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 echocardiography 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 (Figure 2). Laboratory tests revealed brain natriuretic peptide of 2,712 pg/mL and troponin I peaking at 0.62

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. 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. 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. In the majority of cases, a recent emotional or physical stressor is identified prior to manifestation of TC.

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.

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. 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.

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. The in-hospital mortality associated with TC is ~1%, with the recurrence rate predicted to be 10%. 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.

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.

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 gradient as well as a basal to apical gradient. High levels of catecholamines have been demonstrated to result in neurogenic myocardial stunning as a result of a basal to apical gradient.

Keywords: Cough, Takotsubo cardiomyopathy, Stress cardiomyopathy, Cough-induced Takotsubo Syndrome, Apical ballooning syndrome

Conflict of interest: The authors reported no actual or potential conflicts of interest relative to this document.

From the Cardiology Department, Dunedin Public Hospital (S.L., J.P.), and the Department of Medicine, Dunedin School of Medicine, University of Otago (G.T.W.), Dunedin, New Zealand.

Copyright 2018 by the American Society of Echocardiography. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

https://doi.org/10.1016/j.case.2018.03.004

240

CARDIOMYOPATHIES

Cough-Induced Takotsubo (Stress) Cardiomyopathy

Sudish Lal, MBChB, James Pemberton, MD, FASE, and Gerard T. Wilkins, FRACP, Dunedin, New Zealand
of direct toxic effects on the cardiomyocytes.\textsuperscript{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 cardiomyopathy.\textsuperscript{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 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.\textsuperscript{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).\textsuperscript{14,15}
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 occurrence 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.

REFERENCES

1. Dote K, Sato H, Tateishi H, Uchida T, Ishihara M. Myocardial stunning due to simultaneous multivessel coronary spasms: a review of 5 cases. J Cardiol 1991;21:203-14.
2. Kurowski V, Kaiser A, Von Hof K, Killermann DP, Mayer BN, Hartmann F, et al. Apical and midventricular transient left ventricular dysfunction syndrome (takotsubo cardiomyopathy): frequency, mechanisms, and prognosis. Chest 2007;132:809-16.
3. Pilgrim TM, Wyss TR. Takotsubo cardiomyopathy or transient left ventricular apical ballooning syndrome: a systematic review. Int J Cardiol 2008;124:282-92.
4. Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review. Eur Heart J 2006;27:1523-9.
5. Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (takotsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J 2008;155:408-17.
6. Elesber AA, Prasad A, Lennon RJ, Wright S, Lerman A, Rihal CS. Four-year recurrence rate and prognosis of the apical ballooning syndrome. J Am Coll Cardiol 2007;50:448-52.
7. Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med 2005;352:539-48.
8. Kume T, Akasaka T, Kawamoto T, Yositani H, Watanabe N, Neishi Y, et al. Assessment of coronary microcirculation in patients with takotsubo-like left ventricular dysfunction. Circ J 2005;69:934-9.
9. Bybee KA, Murphy J, Prasad A, Wright RS, Lerman A, Rihal CS, et al. Acute impairment of regional myocardial glucose uptake in the apical ballooning (takotsubo) syndrome. J Nucl Cardiol 2006;13:244-50.
10. Kono T, Sabba H. Takotsubo cardiomyopathy. Heart Fail Rev 2014;19:585-93.
11. Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Musha H, Sasaki K. 123I-MIBG myocardial scintigraphy in patients with “takotsubo” cardiomyopathy. J Nucl Med 2004;45:1121-7.
12. Butman SM. Coughing-induced stress cardiomyopathy. Catheter Cardiovasc Interv 2010;76:388-90.
13. Little WC, Reeves RC, Coughlan C, Rogers EW. Effect of cough on coronary perfusion pressure: does coughing help clear the coronary arteries of angiographic contrast medium. Circulation 1982;65:604-10.
14. Sharpey-Schafer EP. Effects of coughing on intrathoracic pressure, arterial pressure and peripheral blood flow. J Physiol 1953;122:351-7.
15. MacDougall JD, Tuxen D, Sale DG, Moroz JR, Sutton JR. Arterial blood pressure response to heavy resistance exercise. J Appl Physiol 1985;58:785-90.