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REVIEW ARTICLE

Biventricular takotsubo cardiomyopathy with asymmetrical wall motion abnormality between left and right ventricle: a report of new case and literature review

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Abstract
Takotsubo cardiomyopathy (TC) is characterized by transient wall motion abnormalities most commonly involving the left ventricle (LV). Although biventricular TC had been considered uncommon condition, recently biventricular TC has been reported as a new variant observed in 19–42% of all TC presentations. Since biventricular TC has a poor prognosis as compared with isolated TC, it is important to distinguish between isolated LV TC and biventricular TC. We present a case of 70-year-old female with dyspnea persisting for 2 days. Electrocardiogram showed symmetrical T-wave inversion in leads V2–V4. Transthoracic echocardiography (TTE) revealed diffuse hypo-kinesis except for the apical inferior LV and LV ejection fraction of 32%. Hyper-kinesis of the right ventricular (RV) basal segment and dys-kinesis of the RV apical segment. 2 weeks after admission, coronary angiography showed no evidence of significant stenosis. LV ejection fraction improved to 51% and wall motion abnormalities of the RV basal and apical segments were ameliorated to normo-kinesis. Electrocardiogram revealed symmetrical and deepened T-wave inversion in leads V2–V3. The presence of a transient abnormality in biventricular wall motion beyond a single coronary artery perfusion territory with new electrocardiographic change met the diagnostic criteria of definite TC defined by Mayo Clinic criteria. 4 weeks after admission, no recurrence of wall motion abnormalities in both ventricles were found and T-wave inversion ameliorated. To our knowledge, this is the first report of biventricular TC with asymmetrical abnormities of wall motion between LV and RV.

Keywords Stress cardiomyopathy · Apical ballooning cardiomyopathy · Ampulla cardiomyopathy · Takotsubo cardiomyopathy · Broken heart syndrome

Introduction

Takotsubo cardiomyopathy (TC) is characterized by transient wall motion abnormalities of left ventricular (LV) apical ballooning without significant coronary artery stenosis. Although biventricular TC has been considered uncommon condition, recent studies suggest that biventricular TC has been reported as a new variant observed in 19–42% of all TC presentations [1–4]. Furthermore, the rates of in-hospital mortality and long-term clinical adverse events were significantly higher in biventricular TC than isolated LV TC [1, 2, 4, 5]. In this context, it is important to distinguish between isolated LV TC and biventricular TC. In previous reports, wall motion abnormalities of LV and RV were symmetric in biventricular TC. Here we present a case of biventricular TC with asymmetrical wall motion between LV and RV.

Case report

A 70-year-old female was admitted to our hospital because of dyspnea persisting for 2 days. She was afebrile, denied any cold symptom, and not aware of chest discomfort such

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as chest pain. The patient had no history of cardiac disease and had taken no medication. She attended her general practitioner, who pointed out cardiomegaly (cardiothoracic ratio 71%) and pulmonary congestion in her chest X-ray. She was referred to our hospital for further evaluation. She had not been aware of the preceding physical and emotional stress. On physical examination, her pulse was irregular at 166 beats/min, blood pressure was 119/95 mmHg, and oxygen saturation was 89% on room air. Distended jugular veins and edema in both lower legs were observed. Laboratory data showed plasma brain natriuretic peptide 452 pg/mL, creatinine kinase 125 IU/L, and negative C-reactive protein. Transthoracic echocardiography (TTE) showed diffuse hypo-kinesis except for the apical inferior left ventricular wall (LV) (Fig. 1a: arrow head). LV ejection fraction was assessed by modified biplane Simpson's method and the value of 32% (Table 1), and no evidence of significant mitral regurgitation. Hyper-kinesis of the right ventricular (RV) free wall basal segment (Fig. 2a: arrow), dys-kinesis of RV mid-portion (Fig. 2a: cross), and akinesis of the RV apical segment (Fig. 2a: arrow head). RV-S′ was as high as 16.5 m/s (Fig. 2a: bottom) possibly due to hyper-kinesis of the RV basal wall motion. Electrocardiogram showed atrial fibrillation with tachycardia (heart rate of approximately 175 beats per minute) and symmetrical and shallow T-wave inversion (Fig. 3a: black arrow) in leads V2–V4 and no significant ST elevation (Fig. 3a). Emergency coronary angiography (CAG) was necessary to exclude ischemic heart disease, but she did not agree to undergo CAG. Furthermore, she refused even minimal invasive examination such as blood examination. She received beta blocker (bisoprolol 2.5 mg) and digoxin 0.125 mg for atrial fibrillation with tachycardia. The following day of administration, heart rate ameliorated to 100 beats per minute. Atrial fibrillation with tachycardia was improved temporarily, it exacerbated and average heart rate was from 120 to 150 beats per minute with ECG monitoring from day 2 of administration. Two weeks after admission, coronary angiography showed no evidence of significant stenosis (Fig. 4). Coronary spasm provocation test was not performed. The wall motion of LV

