Takotsubo Cardiomyopathy in a 22-Year-Old Single-Ventricle Patient

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We report a highly unusual case of a 22-year-old woman with single-ventricle anatomy and a history of Fontan palliation who developed takotsubo cardiomyopathy. To our knowledge, takotsubo cardiomyopathy has not previously been described in a patient with single-ventricle anatomy, or more generally in any patient with congenital heart disease. The patient presented at our clinic for urgent examination after a 2-day history of chest pain that had begun upon the death of her dog. Invasive evaluation was refused by the patient; instead, she underwent electrocardiogram-gated coronary computed tomographic angiography, to rule out obstructive coronary disease.

A physician who suspects takotsubo cardiomyopathy in a patient should look for new-onset chest pain and dyspnea coupled with these features: immediate onset of segmental akinesia in the midventricular or apical aspects of the heart, elevation of brain natriuretic peptide level 12 to 24 hours after onset of akinesia, elevation of troponin level 24 to 48 hours after onset, and disappearance of the segmental akinesia a few days after onset. (*Tex Heart Inst J* 2016;43(1):61-4)

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Takotsubo cardiomyopathy (TC), also known as apical ballooning syndrome, broken-heart syndrome, and stress-induced cardiomyopathy, is a rare disease that presents with chest pain and transient myocardial dysfunction, which typically results in apical ballooning of the heart. First documented in Japan¹ in 1991, takotsubo is a nonischemic cardiomyopathy that occurs in an estimated 1% to 2% of patients who present with suspected ST-segment-elevation acute myocardial infarction (MI).²⁻⁸ It is characterized by symptoms that mimic an acute MI except for the minimal release of cardiac enzymes and the absence of obstructive epicardial coronary artery disease in the vessels leading to the involved territory.^{9,10} The onset of symptoms is typically preceded by a stressful event.^{4,11-15} We report the case of a 22-year-old woman with single-ventricle anatomy (after childhood Fontan palliation) who developed TC.

Case Report

A 22-year-old woman born with double-inlet left ventricle and L-transposition of the great arteries had undergone pulmonary artery banding shortly after birth, and this had been followed, when she was 4 years of age, by lateral-tunnel Fontan palliation. The patient had done well thereafter and had led an active life, working full-time in retail sales and exercising regularly without difficulty.

The patient presented at our clinic for an urgent examination after a 2-day history of chest pain that had begun upon the death of her dog. She at first had experienced hyperventilation and a sharp pain over her left breast that had radiated to her left shoulder; this she rated as “6” on a scale of 1–10. She initially took 2 aspirin tablets, with no relief. The next morning, the pain had abated slightly when she awoke, but with activity it grew so strong that she took 3 tablets of ibuprofen and 1 tablet of clonazepam, again with no relief.

Given her persistent chest pain, she presented at our clinic with an 8/10 pain level and was admitted to the hospital. Deep breathing, coughing, sneezing, and lying supine while drawing her knees to her chest exacerbated the pain. She reported no palpitations, nausea, dizziness, or edema. Her blood pressure was 90/60 mmHg; her heart rate, 78 beats/min; her respiration (regular and shallow), 20 to 28 breaths/min; and her oxygen saturation, 95% on room air. Her physical examination revealed nothing unusual, other than the expected single S₂ consistent with the absence of

Fig. 1 **A)** Patient's electrocardiogram 2 months before takotsubo cardiomyopathy diagnosis shows sinus rhythm with rightward axis and right ventricular hypertrophy. **B)** Patient's electrocardiogram upon presentation with takotsubo symptoms shows sinus rhythm with new T-wave inversions in leads V_2 through V_6 .

Fig. 2 Patient's echocardiograms (apical 4-chamber views) show **A)** normal single-ventricle baseline function one year before takotsubo cardiomyopathy diagnosis and **B)** the typical ballooning in the apex of the heart during her presentation with takotsubo cardiomyopathy.

a functional pulmonary valve. An electrocardiogram (ECG) revealed sinus rhythm at 95 beats/min with right bundle branch block, QTc prolongation, and deep T-wave inversions in leads V_2 through V_6 , II, and aVL (Fig. 1). This ECG was markedly different from a previous outpatient ECG of hers, which had not shown the deep anterolateral T-wave inversions. One sublingual tablet of nitroglycerin produced no change in ECG re-

Fig. 3 Echocardiograms (apical 4-chamber views) show apical hypokinesis during **A)** diastole and **B)** systole. Note ballooning of the apex during systole and normal contractility in the remainder of the myocardium.

