A Case of Broken Heart Syndrome

Patrick C. Bergin, MD, FRCPC

Julia’s Broken Heart

Julia, 66, has an unusual presentation of acute coronary syndrome. Less than 24 hours after her brother-in-law’s death from acute MI, Julia’s husband died tragically following a cardiac arrest.

Later that same day she developed moderately severe retrosternal chest heaviness associated with slight ST elevation anterolaterally (Figure 1), but she was hemodynamically stable. Her discomfort lasted approximately seven hours, apparently unresponsive to nitroglycerine. She was not offered thrombolysis by the initial treating physicians.

Her peak creatine kinase (CK) level was 225 and she had positive troponin I result of 6.3 ug/L.

Pertinent medical history includes diet controlled dyslipidemia and remote history of deep vein thrombosis (DVT). Julia’s mother died of MI at age 50 and she has a brother with life-threatening pulmonary arterial and right atrial thrombosis, who was identified to have heterozygous prothrombin gene mutation.

For more on Julia, see page 28.

CardioCase discussion

Psychologic stress has long been associated with increased cardiac events. This may be facilitated by a coronary vasospasm or plaque rupture caused by increased shear stress within the vessel secondary to increased sympathetic activation. We also see catecholamines implicated in acute coronary syndrome (ACS) as a circadian early morning ischemia phenomenon, or after heavy exertion, such as shovelling snow in colder weather. As clinicians, we have all likely seen patients that have experienced an ischemic cardiac event following a stressful situation. This may be following a fight with their teenage daughter, loss of a job, or news of a loved one’s serious illness or death. Patients will often ask whether stress can cause a heart attack and the answer is, unfortunately, yes.

This article describes a recently identified condition called Takotsubo syndrome, otherwise known as:

- stress cardiomyopathy,
- transient left ventricle (LV) apical ballooning syndrome, or
- Broken Heart syndrome.

It is typically associated with an acutely stressful situation of a personal or emotional nature, but has also been reported with heightened stress associated with natural disasters, as well
as medical conditions associated with excessive catecholamine states.\textsuperscript{3}

**Prevalence and patient demographics**

It was not until the mid 1990s that Japanese authors highlighted the reversible ischemic syndrome of transient LV apical ballooning, angiographically resembling a takotsubo—a Japanese octopus trap.\textsuperscript{3,4} This syndrome is now recognized in the non-Asian populations in Europe and North America.\textsuperscript{4}

The true prevalence is unknown, with retrospective studies likely underestimating at 2\% of ACS presentations. This may be a more common entity unrecognized in a wide array of medical, surgical and critical care populations.\textsuperscript{3} Takotsubo syndrome has been reported in patients with pheochromocytoma, cocaine use and other withdrawal states and has been associated with subarachnoid hemorrhage and head trauma patients.\textsuperscript{5,6} Elderly or postmenopausal women represent > 80\% of cases, with a mean age of 62 to 75 years.\textsuperscript{4,7}

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Proposed Mayo criteria for clinical diagnosis of Takotsubo syndrome</th>
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<td>All of the following 4 criteria must be met: \textsuperscript{4}</td>
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<td>1. Transient akinesis or dyskinesis of the left ventricular apical and mid ventricular segments with regional wall motion abnormalities extending beyond a single epicardial vascular distribution</td>
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<td>2. Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture</td>
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<td>3. New electrocardiographic abnormalities (ST segment elevation or T wave inversion)</td>
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<td>4. Absence of:</td>
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<td>- Recent significant head trauma</td>
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<td>- Intracranial bleeding</td>
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<td>- Pheochromocytoma</td>
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<td>- Obstructive epicardial coronary artery disease</td>
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<td>- Myocarditis</td>
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<td>- Hypertrophic cardiomyopathy</td>
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**About the author...**

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![Figure 1. Acute MI presentation on ECG.](image-url)
Elderly or post-menopausal women represent > 80% of cases, with a mean age of 62 to 75 years.