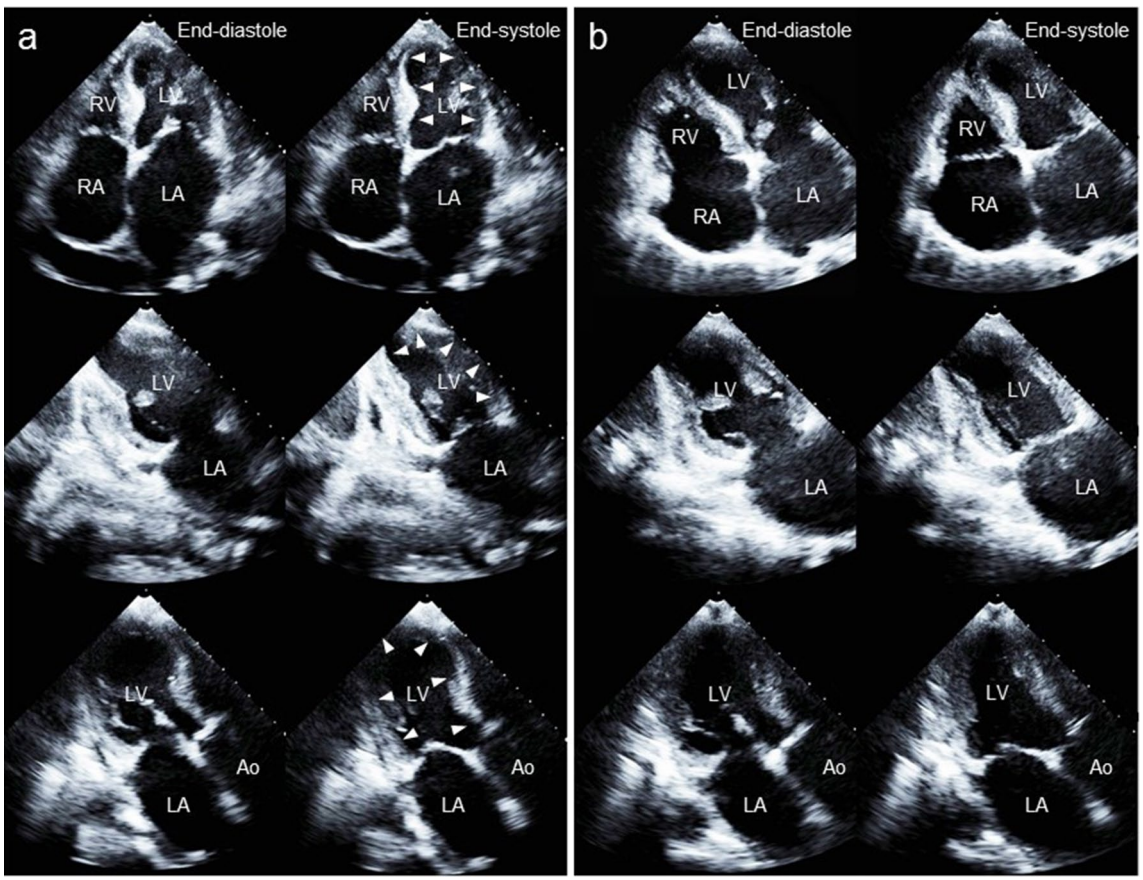

Fig. 1 Echocardiographic change [apical four-chamber view (top), apical two-chamber view (middle), and apical three-chamber view (bottom)] of the presented case **a** on admission and **b** 14 days after admission. **a** Diffuse hypo-kinesis (arrow head) except for the apical inferior LV wall at end-systole. **b** The motion of LV wall segments were ameliorated to normo-kinesis except for LV apical segment (arrow head). *RA* right atrium, *RV* right ventricle, *LA* left atrium, *LV* left ventricle, *Ao* aorta

Table 1 Time course of the laboratory and echocardiographic data of the presented case

	On admission	2 weeks after admission
BNP (pg/mL)	452	96
LVDd (mm)	42	43
LVDs (mm)	32	32
LVEDVi (mL/m^2)	50	34
LVESVi (mL/m^2)	34	16
LVSVi (mL/m^2)	16	17
LVEF (%)	32	51
E (cm/s)	93	106
E′ (cm/s)	8	5
E/*E′* ratio	11	23
TRPG (mmHg)	42	26
RVSP (mmHg)	50	29

BNP brain natriuretic peptide, *LVDd* left ventricular end-diastolic diameter, *LVDs* left ventricular end-systolic diameter, *LVEDVi* left ventricular end-diastolic volume index, *LVESVi* left ventricular end-systolic volume index, *LVSVi* left ventricular stroke volume index, *LVEF* left ventricular ejection fraction, *TRPG* tricuspid regurgitation peak gradient, *RVSP* right ventricular systolic pressure

