Cough-Induced Takotsubo (Stress) Cardiomyopathy

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INTRODUCTION

Takotsubo cardiomyopathy (TC), also known as stress cardiomyopathy or "broken heart syndrome," is an acute transient cardiac condition. It is often associated with an identifiable emotional or physical stressor resulting in a variety of distinct patterns of left ventricular wall contraction abnormality. We describe a rare case demonstrating cough-induced TC that we believe is the first case in which such a temporal relationship between cough and transient left ventricular apical ballooning was documented on serial transthoracic echocardiography.

CASE PRESENTATION

An 85-year-old woman was progressing well when reviewed in the clinic 3 months after uncomplicated bioprosthetic mitral valve replacement. She had a background of atrial fibrillation and previous mild cerebellar stroke. Transthoracic echocardiography on the day of the clinic visit was similar to preoperative imaging, showing that left ventricular systolic function was low normal (ejection fraction ~ 50%), with no obvious regional wall motion abnormality (Figure 1, Video 1). A few hours after her clinic appointment, she started coughing violently for several minutes, to the point of near choking, following accidental aspiration of water while drinking. Immediately after the resolution of her coughing episode, the patient experienced chest tightness and dyspnea, which gradually worsened over the ensuing 2 days. She was admitted, and electrocardiography showed new widespread T-wave inversion (Figure 2). Laboratory tests revealed brain natriuretic peptide of 2,712 pg/mL and troponin I peaking at 0.62 μg/L. Chest radiography, compared with baseline, did not demonstrate any changes suggestive of florid pulmonary edema. Echocardiography now demonstrated moderate left ventricular impairment with a dyskinetic apex (Figure 3, Video 2). Coronary angiography showed no significant coronary artery disease (Figure 4). She was commenced on furosemide, and her bisoprolol and cilazapril doses were increased. Repeat echocardiography 3 months later showed resolution of her left ventricular apical ballooning and recovery of systolic function (Figure 5, Video 3). A diagnosis of cough-induced TC was made.

DISCUSSION

TC is an acute, reversible, nonischemic phenomenon mimicking acute coronary syndrome. The first case reports of TC were described in Japanese patients in the early 1990s.[1] The true prevalence of TC is unknown, however, it is estimated to account for approximately 1–2% of all patients presenting with a presumed diagnosis of acute coronary syndrome.[2] This unique cardiomyopathy is predominantly seen in postmenopausal women, with 90% of cases seen in women with a mean age ranging from 62 to 76 years.[3] In the majority of cases, a recent emotional or physical stressor is identified prior to manifestation of TC.[4]

TC patients usually present with substernal chest pain and electrocardiographic changes (ST-segment elevation in precordial leads present in 68% of patients with diffuse T-wave inversions present in 97% of cases) but with peak troponin levels significantly lower when compared to those with acute myocardial infarction.[3,4]

The diagnosis of TC typically requires clinical suspicion, nonobstructive coronary artery disease (stenosis <50%) on angiography, and characteristic left ventricular wall motion abnormalities in systole and diastole observed on left ventriculography or echocardiography.[5] In the typical form of this disorder, the regional wall abnormality pattern is characterized by distinct transient left ventricular apical ballooning as a result of depressed mid and apical segments with hyperkinesis of basal walls.[3-5]

The treatment for TC is primarily empiric, with standard medications used in the management of heart failure. Angiotensin-converting enzyme inhibitors, β-blockers, and/or diuretics are individualized based on patient characteristics at time of presentation.

TC generally has a very favorable prognosis, with virtually complete recovery of the left ventricular function by 4–8 weeks.[5] The in-hospital mortality associated with TC is ~1%, with the recurrence rate predicted to be 10%.[4,6]

The complications associated with TC are heart failure requiring inotropes or an intra-aortic balloon pump, left ventricular outflow tract obstruction, left ventricular thrombus, left ventricular free wall rupture, right ventricular impairment, ventricular arrhythmia, and rarely death.[3,5] Angiotensin-converting enzyme inhibitors and β-blockers may be continued once the left ventricular function has returned to baseline, but there is paucity of data supporting the long-term use of these pharmacological agents in this subset of patients.

