


Takotsubo syndrome in the same heart before and after heart transplantation

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Abstract

Heart transplantation is an effective therapy for patients with end-stage heart failure. In some cases, Takotsubo syndrome (TTS) was seen in the donor heart. We report a case of TTS in a 40-year-old woman with a history of epileptic seizures who underwent heart transplantation from a donor with TTS. The donor was brain-dead due to severe hypoxic encephalopathy during cardiac arrest with TTS. Fifteen months after heart transplantation, she was readmitted for epileptic seizures. Electrocardiogram showed T-wave inversion, and transthoracic echocardiography showed apical ballooning. Coronary angiography was normal, and endomyocardial biopsy was negative for rejection. Iodine-123 metaiodobenzylguanidine imaging demonstrated a low heart-to-mediastinum ratio and high washout rate. Eighteen days after admission, recovery of left ventricular dysfunction was confirmed, and she was diagnosed with TTS triggered by epileptic seizures. It is important to recognize the risk of recurrent TTS in heart transplantation patients from a donor with TTS.

Keywords Heart transplantation; Takotsubo syndrome; Recurrence

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Introduction

Takotsubo syndrome (TTS) is an acute transient heart failure syndrome with left ventricular (LV) dysfunction and serious complications. Several pathophysiologic mechanisms have been proposed, such as the contributions of the autonomic sympathetic nervous system, circulating catecholamine, or endothelial dysfunction; however, the exact pathophysiology remains unknown. Here, we report a rare case of TTS after heart transplantation from a donor who suffered brain death with TTS. This is the first report of recurrent TTS beyond heart transplantation, which may lead to the elucidation of the mechanistic insight of TTS.

Case report

A 40-year-old woman with end-stage hypertrophic cardiomyopathy underwent heart transplantation following LV assist

device support. She also had several events of epileptic seizures due to a previous cerebrovascular disease.

The donor, who was in her sixties, was brain-dead due to severe hypoxic encephalopathy during cardiac arrest. After resuscitation, electrocardiogram (ECG) revealed ST-segment elevation in leads II, III, and aVF (Figure 1A). Cardiac catheterization showed hyperkinesis of the LV base and akinesia of the apex without coronary artery stenosis (Figure 2A–D). Transthoracic echocardiography (TTE) demonstrated apical ballooning on the initial assessment, which improved during donor management with intra-aortic balloon pumping support. Intra-aortic balloon pumping was successfully weaned 2 days before procurement. Before the procurement (7 days after cardiac arrest), LV dysfunction normalized, leading to the diagnosis of TTS. Cardiac arrest was considered to be due to TTS, and the haemodynamic derangement was considered to be temporary, which suggested the validity of the donor candidate for heart transplantation.

Figure 1 Electrocardiogram of the donor after resuscitation in the first takotsubo syndrome (TTS) event (A). Electrocardiogram of the recipient on the day of admission (B), at 4 AM on the next day of admission (C), and at 6 PM on the next day of admission (D) in the second TTS event.