wall segments was ameliorated to normo-kinesis except for LV apical segment and LVEF improved to 51% (Fig. 1b and Table 1). Wall motion abnormalities of the RV had been already ameliorated to normo-kinesis, and RV-S′ of 11.0 cm/s (Fig. 2b). We could not obtain the same image on admission with satisfactory quality for presentation. Therefore, we referred to subcostal 4-chamber view as an image of close to apical 4-chamber view. Electrocardiogram revealed atrial fibrillation (heart rate of approximately 81 beats per minute) and symmetrical and deepened T-wave inversion (Fig. 3b: black triangle) in leads V2–V3. The presence of a transient abnormality in biventricular wall motion beyond a single epicardial coronary artery perfusion territory with new electrocardiographic change met the diagnostic criteria of definite TC defined by Mayo Clinic criteria [6]. She received diuretics (intravenous administration of furosemide 40 mg) and angiotensin II receptor blocker (telmisartan 20 mg) for heart failure. Since hemodynamics was maintained stable, inotropic agent or support with intra-aortic balloon pump were no longer needed. Heart failure was considered to be improved from the disappearance of pulmonary congestion and reduction of cardiomegaly (cardiothoracic ratio 52%) in her chest X-ray and brain natriuretic peptide of 96 pg/mL. 4 weeks after admission, TTE revealed no recurrence of regional wall motion abnormalities in both ventricles. Atrial fibrillation with tachycardia (heart rate of approximately 121 beats per minute) and T-wave inversion in leads V2–V4 (Fig. 3c: white arrow) were ameliorated. Since normal kinesis in biventricular wall motion was sustained, she was discharged from our hospital 5 weeks after her admission.

