www.nature.com/clinicalpractice/cardio

A case of Takotsubo cardiomyopathy mimicking an acute coronary syndrome

Mark D Metzl, Erik J Altman, Daniel M Spevack, Sanjay Doddamani, Mark I Travin and Robert J Ostfeld*

SUMMARY

Background A 71-year-old woman presented with severe chest pain after an episode of acute emotional distress. Her serum levels of cardiac enzymes were slightly elevated and electrocardiography revealed anterior ST-segment elevations. Significant coronary stenoses were excluded. A left ventriculogram revealed apical ballooning and a hypercontractile basal segment.

Investigations Serum cardiac enzyme measurements, echocardiography, coronary angiography and left ventriculography.

Diagnosis Takotsubo cardiomyopathy

Management Treatment with β-blockers, aspirin, angiotensin-converting-enzyme inhibitors, and intravenous diuretics.

KEYWORDS basal hyperkinesis, left ventricular apical ballooning syndrome, myocardial stunning, Takotsubo cardiomyopathy

CME

MD Metzl is an internal medicine resident at Montefiore Medical Center, Bronx, NY, USA. EJ Altman is a Cardiology Fellow, DM Spevack, S Doddamani and RJ Ostfeld are Assistant Professors of Medicine, and MI Travin is Professor of Clinical Nuclear Medicine and Medicine at Albert Einstein College of Medicine, NY, USA.

Correspondence
*Albert Einstein College of Medicine, Division of Cardiology, 3400 Bainbridge Avenue, Bronx, NY 10467, USA
rostfeld@montefiore.org

Received 19 September 2005 **Accepted** 2 November 2005
www.nature.com/clinicalpractice
doi:10.1038/ncpcardio0414

This article offers the opportunity to earn one Category 1 credit toward the AMA Physician's Recognition Award.

THE CASE

A 71-year-old woman presented to an emergency department with acute, left-sided, substernal chest pain at rest. Her husband had died 4 months previously, causing her severe emotional stress, and she was also in the process of selling her home. Her medical history included peripheral vascular disease, rheumatic heart disease with moderate mitral valve regurgitation, sarcoidosis, type 2 diabetes mellitus, hypertension, hypothyroidism, and rheumatoid arthritis. The patient denied having any history of angina symptoms. She had undergone a nuclear stress test 2 weeks before presentation, but this had not revealed any evidence of ischemia. Her medications included 400 mg pentoxifylline three times daily, and 75 mg clopidogrel, 50 μg levothyroxine sodium, 200 mg hydroxychloroquine sulphate, 25 mg hydrochlorothiazide and 240 mg diltiazem hydrochloride extended-release capsules, all once daily.

On presentation, the patient was afebrile, hypotensive (72/50 mm Hg), and had a heart rate of 72 beats/min, a respiratory rate of 18 breaths/min and an oxygen saturation of 99%. Physical examination revealed a grade 2/6 systolic murmur at the apex of the heart, without radiation. No jugular venous distention or lower-extremity edema was noted, and the lungs were clear on auscultation. The patient's complete blood count, basic metabolic panel and liver-function tests were all within the normal range. Two sets of myocardial enzyme assays showed an increase in creatine phosphokinase from 84 U/l to 121 U/l (normal range 24–170 U/l), and in troponin I from 0.46 μg/l to 1.26 μg/l (normal range 0–0.05 μg/l) over 2 h. Electrocardiography revealed ST-segment elevation in the precordial leads (Figure 1).

Administration of a 1 l normal saline bolus failed to normalize the patient's blood pressure; therefore, intravenous dobutamine therapy

