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CASE REPORT

Takotsubo cardiomyopathy in a young adult with transplanted heart: what happened to denervation?

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Abstract

This manuscript describes the first report of takotsubo cardiomyopathy in a young heart transplant recipient following angry debate. Our patient is a 21-year-old woman with cardiac transplant performed owing to right ventricular failure in congenital heart disease. Positive echocardiography with typical asymmetry of regional function, positive enzymes, and negative biopsy and angiography met the criteria for the diagnosis of takotsubo cardiomyopathy. Patient was discharged after 1 week in good clinical conditions and fully recovered cardiac function. The development of takotsubo cardiomyopathy in transplanted heart suggests that re-innervation occurs, thus representing a target for catecholamine-induced cardiac dysfunction.

Keywords Stress-induced cardiomyopathy; Echocardiography; Coronary angiography; Transient dysfunction

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Introduction

Takotsubo syndrome (TS) is a transient reversible stress-induced heart failure syndrome secondary to increased sympathetic activity caused by excessive release of catecholamines.[1] Diagnostic criteria for TS were recently updated by the European Society of Cardiology and include[2] the following: (i) transient wall motion abnormalities, often preceded by emotional stress, (ii) wall motion abnormalities extended beyond a single coronary artery distribution, (iii) absence of culprit coronary artery disease, (iv) acute and reversible electrocardiographic changes, (v) elevated BNP, (6) mild troponin elevation, and (7) recovery of systolic function during follow-up.

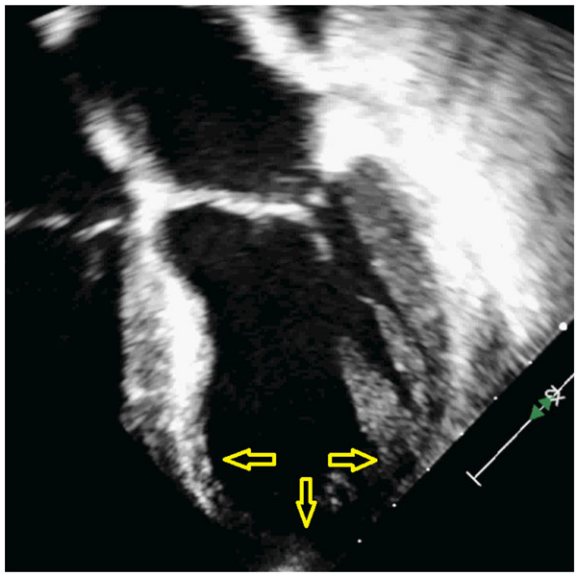
Case Report

We report the case of a 21-year-old woman with cardiac transplant performed in 2007 owing to progressive right ventricular failure following Mustard surgery for transposition of the great arteries. Reviewing the patient's chart, we found no evidence of acute episodes of heart failure associated with regional wall motion abnormalities, suggesting no previous episodes of TS. The patient developed progressive severe systemic right ventricular failure, a known complication after the Mustard palliation surgery. After successful cardiac transplant, the patient was followed up regularly by clinical evaluation, laboratory testing, and echocardiography every 3 months, while coronary angiography and intravascular ultrasound was performed every 12–18 months, according to current guidelines, in order to establish progression of coronary disease (i.e. Stanford score). During follow-up, one hospitalization was reported in 2014 for bacterial pneumonia, while no acute heart failure events and/or cardiac rejection occurred. The last follow-up visit before the reported event was performed in November 2016. Clinical and echocardiographic examination showed optimal clinical conditions, New York Heart Association class I, normal biventricular function with absence of wall motion abnormalities, and no pericardial effusion. Angiography demonstrated mild-to-moderate coronary artery disease (Stanford II) with absence of significant coronary artery stenosis.