Discussion

The pattern of the wall motion abnormality in RV observed in this case was a typical feature of right ventricular TC, but diffuse hypo-kinesis in LV was uncommon as TC. It had been also suspected that LV wall abnormality might be attributed to tachycardia-induced cardiomyopathy (TIC). TIC is defined as the presence of tachycardia (heart rate from 120 to 200 beats per minute), which persists for more than 10–15% of the day [7]. In this case, TIC was not completely excluded because we could not present all of the records of heart rate during entire hospitalization and the rate of tachycardia in a day. But the pattern of biventricular wall motion abnormality would be atypical as TIC and further it was improved despite the continuation of tachycardia. TC is defined by Mayo Clinic criteria as follows: the presence of a transient abnormality in LV wall motion beyond a single epicardial coronary artery perfusion territory with new electrocardiographic abnormalities, modest elevation in cardiac troponin, or absence of obstructive coronary disease [6]. In this context, it is our firm belief that wall motion abnormality in LV was attributed to TC. TC includes various types according to the affected region in LV such as apical ballooning type, mid-ventricular ballooning type, basal ballooning type, apical hyper-contractility type, and multiple segments affected type [8]. Recently, these previous conditions are represented as takotsubo syndrome [9]. Our case is compatible as multiple segments affected type of TC. Wall motion abnormalities typically occur in LV, but it can also affect RV as well and show some variant forms, such as isolated right ventricular type [10, 11] or biventricular type. The biventricular TC was first reported in 2004 [12] and has been recognized as a very rare form, but the number of reports on biventricular TC has been increasing over time possibly because of its increasing recognition. Biventricular TC constitutes approximately 19–42% of all TC presentations [1–4]. Several possible mechanisms of isolated TC have been reported such as coronary artery spasm [13], coronary artery microvascular dysfunction [14] and catecholamine cardiotoxicity [15], but the precise cause remains unclear. The precise mechanism of biventricular TC also remains to be explained. In the case report literature between 2004 (first report) and 2018, 39 cases of biventricular TC have been reported including the present case. Biventricular TC cases consisted of 4 men (10%) [1, 16–18] and 35 women (90%) [1, 12, 19–42], age from 36 to 89 years (median age was 78.0 years), and LVEF of 35.9 ± 10.5% at the first presentation. In all cases except for ours, the wall motion abnormalities of apical ballooning akinesis and basal