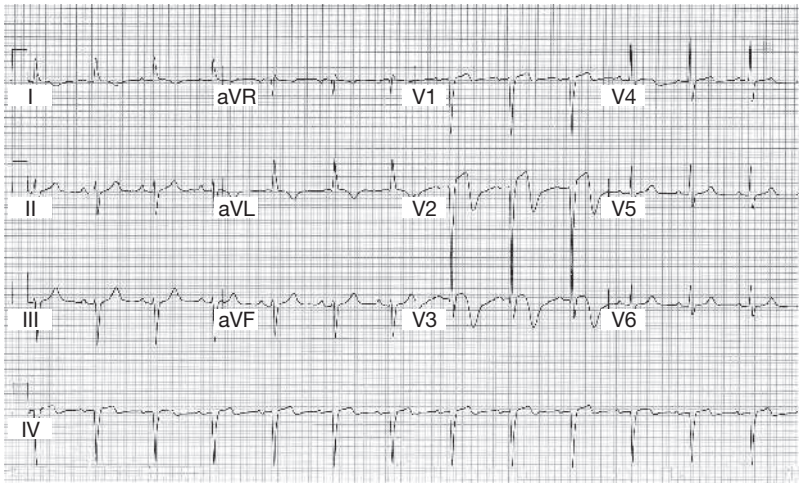

Figure 1 A 12-lead electrocardiogram showing ST-segment elevations and T-wave inversions in the right precordial leads, which is a typical pattern observed in Takotsubo cardiomyopathy. T-wave inversions are also evident in leads I and aVL, and the QT interval is prolonged.

was started at 6 μg/kg/min concomitantly with 325 mg aspirin. She also underwent thrombolysis with tenecteplase and was given heparin via intravenous drip.

While being transferred to a tertiary care center, the patient became tachycardic to 119 beats/min and required a 100% oxygen non-rebreather mask to maintain oxygen saturation greater than 90%. Diffuse crackles were detected bilaterally and the patient was given 80 mg furosemide intravenously. On arrival at the center, her oxygen saturation was 83% with 100% oxygen administered by non-rebreather mask; she was immediately intubated.

Cardiac catheterization revealed Thrombolysis in Myocardial Infarction grade III flow in all coronary arteries and a 40% lesion in the proximal right coronary artery. The left anterior descending (LAD) artery wrapped around the apex of the heart. Left ventriculography revealed left ventricular ballooning in the mid, distal and apical segments, with vigorous contraction of the basal segment (Figure 2). A 45 mm Hg dynamic intracavitary left ventricular gradient was detected, which decreased to 25 mm Hg when dobutamine therapy was stopped. The patient's blood pressure subsequently improved. A transthoracic echocardiogram showed similar wall motion to that observed by ventriculogram, systolic anterior motion of the mitral valve leaflets, and a left ventricular ejection fraction of 35%. A diagnosis of Takotsubo cardiomyopathy was considered, pending improvement of left ventricular function. In the coronary care unit the patient received 325 mg aspirin daily, heparin by intravenous drip, insulin by intravenous drip, 2.5 mg lisinopril daily, 25 mg metoprolol tartrate every 12 h, 40 mg simvastatin daily, and 50 μg levothyroxine sodium daily. The patient's condition improved and she was extubated within 24 h. Transthoracic echocardiography performed 3 days after initial presentation revealed improved left ventricular wall motion, no systolic anterior motion of the mitral valve, and a left ventricular ejection fraction of 45%. Follow-up echocardiography at 6 weeks revealed normal left ventricular function and an ejection fraction of 55%.

DISCUSSION OF DIAGNOSIS

Takotsubo cardiomyopathy is a syndrome with distinctive features (Box 1) that mimics acute myocardial infarction at clinical presentation; symptoms are acute chest pain and dyspnea, and ST-segment elevations can be seen on electrocardiograms. Cardiac catheterization should reveal a characteristic left ventricular wall-motion pattern without evidence of obstructive atherosclerotic coronary disease.

Dote *et al.*[1] first described this syndrome in Japanese patients; the name relates to the peculiar shape of the left ventricle, which resembles an octopus-fishing pot called a Takotsubo, and can be visualized by end-systolic ventriculography. This cardiomyopathy is becoming increasingly recognized around the world,[2–7] and clinicians should include it in the differential diagnosis of patients presenting with a suspected acute coronary syndrome.

Although the worldwide incidence is unknown, Takotsubo cardiomyopathy accounts for approximately 1% of admissions for suspected acute myocardial infarction in Japan;[6] most cases are reported in postmenopausal women aged 60–75 years.[2–7] Acute emotional or physiological stressors generally precede symptoms,[5–7] and the death of a close relative is the stressor reported most frequently.[2,7]

Presenting with overlapping symptoms and initial findings, it is difficult to distinguish Takotsubo cardiomyopathy from an acute coronary syndrome. A history of recent emotional trauma can prompt a clinician to consider Takotsubo cardiomyopathy; however, emotional triggers have also been associated with acute coronary syndromes.[8] Progression of electrocardiographic changes

can also be similar, with anterior Q-wave formation and T-wave inversions occurring in the precordial leads.[9] In the case described, electrocardiography revealed ST-segment elevations and T-wave inversions in the right precordial leads, mimicking an ST-elevation myocardial infarction (STEMI). A prolonged QT interval was also observed; this feature is described in several other cases of Takotsubo cardiomyopathy.[10]

Elevations in the levels of creatine phosphokinase and troponin are typically less than those observed in acute anterior STEMI,[4,5,7] but this difference cannot be used to exclude an acute coronary syndrome.