Supplemental motion images are available for [Figures 3A](#) and [3B](#).

sults or relief in symptoms. The patient's troponin I and creatine kinase-MB isoenzyme levels were 0.07 ng/mL and 0.5 ng/mL, respectively; and her brain natriuretic peptide level was 188 pg/mL.

Echocardiography with contrast medium revealed akinesis and ballooning of the cardiac apex, with normal contractility in the remainder of the myocardium (Figs. 2 and 3). The estimated left ventricular ejection fraction (LVEF) was 0.35 to 0.40; that figure had previously been 0.55. We chose ECG-gated coronary computed tomographic angiography (CTA) over cardiac catheterization, given the low pre-test likelihood

of obstructive coronary artery disease and the family's preference. On the basis of the CTA, the left anterior descending coronary artery appeared to supply the apical portion of the ventricle, and there was no evidence of obstructive coronary artery disease in this study (Fig. 4). The patient, after treatment with metoprolol, aspirin, and a benzodiazepine, experienced gradual relief of chest pain and was discharged from the hospital. Two days later, she returned for a repeat echocardiogram, which indicated improved wall motion (only mild hypokinesis of the left ventricular apex) and an LVEF of 0.50 to 0.55. Repeat cardiac enzyme assays were negative. Two weeks later, a repeat echocardiogram revealed normal wall motion, complete resolution of apical hy-

Fig. 4 Computed tomographic angiograms with electrocardiographic gating show the **A**) right and **B**) left coronary arteries after the diagnosis of takotsubo cardiomyopathy. Note that the left anterior descending coronary artery appears to supply the apical portion of the ventricle.

pokinesis, and an LVEF of 0.50 to 0.55; moreover, her ECG studies had normalized (Fig. 5).

Discussion

To our knowledge, TC has not previously been described in a patient with single-ventricle anatomy or, more generally, in a patient with congenital heart disease. Our patient manifested typical signs and symptoms of TC, including T-wave changes, ST-segment elevation or depression, trivial elevations of cardiac enzymes, and apical ballooning on echocardiographic examination.^{1,4,10,11,14-21} It should be noted that the prognosis of patients with TC is good: most such patients experience complete resolution of symptoms and of echocardiographic and ECG changes.^{15-18,21} Our patient was successfully treated with conservative measures: rather than undergo invasive evaluation, she underwent ECG-gated coronary CTA to rule out obstructive coronary disease. It has been suggested that the apical and mid-ventricular forms of TC have strong associations with transient endothelial dysfunction, a condition that can be tested by study of coronary response to acetylcholine testing.²² Experienced cardiovascular centers are moving toward elective predischarge catheterization and acetylcholine testing; however, in this case our adjunctive use of CTA enabled us to avoid cardiac catheterization and

Fig. 5 Echocardiograms from the **A**) apical 4-chamber view and **B**) parasternal long-axis view show the resolution of takotsubo cardiomyopathy.

Supplemental motion images are available for [Figures 5A and 5B](#).

acetylcholine testing: the likelihood (and usefulness) of an interpretable study in the presence of a single ventricle is probably low.

We should bear in mind that echocardiography performed with contrast medium can provide good views of the apical aspect of the heart when cardiac catheterization is not an option. A physician who suspects TC in a patient should look for new-onset chest pain and dyspnea coupled with these features: immediate onset of segmental akinesia in the midventricular or apical aspects of the heart, elevation of brain natriuretic peptide level 12 to 24 hours after onset, elevation of troponin level 24 to 48 hours after onset, and disappearance of the segmental akinesia a few days after onset.