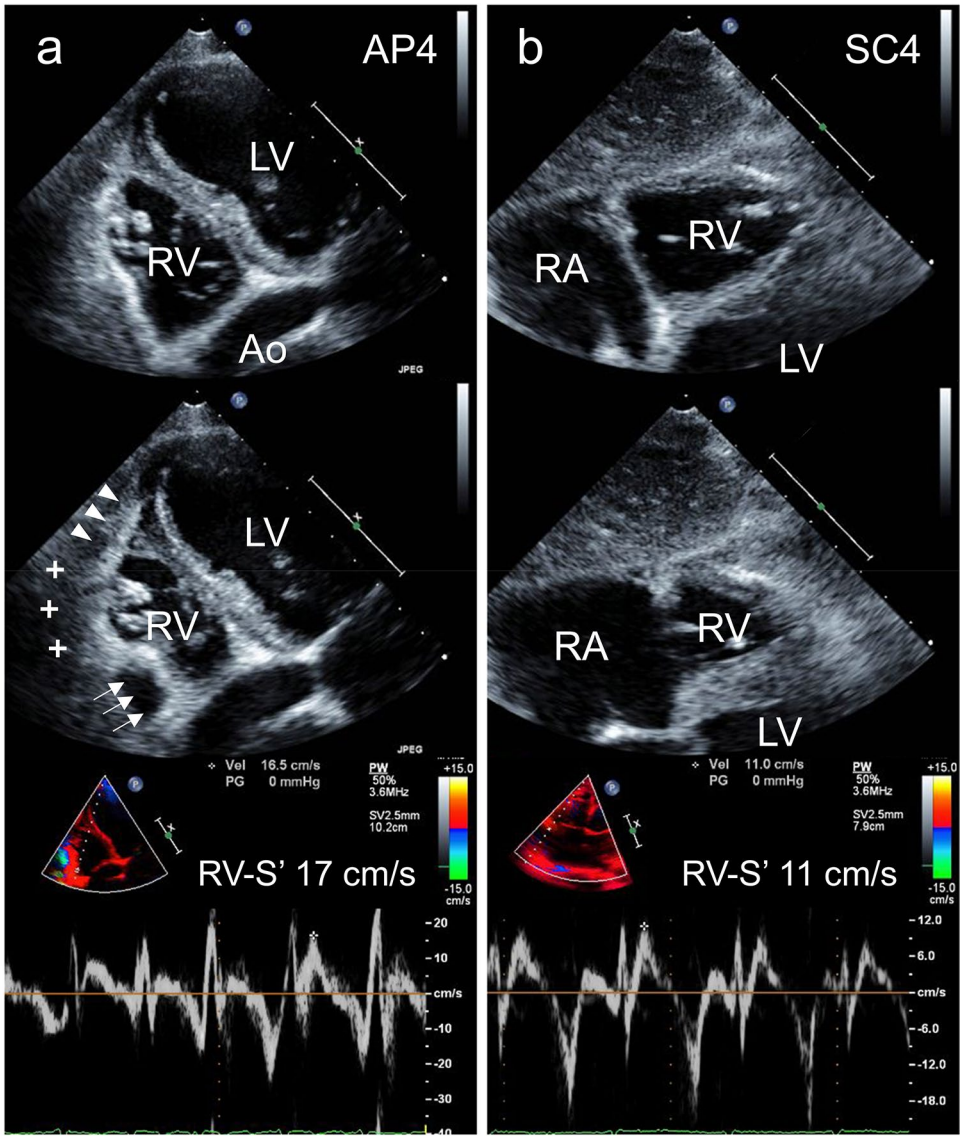

Fig. 2 Echocardiographic change [RV-focused apical four-chamber view at end-diastole (top), RV-focused apical four-chamber at end-systole (middle), and tissue Doppler imaging for measurement of RV-S′ (bottom)] of the presented case **a** on admission and **b** 14 days after admission. **a** Hyper-kinesis of the RV free wall basal segment (arrow), dys-kinesis of RV mid-portion (Fig. 2a: cross), and akinesis of the RV apical segment (arrow head) at end-systole. RV-S′ was 17 cm/s on admission. **b** The motion of RV free wall basal segment was ameliorated to normo-kinesis and RV-S′ of 11.0 cm/s at 14 days after admission. *AP4* apical four-chamber view, *SC4* subcostal four-chamber view, *RA* right atrium, *RV* right ventricle, *LV* left ventricle, *Ao* aorta

hyper-kinesis were symmetrical between LV and RV (only one case [19] was inverted TC, which was also symmetrical wall motion). Biventricular TC has a potential to cause the critical complications, such as cardiac rupture [23, 24] and requirement of hemodynamic support with intra-aortic balloon pump [35]. Some previous data indicate that biventricular TC portends poor prognosis. Biventricular TC was more likely to require inotropic support upon admission [5] and showed higher rate of in-hospital mortality and the long-term clinical adverse events (cardiac death, recurrence of TC, and re-hospitalization due to heart failure) compared to isolated LV TC [4]. Moreover, RV involvement was an independent predictor of the following end point, all-cause death, re-hospitalization due to heart failure and recurrence of TC clinical adverse event in multivariate analysis. [4]. From those findings [1, 2, 4], it is pivotal to distinguish between isolated LV TC and biventricular TC. Until now, all of the reported cases with biventricular TC showed symmetric abnormalities of wall motion between LV and RV. To our knowledge, this is the first case of biventricular TC with diffuse LV hypo-kinesis and asymmetrical wall motion between LV and RV. Encountering patients with TC much attention should be paid to biventricular type as a differential diagnosis. Further investigation is warranted to further address various issues regarding biventricular TC with asymmetrical abnormities of wall motion between LV and RV including its long-term prognosis.

Conclusions

We presented a case of biventricular TC with hypo-kinesis of diffuse LV. To our knowledge, this is the first report of biventricular TC with asymmetrical abnormities of wall