In mid-January 2017, the patient was admitted to the hospital owing to acute worsening of her clinical conditions

characterized by reduced tolerance to activity and fatigue. The day before the onset of symptoms, she reported having an angry debate. Physical examination evidenced fair general clinical conditions, borderline tachycardia with a heart rate of 100 b.p.m., an oxygen saturation of 98%, and a cuff blood pressure of 130/87 mmHg. The electrocardiogram showed right bundle branch block (already present in her previous tracings) with new evidence of negative T waves in all precordial leads (*Figure 1*). Echocardiography revealed a dilated left ventricle with severely depressed ejection fraction (34%); there was evident asymmetry of regional function with typical akinetic mid-to-apical segments and normally contracting basal segments (*Figure 2*; *Video S1*), resembling the traditional Japanese octopus trap (i.e. 'takotsubo'). Right ventricular function was low to normal (fractional area change of 34%) with no pericardial effusion. Troponin was still normal at admission but turned moderately positive within the following hours, reaching 108 pg/mL (normal range 0–17 pg/mL), with markedly elevated BNP (1780 pg/mL). With the aim of ruling out ischaemic cardiomyopathy and/or acute rejection, epicardial vessels coronary angiography and myocardial biopsy were performed. No evidence of coronary obstruction was found (*Figure 3*); thus, with acute graft rejection being suspected, patient was started on i.v. milrinone and diuretics, to sustain circulation and prevent the expected development of right ventricular dysfunction, as previously described in acute cardiac rejection patients.[3] After 2 days, cardiac histological examination was available showing no signs of acute rejection. Accordingly, diagnosis of TS cardiomyopathy was made, and the patient was switched to oral therapy with enalapril and furosemide. As expected, within 7 days, heart rate decreased to 80 b.p.m., and echocardiography showed normal left ventricular volume and improved systolic function with 55% ejection fraction, with a significant reduction in apical hypokinesia. After 20 days, follow-up evaluation showed fully recovered systolic function with a 65% ejection fraction and no more apical dysfunction (*Figure 4*; *Video S2*); thus, preventive treatment with carvedilol and enalapril was undertaken. At present, patient undergoes regular follow-up visits. No additional acute events have been reported, and she is currently asymptomatic and in good general clinical conditions.

Figure 2 Acute apical dysfunction on admission echocardiography (end-systole).



Discussion

Sympathetic activation and catecholamines have a central role in the pathophysiology of TS, producing a complex

Figure 1 Electrocardiogram tracing at the time of admission.

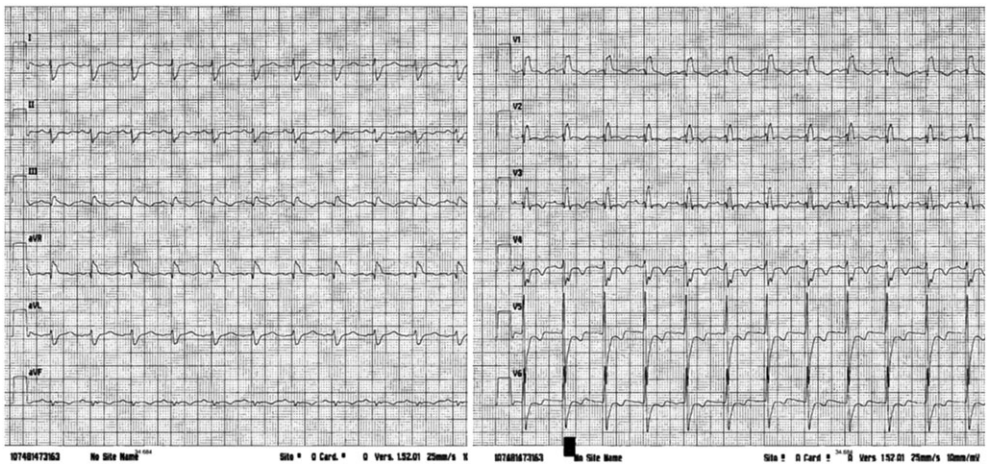


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Figure 3 Negative angiography.