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 [in Japanese]. *J Cardiol* 1991;21(2):203-14.
2. Eshtehardi P, Koestner SC, Adorjan P, Windecker S, Meier B, Hess OM, et al. Transient apical ballooning syndrome--clinical characteristics, ballooning pattern, and long-term follow-up in a Swiss population. *Int J Cardiol* 2009;135(3):370-5.
3. Pilgrim TM, Wyss TR. Takotsubo cardiomyopathy or transient left ventricular apical ballooning syndrome: a systematic review. *Int J Cardiol* 2008;124(3):283-92.
4. Bybee KA, Prasad A, Barsness GW, Lerman A, Jaffe AS, Murphy JG, et al. Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning syndrome. *Am J Cardiol* 2004;94(3):343-6.
5. Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Musha H, Sasaka K. 123I-MIBG myocardial scintigraphy in patients with "takotsubo" cardiomyopathy. *J Nucl Med* 2004;45(7):1121-7.
6. Matsuoka K, Okubo S, Fujii E, Uchida F, Kasai A, Aoki T, et al. Evaluation of the arrhythmogenicity of stress-induced "takotsubo cardiomyopathy" from the time course of the 12-lead surface electrocardiogram. *Am J Cardiol* 2003;92(2):230-3.
7. Ito K, Sugihara H, Katoh S, Azuma A, Nakagawa M. Assessment of takotsubo (apical) cardiomyopathy using 99mTc-tetrofosmin myocardial SPECT--comparison with acute coronary syndrome. *Ann Nucl Med* 2003;17(2):115-22.
8. Kawai S, Suzuki H, Yamaguchi H, Tanaka K, Sawada H, Aizawa T, et al. Apical cardiomyopathy ('takotsubo' [sic] cardiomyopathy)--reversible left ventricular dysfunction: with ST segment elevation. *Jpn Circ J* 2000;64(2):156-9.
9. Pernicova I, Garg S, Bourantas CV, Alamgir F, Hoye A. Takotsubo cardiomyopathy: a review of the literature. *Angiology* 2010;61(2):166-73.
10. Abe Y, Kondo M, Matsuoka R, Araki M, Dohyama K, Tanio H. Assessment of clinical features in transient left ventricular apical ballooning. *J Am Coll Cardiol* 2003;41(5):737-42.
11. 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(13):1523-9.
12. Prasad A. Apical ballooning syndrome: an important differential diagnosis of acute myocardial infarction. *Circulation* 2007;115(5):e56-9.
13. Buchholz S, Rudan G. Tako-tsubo syndrome on the rise: a review of the current literature. *Postgrad Med J* 2007;83(978):261-4.
14. Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Sasaka K. Reversible left ventricular dysfunction "takotsubo" cardiomyopathy related to catecholamine cardiotoxicity. *J Electrocardiol* 2002;35(4):351-6.
15. Tsuchihashi K, Ueshima K, Uchida T, Oh-mura N, Kimura K, Owa M, et al. 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* 2001;38(1):11-8.
16. Bybee KA, Kara T, Prasad A, Lerman A, Barsness GW, Wright RS, Rihal CS. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Ann Intern Med* 2004;141(11):858-65.
17. Seth PS, Aurigemma GP, Krasnow JM, Tighe DA, Untereker WJ, Meyer TE. A syndrome of transient left ventricular apical wall motion abnormality in the absence of coronary disease: a perspective from the United States. *Cardiology* 2003;100(2):61-6.
18. Kurisu S, Sato H, Kawagoe T, Ishihara M, Shimatani Y, Nishioka K, et al. Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: a novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J* 2002;143(3):448-55.
19. Shimizu M, Takahashi H, Fukatsu Y, Tatsumi K, Shima T, Miwa Y, et al. Reversible left ventricular dysfunction manifesting as hyperkinesis of the basal and the apical areas with akinesis of the mid portion: a case report [in Japanese]. *J Cardiol* 2003;41(6):285-90.
20. Iga K, Hori K, Kitaguchi K, Matsumura T, Gen H, Tomonaga G, Tamamura T. Transient segmental asynergy of the left ventricle of patients with various clinical manifestations possibly unrelated to the coronary artery disease. *Jpn Circ J* 1991;55(11):1061-7.
21. Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Koike H, Sasaka K. The clinical features of takotsubo cardiomyopathy. *QJM* 2003;96(8):563-73.
22. Angelini P. Takotsubo cardiomyopathy: what is behind the octopus trap? *Tex Heart Inst J* 2010;37(1):85-7.