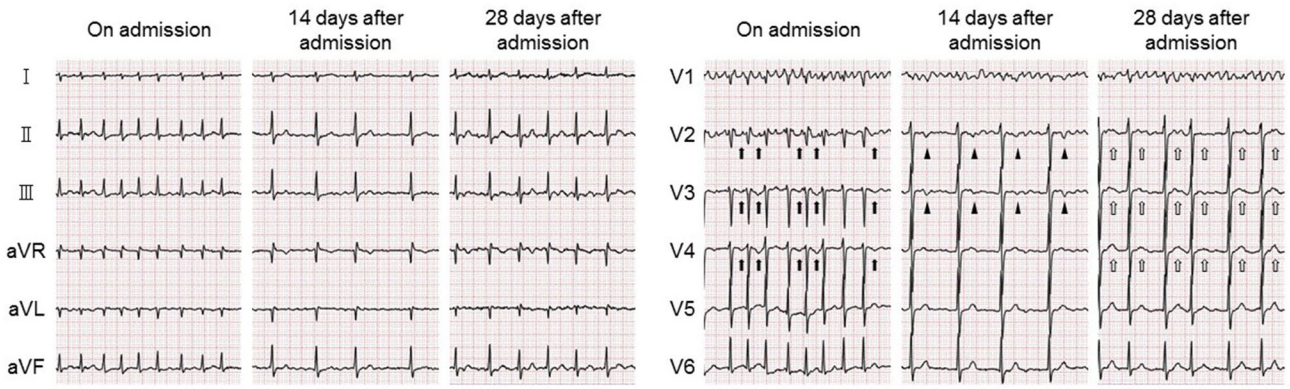

Fig. 3 Electrocardiography of the presented case on admission, 14 days after admission, and 28 days after admission. Atrial fibrillation with tachycardia (heart rate of approximately 175 beats per minute) and symmetrical and shallow T-wave inversion (black arrow) in leads V2–V4 and no significant ST elevation on admission. Atrial fibrillation (heart rate of approximately 81 beats per minute) and symmetrical and deepened T-wave inversion (arrow head) in leads V2–V3 at 14 days after admission. Atrial fibrillation with tachycardia (heart rate of approximately 121 beats per minute) and T-wave inversion ameliorated (white arrow) in leads V2–V4 at 28 days after admission

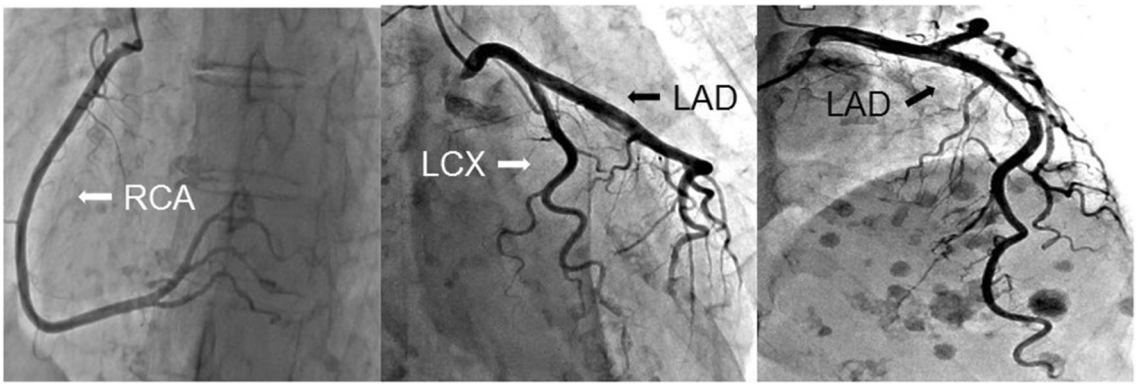

Fig. 4 Coronary angiography of the presented case. It showed no evidence of significant stenosis. *RCA* right coronary artery, *LCX* left circumflex artery, *LAD* left anterior descending artery

motion between LV and RV. Comprehensive assessment of both ventricles is crucial since biventricular TC shows worse prognosis than isolated LV TC.

Compliance with ethical standards

Conflict of interest Toshimitsu Tsugu, Yuji Nagatomo, Yuki Nakajima, Toshimi Kageyama, Jin Endo, Yuji Itabashi, and Takashi Kawakami declare that they have no conflict of interest.

Human rights statement This article does not contain any studies with human or animal subjects performed by any of the authors.

Informed consent Informed consent was obtained from the patient for being included in this report.