The exact pathogenic mechanism of TC remains unknown, however, excessive sympathetic stimulation, microvascular dysfunction, and metabolic abnormalities have been speculated to be associated with this disorder.[7,8,9] The most widely accepted postulation is that an endogenous catecholaminergic surge during emotional distress is integral to the development of TC. The left ventricle has the greatest density of sympathetic receptors with an epicardial to endocardial as well as a basal to apical gradient.[10] High levels of catecholamines have been demonstrated to result in neurogenic myocardial stunning as a result

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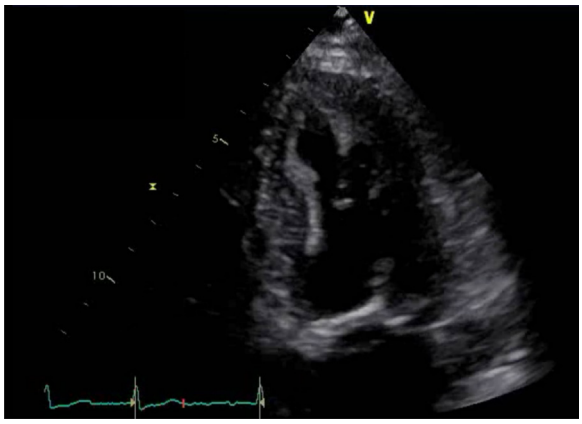

Figure 1 Transthoracic echocardiography: apical four-chamber view during end-systole before coughing episode showing no obvious left ventricular regional wall motion abnormality.

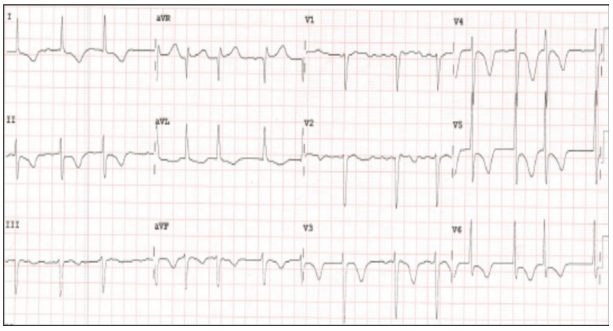

Figure 2 Electrocardiogram showing widespread T-wave inversion.

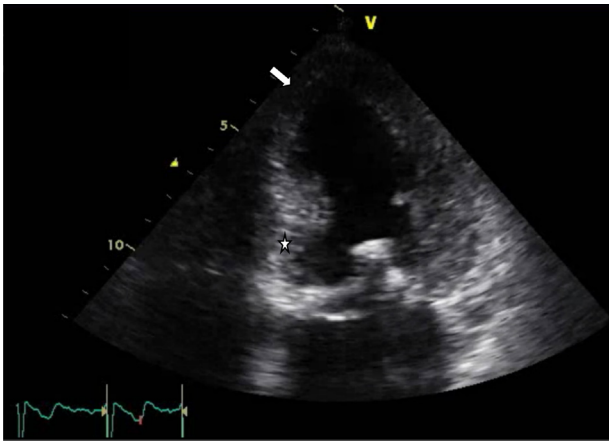

Figure 3 Transthoracic echocardiography: apical four-chamber view during end-systole after coughing episode demonstrating apical ballooning (*arrow*) with preserved contractilty of the basal segment (*star*).

of direct toxic effects on the cardiomyocytes.[10,11] While various physical stressors have been identified to potentially cause TC, there is only one other case report in the literature of cough as an innocuous event causing such a cardioyopathy.[12] Our patient satisfies all of the criteria for TC and uniquely had an echocardiogram performed, with normal wall motion noted, a few hours before an intense coughing episode. It