Diagnosis and clinical features

Patients usually present with the acute onset of visceral chest pain and dyspnea following excessive stress. They typically suffer a small MI but may be complicated by:

- heart failure,
- ventricular tachycardia,
- cardiogenic shock,
- mitral insufficiency,
- LV mural thrombus,
- LV free wall rupture and
- cardiac arrest/death.\(^4\)

Normal vessels or subcritical lesions are seen on coronary angiography despite an apparent classic presentation of cardiac type chest pain, positive biomarkers (86% to 100%), elevated cardiac enzymes (74%), with or without EKG changes (82% with ST elevation).\(^4,8\) Takotsubo syndrome classically manifests with LV apical ballooning seen on initial or early angiography, that is usually reversible within several months.\(^4\)

Mechanism of injury

It has been proposed that the majority, if not all of Takotsubo patients have a Type 3 “wrap around” left anterior descending (LAD) artery.\(^5\) The coronary ischemia is likely secondary to vasospasm of the distal LAD, but distal thrombus, not visualized by angiography, has also been postulated.\(^5\) It appears similar to animal models of coronary ischemia, secondary to induced vasospasm or excess catecholamine states.

The characteristic ballooning of the LV apex is felt to be caused by transient myocardial injury or stunning of the distal apical myocardium, with compensatory hyperkinetic contraction in the mid and basal LV regions.\(^3,4,5\) However, the nature and extent of the ballooning of the LV apical segments has been difficult to explain solely on involvement of the LAD coronary artery.\(^3,5,8,9\) Impaired multivessel coronary microcirculation, calcium overload with direct myocyte damage and abnormal fatty acid metabolism with prolonged myocardial stunning have all been proposed as possible mechanisms.\(^8,9\)

Reverend Thomas Bayes (author of the Bayesian Theory) suggests that rare presentations of common problems are more common than common presentations of rare problems.\(^6\)

It seems logical to assume that excessive...
catecholamine-induced states may be causing coronary vasospasm. However, these patients meet the criteria for diagnosis of MI using American Heart Association (AHA)/American College of Cardiology (ACC) and World Health Organization (WHO) criteria\(^5,10\) and an atherothrombotic ischemic etiology should still be considered. A recent intravascular ultrasound study involving five patients diagnosed with Takotsubo syndrome demonstrated all five patients to have a disrupted eccentric atherosclerotic plaque in the middle portion of the LAD artery that was not visible on coronary angiography.\(^5\)

**Treatment and prognosis**

Prognosis is generally very good, with the majority of patients demonstrating significant improvement and often completely normalizing LV function.\(^3\) Treatment generally is supportive when hemodynamically unstable. Some authors suggest a preference for intra-aortic balloon counterpulsation over inotropes because of the potential role of catecholamine excess in its origin.\(^3\) Diuretics, β-blockers and angiotensin-converting enzyme (ACE) inhibitors are used until recovery of LV function. At present, there is no available evidence that supports long-term use of ACE inhibitors or β-blockers once LV function normalizes. Intuitively, antiplatelet agents should be considered until a thrombotic pathogenesis is more definitively excluded. Anticoagulation should be considered until

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<td><strong>Summary of characteristic features of Takotsubo syndrome</strong></td>
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<td>1. Postmenopausal females</td>
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<td>2. Associated with acute significant stressor</td>
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<td>3. Positive troponin with elevated CK, with or without typical EKG features of acute MI</td>
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<td>4. Absence of significant coronary artery disease on angiography</td>
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<td>5. Develops early characteristic LV apical ballooning with compensatory hyperkinetic basal and mid LV motion giving rise to appearance resembling a takotsubo</td>
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<td>6. LV dysfunction reversible with good long term prognosis</td>
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Figure 2. ECG six weeks post MI.
apical akinesia or dyskinesis resolves to minimize cardioembolic risk.\textsuperscript{3,9}

Takotsubo or Broken Heart syndrome suggests there is a significant role that stress plays in the progression of cardiovascular disease. Atherosclerotic disease progression may follow a series of plaque ruptures that largely remain clinically silent, possibly precipitated or aggravated by life’s stressors, with clinically identifiable cases only representing the “tip of the iceberg.” Identifying and learning more about the pathogenesis of Takotsubo syndrome may help us in managing stress as a modifiable risk factor in cardiovascular disease progression.

References
7. UpToDate Online. Takotsubo Stress Cardiomyopathy.