Given that Takotsubo syndrome is characteristically precipitated by emotional stress, elevated catecholamine levels might be useful in its diagnosis. In a small cohort of patients, Wittstein *et al.*[6] found that women presenting with Takotsubo cardiomyopathy had significantly higher catecholamine levels than women presenting with classic acute myocardial infarction, despite experiencing similar episodes of emotional stress.

In the case described here, echocardiography revealed akinesis of the apex and the mid-ventricle as well as basal hyperkinesis, wall-motion abnormalities extending beyond the region supplied by one coronary artery. This feature is characteristic of Takotsubo cardiomyopathy, whereas wall-motion abnormalities observed in acute myocardial infarction are often more localized. Myocardial viability is preserved in Takotsubo cardiomyopathy, which can be demonstrated using cardiac MRI.[6] Although nonobstructive atherosclerotic lesions have been observed with this condition, they have all been smaller than 50% of the luminal diameter, as in the case described here.[6] Interestingly, Ibanez *et al.*[11] suggest that this cardiomyopathy might result from a transient LAD obstruction caused by a ruptured artherosclerotic plaque located proximally in a large LAD that extends to the diaphragmatic surface of the left ventricle.[11] They observed this phenomenon on intravascular ultrasonograms of five patients. Takotsubo cardiomyopathy might, therefore, be an acute coronary syndrome arising in patients with an unusual LAD anatomy. Early reperfusion follows, resulting in a widely stunned, rather than infarcted myocardium. Takotsubo cardiomyopathy has, however, been observed in patients without this type of LAD anatomy,[3,4] bringing into question whether this pathophysiology is involved in all cases.

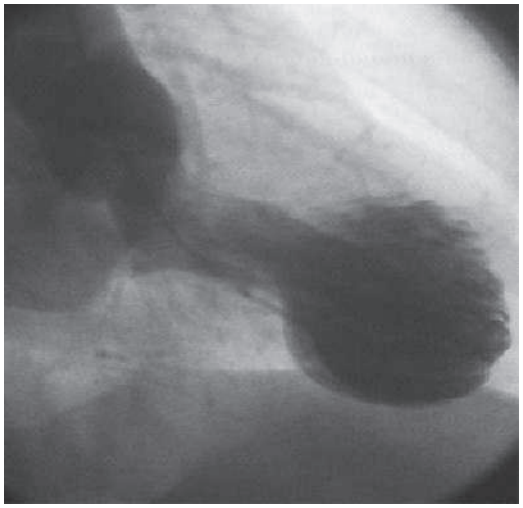

Figure 2 Left ventriculogram of the patient during systole showing mid, distal and apical left ventricular ballooning, with vigorous contraction of the basal segment as seen in Takotsubo cardiomyopathy.

Box 1 Clinical features of Takotsubo cardiomyopathy.

- Presentation of acute chest pain or dyspnea after emotional or physiological stress
- Electrocardiographic abnormalities that mimic an acute myocardial infarction
- Transient akinesis or hypokinesis of the left ventricular apex and mid ventricle with basal hyperkinesis
- Absence of obstructive coronary lesions on coronary angiography
- Absence of other catecholamine-surge state, including pheochromocytoma, recent head trauma and intracranial bleeding
- Recovery of left ventricular function within 2–4 weeks of presentation

Although the etiology of Takotsubo cardiomyopathy is unclear, the transient left ventricular apical ballooning observed is generally considered to be a form of myocardial stunning. Several mechanisms have been proposed, including catecholamine surges leading to left ventricular dysfunction, which have been described in pheochromocytoma and in

Competing interests
The authors declared they have no competing interests.

neurogenic-stunned myocardium syndrome after subarachnoid hemorrhage.[12,13] Coronary vasospasm does not appear to play a significant part in the disorder,[2,3] and the reperfusion hypothesis proposed by Ibanez *et al.*[11] warrants further investigation.