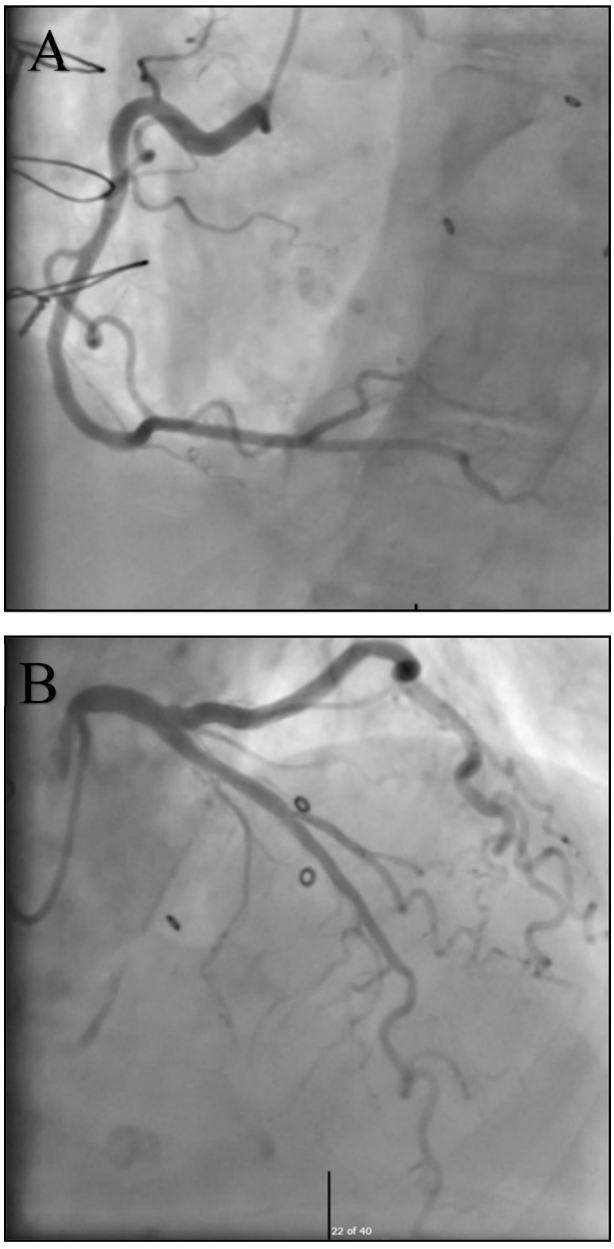

Figure 4 Coronary angiography showing no significant obstructive disease of the **(A)** right coronary artery and **(B)** left main stem, left anterior descending coronary artery, and left circumflex coronary artery.

is possible that sympathetic activity was markedly increased by the sensation of coughing, which would account for the occurrence of TC in this patient. It has been shown that coughing decreases coronary perfusion pressure in hemodynamically stable subjects due to a greater rise in right atrial pressure compared to aortic pressure.[13] Another plausible theory in this particular instance could be that reduced coronary perfusion, in combination with a sympathetic surge, could have led to myocardial microvascular and metabolic dysfunction contributing to the development of TC. Alternatively, this case may provide insight into a different explanation for TC. It has been known for decades that cough and marked Valsalva maneuvers against resistance can acutely raise blood pressure to extreme levels (systolic pressures from 250 to over 400 mm Hg).[14,15]

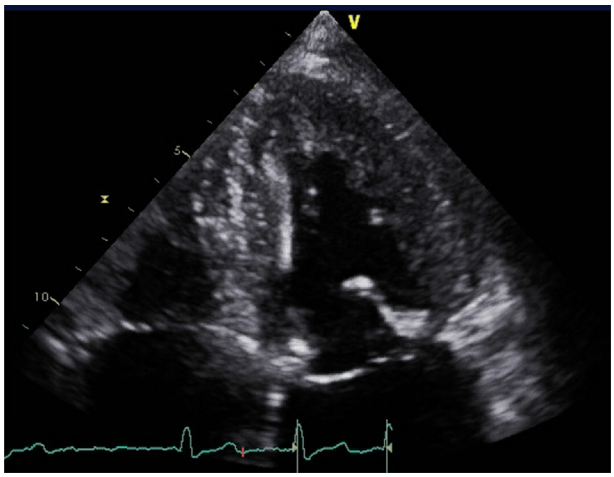

Figure 5 Transthoracic echocardiography: apical four-chamber view during end-systole showing resolution of the apical wall motion abnormality after 3 months.

Such a rise in blood pressure may have been generated in this situation, resulting in the expansion of the apical left ventricular region without necessarily implicating excess sympathetic stimulation as the mediator. We would postulate that the apex may be prone to expansion as this area generally has a thinner left ventricular wall thickness, as dictated by the LaPlace relation. Finally, it is possible that a combination of all the above is responsible for the occurence of TC in this unique case.

CONCLUSION

This case demonstrates cough as an extremely rare but notable cause of TC. The speculative mechanisms responsible for this include catecholamine surge, cardiac microvascular and metabolic dysfunction, and extreme hemodynamic stress. This case adds to the growing list of unusual circumstances identified in the causation of this phenomenon and highlights considering cough as a potential etiology in the differential diagnosis of TC. It raises the question of whether severe coughing episodes may contribute to cases of TC when no clear inciting event is identified as well as subclinical cases that go unidentified.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2018.03.004.

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