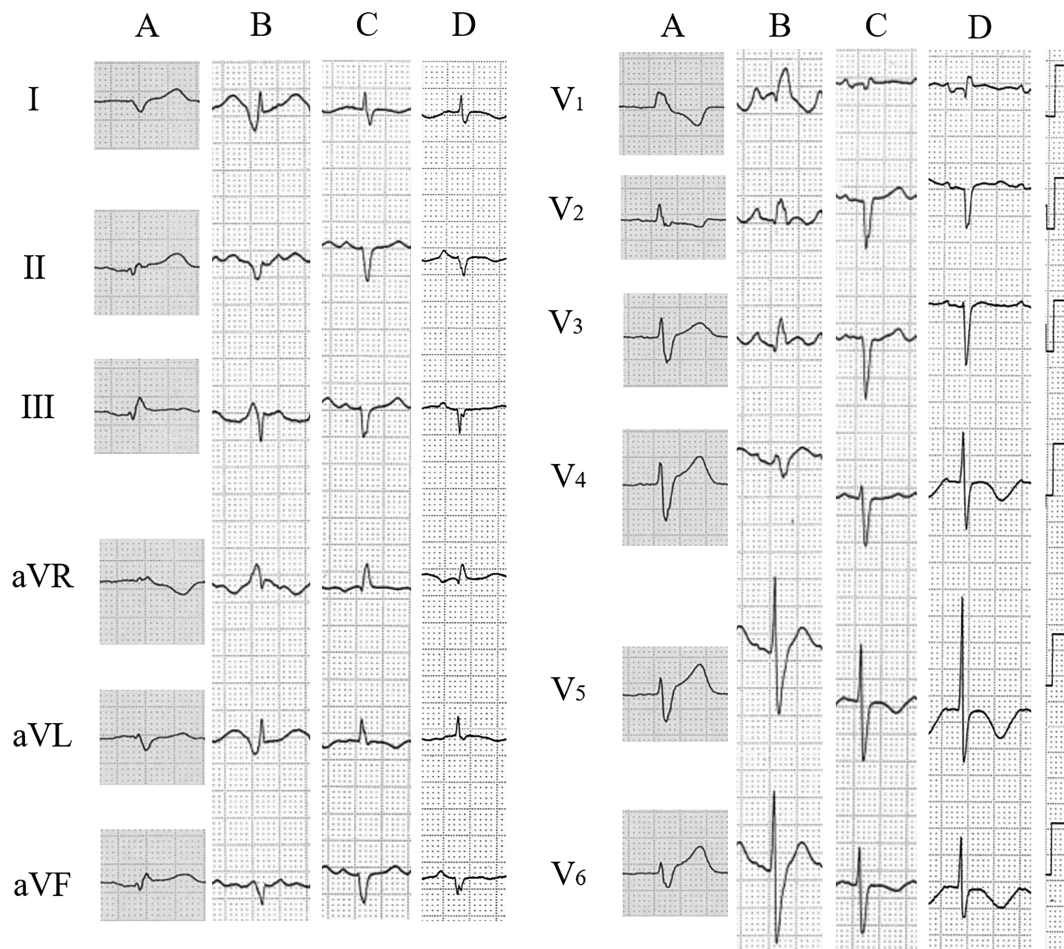
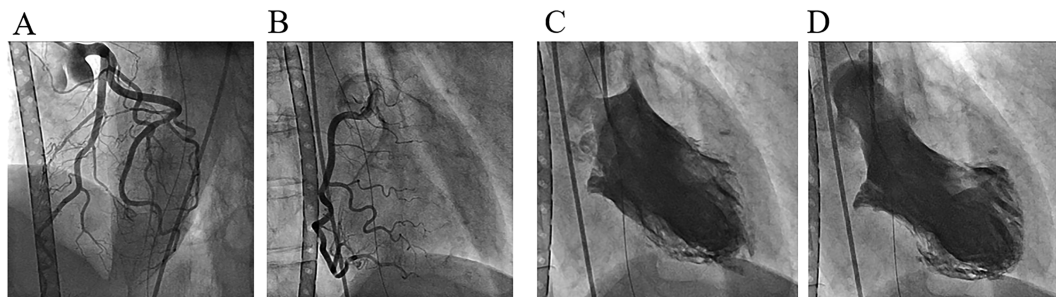


Figure 2 Coronary angiography of the donor after resuscitation showed no significant stenosis in the left coronary artery (A) or right coronary artery (B) in the first takotsubo syndrome (TTS) event. Left ventriculography in the first TTS event showed hyperkinesis of the left ventricular base and akinesia of the apex: at end-diastole (C) and end-systole (D).



The recipient received the marginal donor heart because of haemodynamic instability due to aortic insufficiency under LV assist device support and underwent orthotopic heart

transplantation using the modified bicaval technique. Within 6 months after heart transplantation, there was no overt problem in the transplanted heart. However, she was

admitted three times for epileptic seizures, and her epilepsy was controlled with antiepileptic drugs (i.e. levetiracetam and zonisamide).

Nine months after the last episode of epileptic seizure, she was readmitted for epileptic seizure recurrence. On admission, her heart rate was 135 beats/min, and her blood pressure was 140/100 mmHg. Endotracheal intubation was performed to maintain the airway. ECG revealed sinus tachycardia with right bundle branch block (Figure 1B).

On the next day, ECG revealed T-wave inversion in leads I, aVL, V5, and V6 (Figure 1C,D). High-sensitivity troponin I was 1872.1 pg/mL (normal, <26.2 pg/mL), and brain natriuretic peptide was 1005.7 pg/mL (normal, <18.4 pg/mL). TTE demonstrated apical ballooning (Figure 3A,B). We calculated the InterTAK diagnostic score value of 59 points and suspected TTS rather than acute coronary syndrome.¹

Dobutamine was administered at a rate of 2.8 µg/kg/min, and intravenous furosemide was used for heart failure treatment. Successful extubation was achieved on Day 2. Repeated TTE showed a gradual improvement in LV contraction, and dobutamine administration was discontinued on Day 4.

Coronary angiography showed no significant stenosis (Figure 3C,D). Right ventricular endomyocardial biopsy showed partial fibrosis, sparse lymphocyte infiltration, and hemosiderin deposition, which were considered as artefacts due to injury evoked by previous biopsies. There were no findings suggesting acute cellular or antibody-mediated rejection. On Day 18, TTE revealed recovery of LV dysfunction (Figure 3E,F), confirming the diagnosis of TTS triggered by epileptic seizures. On Day 49, iodine-123 metaiodobenzylguanidine (MIBG) imaging demonstrated

uptake reduction in the inferior–posterior, lateral, and apex regions (Figure 3G,H). The heart-to-mediastinum ratios in the early and delayed phases were 1.55 and 1.25, respectively. The total washout rate was 39.0%, and in the apical region, it was >40%. The patient was discharged on Day 63 with stable condition.

