Overtures to Takotsubo's Cardiomyopathy

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Takotsubo's cardiomyopathy (TCM) is a condition with characteristic left ventricular wall motion abnormalities that occurs in the absence of critical atherosclerosis by coronary angiography. The term *takotsubo* is a fishing pot with a rounded bottom and a narrow neck used for trapping octopus in Japan and resembles the left ventricular appearance in systole observed in the common form of the disease.¹ Typical akinesia/dyskinesia involves both the mid and apical portions of the left ventricle (LV) in about 75% of cases when compared to the atypical pattern, where segmental contraction abnormalities are confined to either the mid or apical LV.² Often, a strong emotional or occasionally physical stress precedes the occurrence of TCM that has led to the use of the alternative term *broken heart syndrome*. It seems to occur more commonly in postmenopausal women.³ In the current issue of *Clinical Cardiology*, Kumar et al. reported a case of cardiac rupture (CR) in a patient with TCM, and expanded the literature search of sporadic cases published worldwide.⁴ A cohort of 12 cases of reported TCM and CR was identified and compared to a group without rupture selected by random sampling. Rupture was confirmed on autopsy in 5 patients, suspected by catheterization in 2 patients, and suggested by echocardiography in 5 patients. More patients with CR had ST elevation in lead II and were all older females (76 ± 9 years). Also, systolic blood pressure, double product, and peak creatine kinase were significantly higher in the CR group compared to controls. However, the difference in troponin I was not statistically significant. Furthermore, the use of β -blockers was less frequent in the CR group. These features of rupture in TCM are similar to those known to occur with rupture following myocardial infarction (MI).

TCM tends to have a clinical presentation similar to an acute MI, with substernal chest pain and dyspnea and mild elevation of markers of myocardial necrosis. The diagnosis will ultimately depend on demonstrating the lack of occlusive coronary lesions with matching wall motion abnormalities.³ Multiple etiologies have been proposed, including the concept of myocardial stunning following a transient spontaneous multivessel coronary artery spasm, a dysfunction affecting myocardial microcirculation or possibly a direct catecholamine-mediated myocyte injury. Exaggerated sympathetic stimulation probably plays a cardinal role in TCM. When measured early in the course of TCM, plasma catecholamine levels have been reported elevated in most patients.³

Despite earlier reports of expected recovery in the majority of TCM patients, acute phase complications have been

reported in as high as 19% of patients, most commonly shock, including cardiogenic shock, ventricular fibrillation, intracavitary thrombus formation, and stroke.^{3,5} Overall, survival of TCM patients is reduced compared to that of an age- and sex-matched general population, mostly due to noncardiac diseases (predominantly cancer).² In their cohort, Kumar et al. report that wall motion abnormalities were confined to mid and apical regions as opposed to the atypical (midventricular) form of TCM, which may indicate that the atypical form of TCM is less prone to rupture.⁴ Another important observation is the pathology findings of myocardial necrosis at the site of CR. Authors have described contraction bands seen in 2 cases as indicative of high catecholamine states and acknowledged that they could be seen with MI. This form of myocardial necrosis, termed contraction band necrosis, can result primarily from severe ischemia followed by reflow.⁶ This may reconcile with another intriguing hypothesis to explain TCM, and that is the concept of aborted MI, indicating coronary emboli/thrombosis with spontaneous lysis. Ibanez et al. reported on 5 TCM patients in which disrupted eccentric atherosclerotic plaques of the left anterior descending coronary artery had been visualized by intravascular ultrasound but were not visible by contrast angiography.⁷ Also, we have recently demonstrated that cholesterol crystals released during plaque rupture can shower downstream, injuring the intima and leading to unopposed vasoconstriction.⁸ Such arterial lesions may not always be visible by angiography. Because of the potential role of catecholamines and excessive sympathetic stimulation in the pathogenesis of TCM, β -blockers would be expected to benefit these patients and have been suggested by Kumar et al. to play a protective role against CR.⁴ Overall, management of TCM is largely empirical, supportive, and should be individualized according to the patient characteristics at initial presentation.³ Typically, this includes β -blockers and aspirin. To date, no long-term studies of pharmacotherapies have been conducted in humans, and some observational data have failed to determine whether any cardioactive drugs could provide risk reduction.²

The rarity of reported CR may be due to a lack of wall thinning in TCM. Interestingly, Kumar et al. reported the location of rupture to be the LV apex in 2 patients, anterior wall in 1 patient, posterior wall in 1 patient, and apical-posterior wall in 1 patient.⁴ According to the LaPlace principle, the localized increase in ventricular cavity increases wall tension, a factor that may increase the risk of rupture. Perhaps one would expect ruptures to occur more in the apex because it has the thinnest wall in the LV.

In another case report in this issue, Taylor et al. reported an intriguing phenomenon of a TCM-like condition occurring following watching a three-dimensional (3D)

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action movie at a local theater.⁹ The 55-year-old female, who had previously been healthy, had a sudden onset of dyspnea, palpitations, nausea, and vomiting 30 minutes into the movie. She had an extensive work-up that included coronary angiography, which demonstrated the lack of coronary flow limiting disease, and cardiac magnetic resonance imaging with a lack of delayed hyperenhancement that could be seen with active inflammation or myocardial fibrosis. At 49 days from presentation, she had a return of normal left ventricular function. Emotional stressors reported to cause TCM range from confrontational arguments to catastrophic events. Nevertheless, in approximately one third of patients, no preceding emotional or physical stressful events have been identified.³ Whether this case of TCM resulted from the emotional distress induced by the movie or merely the visual stimulation of the new 3D technology will be determined by developments of further events given the proliferation of 3D to local theaters, and soon possibly homes.

The etiology of TCM remains a challenge, and as more cases are diagnosed in the catheterization labs, recognition of potential etiologies and complications is expected to rise. Overall, it seems that the number of TCM cases appears to be rising, either due to improved recognition of the entity or related to the etiology of the condition that have not yet been elucidated. Future work would be enhanced by developing

a model of TCM to help study potential mechanisms and etiologies of this condition.

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