References

1. Haghi D, Athanasiadis A, Papavassiliu T, et al. Right ventricular involvement in Takotsubo cardiomyopathy. Eur Heart J. 2006;27:2433–9.
2. Elesber AA, Prasad A, Bybee KA, et al. Transient cardiac apical ballooning syndrome: prevalence and clinical implications of right ventricular involvement. J Am Coll Cardiol. 2006;47:1082–3.
3. Eitel I, von Knobelsdorff-Brenkenhoff F, Bernhardt P, et al. Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy. JAMA. 2011;306:277–86.
4. Kagiyama N, Okura H, Tamada T, et al. Impact of right ventricular involvement on the prognosis of takotsubo cardiomyopathy. Eur Heart J Cardiovasc Imaging. 2016;17:210–6.
5. Becher T, El-Battrawy I, Baumann S, et al. Characteristics and long-term outcome of right ventricular involvement in Takotsubo cardiomyopathy. Int J Cardiol. 2016;220:371–5.

6. Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J. 2008;155:408–17.
7. Fenelon G, Wijns W, Andries E, et al. Tachycardiomyopathy: mechanisms and clinical implications. Pacing Clin Electrophysiol. 1996;19:95–106.
8. Castillo Rivera AM, Ruiz-Bailen M, Rucabado Aguilar L. Takotsubo cardiomyopathy—a clinical review. Med Sci Monit. 2011;17:RA135–47.
9. Lyon AR, Bossone E, Schneider B, et al. Current state of knowledge on takotsubo syndrome: a position statement from the taskforce on Takotsubo syndrome of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2016;18:8–27.
10. Kagiyama N, Okura H, Kume T, et al. Isolated right ventricular takotsubo cardiomyopathy. Eur Heart J Cardiovasc Imaging. 2015;16:285.
11. Sumida H, Morihisa K, Katahira K, et al. Isolated Right ventricular stress (takotsubo) cardiomyopathy. Intern Med. 2017;56:2159–64.
12. Nishikawa S, Ito K, Adachi Y, et al. Ampulla ('takotsubo') cardiomyopathy of both ventricles: evaluation of microcirculation disturbance using 99mTc-tetrofosmin myocardial single photon emission computed tomography and doppler guide wire. Circ J. 2004;68:1076–80.
13. Nojima Y, Kotani J. Global coronary artery spasm caused takotsubo cardiomyopathy. J Am Coll Cardiol. 2010;55:e17.
14. Vitale C, Rosano GM, Kaski JC. Role of coronary microvascular dysfunction in takotsubo cardiomyopathy. Circ J. 2016;80:299–305.
15. Borchert T, Hubscher D, Guessoum CI, et al. Catecholamine-dependent beta-adrenergic signaling in a pluripotent stem cell model of takotsubo cardiomyopathy. J Am Coll Cardiol. 2017;70:975–91.
16. Hwang HJ, Lee HM, Yang IH, et al. Evolutionary change mimicking apical hypertrophic cardiomyopathy in a patient with takotsubo cardiomyopathy. Echocardiography. 2014;31:E293–5.
17. Behnes M, Baumann S, Borggrefe M, et al. Biventricular takotsubo cardiomyopathy in a heart transplant recipient. Circulation. 2013;128:e62–3.
18. Nagao T, Ito K, Tsuboi H, et al. Biventricular takotsubo cardiomyopathy. Intern Med. 2012;51:1435–6.
19. Abroug F, Ouanes I, Maatouk M, et al. Inverted Takotsubo syndrome in *Androctonus australis* scorpion envenomation. Clin Toxicol (Phila). 2018;56:381–3.
20. Tibrewala A, Freed BH, Akhter N. Importance of temporal changes in myocardial strain in Takotsubo cardiomyopathy. BMJ Case Rep. 2017. https://doi.org/10.1136/bcr-2017-220719
21. De Gennaro L, Ruggiero M, Musci S, et al. Biventricular thrombosis in biventricular stress(takotsubo)-cardiomyopathy. J Thromb Thrombolysis. 2017;44:234–7.
22. Morawiec B, Degrauwe S, Iglesias JF, et al. First report on biventricular stress cardiomyopathy with concomitant atrio-ventricular high-grade conduction disorder. Cardiol J. 2017;24:98–100.