TREATMENT AND MANAGEMENT

No consensus exists regarding appropriate therapy for Takotsubo cardiomyopathy because the number of reported cases is low and the disorder is possibly underdiagnosed. Most data regarding treatment have been derived by observing patients initially treated for STEMI, and diagnosed later as having Takotsubo cardiomyopathy. Since differentiation between this cardiomyopathy and an acute coronary syndrome is often difficult at initial presentation, we tend to treat patients conservatively to avoid complications that might arise by failing to treat an anterior wall myocardial infarction. Patients receive aspirin, β-blockers, angiotensin-converting-enzyme inhibitors, cardiac catheterization and intravenous diuretics if needed.

When a patient presents with hypotension, intravenous pressors might be required, and sometimes treatment with intra-aortic balloon pumps and left ventricular assist devices is necessary. Those with hypotension should be evaluated by echocardiography or cardiac catheterization for an intra-cavitary gradient, which in this case was exacerbated by dobutamine and resulted in a dynamic left ventricular mid-cavity obstruction. If a dynamic intraventricular pressure gradient is detected, inotropic drug therapy should be discontinued and intravenous β-blockers administered to increase diastolic filling time and left ventricular end-diastolic volume.[14] Thickening of the mid ventricular septum is reported to be a predisposing factor for developing an intracavitary gradient,[15] but was not observed in this case.

Patients with Takotsubo cardiomyopathy must be monitored for symptoms of cardiogenic shock, heart failure and arrhythmias. Rare cases of sudden death have been reported and can result from catecholamine-mediated arrhythmias, *torsade de pointes*,[10] ventricular rupture, tamponade and pulmonary edema. Most patients, however, experience improvements in left ventricular function within 2–4 weeks of symptom onset. [2]

CONCLUSION

This case illustrates the challenges of distinguishing Takotsubo cardiomyopathy from an acute coronary syndrome, and the management of hypotension caused by a dynamic intraventricular gradient. Further studies will hopefully enable early diagnosis of Takotsubo cardiomyopathy, clarify its etiology, refine therapy regimens and aid in its prevention.

References

1 Dote K *et al.* (1991) Myocardial stunning due to simultaneous multivessel coronary spasm: a review of 5 cases. *J Cardiol* **21:** 203–214
2 Tsuchihashi K *et al.* (2001) Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina Pectoris-Myocardial Infarction Investigations in Japan. *J Am Coll Cardiol* **38:** 11–18
3 Kurisu S *et al.* (2002) Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: a novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J* **143:** 448–455
4 Desmet WJR *et al.* (2003) Apical ballooning of the left ventricle: first series in white patients. *Heart* **89:** 1027–1031
5 Bybee KA *et al.* (2004) Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning syndrome. *Am J Cardiol* **94:** 343–346
6 Sharkey SW *et al.* (2005) Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation* **111:** 472–479
7 Wittstein IS *et al.* (2005) Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* **352:** 539–548
8 Rosengren A *et al* (2004) INTERHEART investigators. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* **364:** 953–962
9 Kurisu S *et al.* (2004) Time course of electrocardiographic changes in patients with tako-tsubo syndrome—comparison with acute myocardial infarction with minimal enzymatic release. *Circ J* **68:** 77–81
10 Denney SD *et al.* (2005) Long QT syndrome and *torsade de pointes* in transient left ventricular apical ballooning syndrome. *Int J Cardiol* **100:** 499–501
11 Ibanez B *et al.* (2005) Tako-tsubo transient left ventricular apical ballooning: is intravascular ultrasound the key to resolve the enigma? *Heart* **91:** 102–104
12 Scott IU and Gutterman DD (1995) Pheochromocytoma with reversible focal cardiac dysfunction. *Am Heart J* **130:** 909–911
13 Kono T *et al.* (1994) Left ventricular wall motion abnormalities in patients with subarachnoid hemorrhage: neurogenic stunned myocardium. *J Am Coll Cardiol* **24:** 636–640
14 Kyuma M *et al.* (2002) Effect of intravenous propranolol on left ventricular apical ballooning without coronary artery stenosis (ampulla cardiomyopathy): three cases. *Circ J* **66:** 1181–1184
15 Merli E *et al.;* Tako-Tsubo cardiomyopathy: New insights into the possible underlying pathophysiology. *Eur J Echocardiogr*, in press