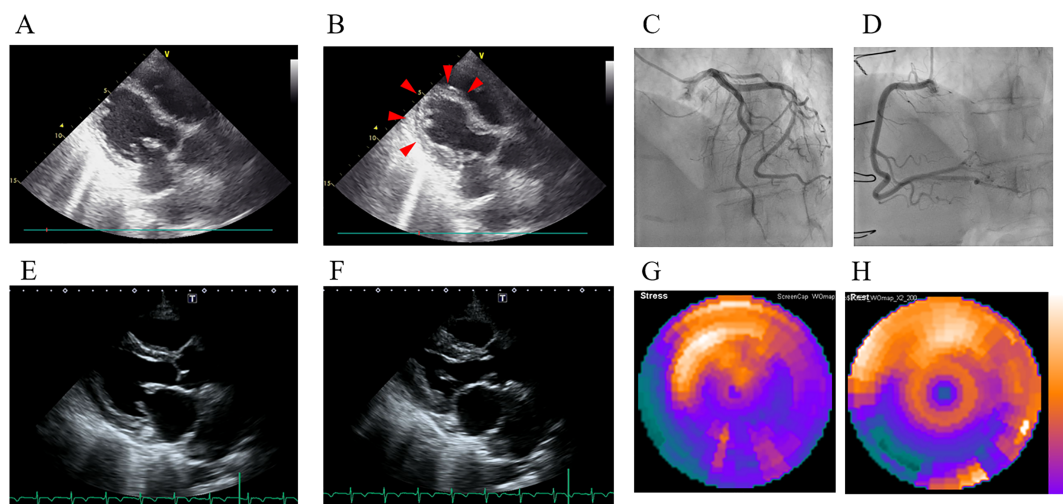
Discussion

Takotsubo syndrome is an acute cardiac condition triggered by emotional and physical stress characterized by reversible LV dysfunction.^{2,3} International diagnostic criteria help to improve the identification and stratification of TTS.⁴ Cerebrovascular disease and epilepsy are the most frequent central nervous system diseases triggering TTS.⁵

This case had two novel points: first, TTS developed in a transplanted heart, and second, TTS recurred after heart transplantation.

A transplanted heart is completely denervated at the time of the transplant operation. Transplanted heart, not all the heart, gradually reinnervated. Sympathetic reinnervation extends from the base to the apex of the anterior and septal walls.⁶ The lateral and inferior walls appear to be involved later.⁶ MIBG findings in this case revealed partial reinnervation of the sympathetic nerve, which corresponded to previous reports.⁷ According to the impact on the development of TTS, the reinnervation of the sympathetic nerve may be necessary in developing TTS⁸ and could possibly explain the rationale for the absence of TTS events in previous epileptic

Figure 3 Two-dimensional transthoracic echocardiography in the second takotsubo syndrome (TTS) event at admission demonstrated apical ballooning (red arrowheads) at end-diastole (A) and end-systole (B). Coronary angiography showed no significant stenosis in the left (C) and right (D) coronary arteries in the second TTS event. Two-dimensional transthoracic echocardiography in the second TTS event on Day 18 demonstrated recovery of left ventricular dysfunction at end-diastole (E) and end-systole (F). A bull's-eye map of iodine-123 metaiodobenzylguanidine imaging after the second TTS event demonstrated uptake reduction in the inferior–posterior, lateral, and apex regions in the early (G) and delayed (H) phases.



seizures after heart transplantation. In the case of TTS, neuronally transmitted norepinephrine was a prerequisite, along with an increased concentration of circulating catecholamine. The reduced MIBG uptake in the inferior–posterior and lateral regions may be due to incomplete sympathetic reinnervation, and the susceptibility to TTS after heart transplantation may be significantly affected by the pattern of sympathetic reinnervation, which may change over time after heart transplantation. However, the absence of MIBG uptake was also affected by myocardial injury from the TTS event.

The TTS recurrence rate is reported to be 1.8% per patient year.³ Neurologic and psychiatric disorders were independent predictors of recurrence, and triggering factors and ballooning patterns could change during recurrence.⁹ Indeed, the first TTS event in this case seemed to be the primary one, whereas the second event was secondary to epileptic seizures. ECG abnormalities also differed between the first and second TTS events: ST-segment elevation in the first and right bundle branch block with T-wave inversion in the second. Although ECG was modified after heart transplantation, it

was not clear why the ECG abnormalities were different despite similar wall motion abnormalities of ballooning.

Notably, the trait of TTS susceptibility was unexpectedly inherited from the donor by the recipient through the transplanted myocardium. The contributing factors for the occurrence of TTS in this case were considered: the donor's myocardium, recipient's sympathetic nervous system, and recipient-derived trigger.

To the best of our knowledge, this is the first report on recurrent TTS after heart transplantation from a donor with TTS. It is important to recognize that epileptic seizures are a predisposing factor for recurrent TTS and should be controlled well.

Conflict of interest

None declared.

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