevation in leads II, III, and AVF, ST depression in leads V2-V3, ST elevation in leads V7-V8	Normal except 20% proximal RCA 20 mm Hg	Hypokinesis of anterolateral and inferior wall (midventricular ballooning)	1 day later, no WMA, EF 60%
3	42 Male White	None	14.31	1 mm ST elevation in leads II, III, and AVF	Normal except 30% distal RCA 24 mm Hg	Hypokinesis of posterobasal wall (posterobasal ballooning)	1 day later, no WMA, EF 60%
4	74 Female White	Acute cholecystitis	3.95	Atrial fibrillation, ST elevation in leads II, III, and aVF, inverted T wave in leads I and aVL	Normal coronaries 18 mm Hg	Hypokinetic anterolateral, apical, and diaphragmatic walls (apical ballooning)	1 month later, no WMA, EF 60%
5	51 Female East Indian	Argument with colleague at work	0.85	1 mm ST depression in leads II, III, and aVF, inverted T wave in leads I and aVL	Normal coronaries 20 mm Hg	Dyskinetic anterolateral and inferior walls, apex spared (midventricular ballooning)	1 week later, normal echocardiogram, no WMA, EF 60%
6	68 Female White	Excessive exercise (ballroom dancing)	0.09	Diffuse broad inverted T waves	Normal coronaries 32 mm Hg	Severe hypokinesis to akinesis of anterolateral and diaphragmatic inferior walls (midventricular ballooning)	2 days later, no WMA, EF 65%

(Continued)

Table 1
Patient Characteristics (Continued)

Patient Number	Age/Sex/ Ethnicity	Stressor	Troponin	Electrocardiogram	Angiogram/LV End-Diastolic Pressure	Ventriculogram	Follow-Up Echocardiogram
7	68 Female White	Small subarachnoid hemorrhage	9.2	Hyperacute T wave in leads V3-V6, inverted T wave in II, III, and aVF	Patent LAD artery stent 32 mm Hg	Akinetic anterolateral, apical, and diaphragmatic walls (apical ballooning)	1 month later, no WMA, EF 55%
8	48 Male White	Argument with wife	0.04	Normal ECG. Abnormal rest perfusion scan	Normal coronaries 17 mm Hg	Global hypokinesis	2 months later, normal LV function, EF 60%
9	69 Female White	Motor vehicle accident	1.41	1.5 mm ST elevation in leads I, AVL, and V5-V6	99% distal circumflex artery stenosis 30 mm Hg	Akinetic anterolateral, apical, and diaphragmatic walls (apical ballooning)	3 weeks later, no WMA, EF 60%
10	40 Female Hispanic	Son injured in a motor vehicle accident	0.74	No ST-T changes	Normal coronaries, except 30% ostial first diagonal 24 mm Hg	Marked hypokinesis of anterolateral wall (anterolateral ballooning)	1 month later, no WMA, EF 65%
11	79 Female White	None	1.43	1 mm ST elevation in leads V2-V4	Chronic 60% ostial RCA with collateral from LAD artery with normal LAD and circumflex arteries 30 mm Hg	Severe hypokinesis of anterior, anteroseptal, apical, and inferior walls (apical ballooning)	1 month later, no WMA, EF 50%
12	57 Female White	None	12.08	ST depression in leads V3-V6, inverted T wave in leads I and aVL	Normal coronaries 31 mm Hg	Dyskinetic posterobasal wall (posterobasal ballooning)	1 month later, no WMA, EF 65%

ECG, electrocardiogram; WMA, wall motion abnormality; EF, ejection fraction; LAD, left anterior descending; RCA, right coronary artery.

ballooning, localized ballooning of the posterobasal or anterolateral walls, and global hypokinesis. These variations may all have as a common genesis the variable sensitivity of the LV segments to catecholamines or localized coronary spasm. Further investigation may clarify this yet unexplained mechanism. ■

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Main Points

- Takotsubo syndrome is characterized by chest discomfort and acute myocardial infarction that is induced by emotional or physical stress.
- The exact etiology remains unclear, but potentially it could be explained by microvascular coronary spasm induced by excess catecholamine production, myocarditis, or aborted myocardial infarction due to spontaneous thrombolysis and stunned myocardium.
- In this case series of 12 patients, 8 had a triggering stressor. For 5 patients, it was emotional stress, and for 3 it was physical stress.
- Stress-induced cardiomyopathy has generally been associated with apical ballooning. In this case series, however, midventricular ballooning was seen.
- The distribution of left ventricular wall motion abnormality in patients with apical ballooning, global hypokinesis, and midventricular ballooning does not correlate with the specific coronary distribution.