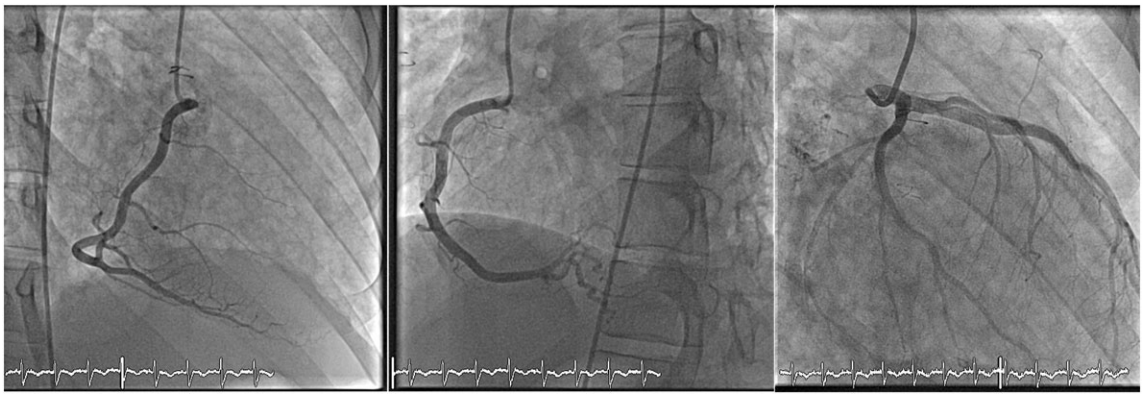
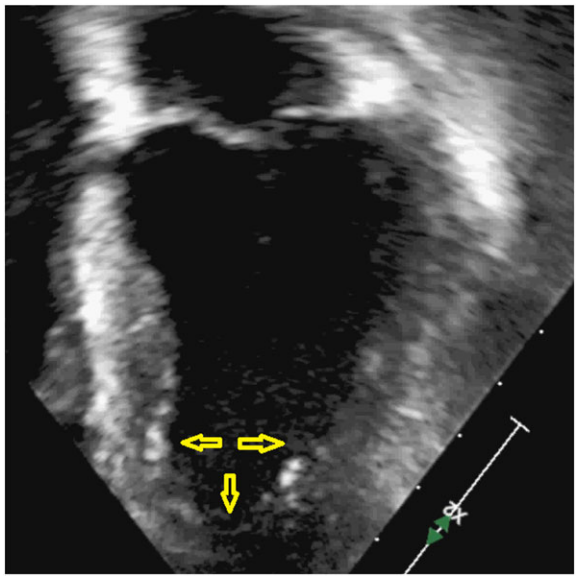


Figure 4 Cardiac function improvement at follow-up echocardiography (end-systole).



interaction with cardiovascular system. Thus, the evidence of TS cardiomyopathy in transplanted patients is somewhat surprising given the complete denervation occurring during transplantation. However, it should be underlined that an elegant study by Buendia-Fuentes[4] demonstrated that sympathetic re-innervation occurs in nearly 40% of transplant recipients within 1 year from transplant. Of note, our patient did not report chest pain, as usually reported in TS, but just symptoms related to heart failure (fatigue and reduced exercise tolerance). It is possible thus to speculate that in our patient, sympathetic re-innervation had already occurred, while the nociceptive sensory afferences had not. This is the first report of TS cardiomyopathy in a young heart transplant recipient following angry debate, as only one previous case has been reported in literature on a 64-year-old man following iatrogenic physical stress determined by transcatheter intervention.[5] In addition, our patient developed TS in pre-menopausal age, which is quite unusual since post-menopausal women are more likely to be prone to TS.

Conflict of interest

None declared.

Supporting information

Additional Supporting Information may be found online in the supporting information tab for this article.

Video S1. Acute apical dysfunction on admission echocardiography.
Video S2. Cardiac function improvement at follow-up echocardiography.

References

1. Chen W, Dilsizian V. Exploring the pathophysiology of takotsubo cardiomyopathy. *Curr Cardiol Rep* 2017; **19**: 53.
2. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GM, Ruilope LM, Ruschitzka F, Rutten

FH, van der Meer P. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2016; **37**: 2129–2200.
3. Stobierska-Dzierzek B, Awad H, Michler RE. The evolving management of acute right-sided heart failure in cardiac transplant recipients. *J Am Coll Cardiol* 2001; **38**: 923–931.
4. Buendia-Fuentes F, Almenar L, Ruiz C, Vercher JL, Sánchez-Lázaro I, Martínez-Dolz L, Navarro J, Bello P, Salvador A. Sympathetic reinnervation 1 year after heart transplantation, assessed using iodine-123 metaiodobenzylguanidine imaging. *Transplant Proc* 2011; **43**: 2247–2248.
5. Behnes M, Baumann S, Borggrefe M, Haghi D. Biventricular takotsubo cardiomyopathy in a heart transplant recipient. *Circulation* 2013; **128**: e62–e63.