23. Sung JM, Hong SJ, Chung IH, et al. Rupture of right ventricular free wall following ventricular septal rupture in takotsubo cardiomyopathy with right ventricular involvement. Yonsei Med J. 2017;58:248–51.
24. Rodriguez AE, Fernandez-Pereira C, Mieres J, et al. Ventricular septal perforation after biventricular takotsubo cardiomyopathy successfully repaired with an Amplatzer device: first report in the literature. Case Rep Cardiol. 2016;2016:3251032.
25. Crimizade U, Messas N, Blondet C, et al. Biventricular takotsubo cardiomyopathy triggered by myocardial ischemic injury: insights from multimodal imaging approach. Int J Cardiol. 2016;207:104–6.
26. Kochanowski J, Piatkowski R, Budnik M, et al. Biventricular takotsubo cardiomyopathy in an elderly woman with uncontrolled type 2 diabetes: the biphasic echocardiographic and clinical pattern. Acta Diabetol. 2016;53:1061–3.
27. Messas N, Morel O, Collange O, et al. Biventricular takotsubo cardiomyopathy and "eclipsed" tricuspid regurgitation: insights from contrast right ventriculography. EuroIntervention. 2016;12:e1072.
28. Koo N, Yoon BW, Song Y, et al. Biventricular takotsubo cardiomyopathy associated with epilepsy. J Cardiovasc Ultrasound. 2015;23:262–5.
29. Ayoub C, Chang M, Kritharides L. A case report of ventricular dysfunction post pericardiocentesis: stress cardiomyopathy or pericardial decompression syndrome? Cardiovasc Ultrasound. 2015;13:32.
30. Perkins MJ, Schachter DT. Biventricular takotsubo cardiomyopathy in graves hyperthyroidism. J Invasive Cardiol. 2014;26:E35–6.
31. Hwang HJ, Sohn IS. A case of biventricular involvement of takotsubo cardiomyopathy: 3D echocardiographic imaging. J Echocardiogr. 2014;12:48–9.
32. Groves EM, Kim JK. Biventricular failure due to stress cardiomyopathy after pericardiectomy for constrictive pericarditis. Case Rep Med. 2013;2013:106757.
33. Vizzardi E, Bonadei I, Piovanelli B, et al. Biventricular Tako-Tsubo cardiomyopathy: usefulness of 2D speckle tracking strain echocardiography. J Clin Ultrasound. 2014;42:121–4.
34. Angelini P, Monge J, Simpson L. Biventricular takotsubo cardiomyopathy: case report and general discussion. Tex Heart Inst J. 2013;40:312–5.
35. Daoko J, Rajachandran M, Savarese R, et al. Biventricular takotsubo cardiomyopathy: case study and review of literature. Tex Heart Inst J. 2013;40:305–11.
36. Robaei D, Buchholz S, Feneley M. Biventricular stress-induced (Tako-tsubo) cardiomyopathy complicated by right ventricular thrombus. J Echocardiogr. 2012;10:104–5.
37. Korlakunta H, Butkevich A, Muthupillai R, et al. Biventricular takotsubo cardiomyopathy: cardiac magnetic resonance imaging as useful diagnostic tool. Tex Heart Inst J. 2011;38:88–9.
38. Eitel I, Schuler G, Gutberlet M, et al. Biventricular stress-induced (takotsubo) cardiomyopathy with left midventricular and right apical ballooning. Int J Cardiol. 2011;151:e63–4.
39. Citro R, Caso I, Provenza G, et al. Right ventricular involvement and pulmonary hypertension in an elderly woman with tako-tsubo cardiomyopathy. Chest. 2010;137:973–5.
40. Bar H, Katus HA, Mereles D. Biventricular involvement in transient apical ballooning syndrome. Int J Cardiol. 2009;133:e79–80.
41. Novak G, Kross K, Follmer K, et al. Transient biventricular apical ballooning: a unique presentation of the "broken heart". Clin Cardiol. 2007;30:355–8.
42. Kurisu S, Inoue I, Kawagoe T, et al. Takotsubo-like transient biventricular dysfunction with pressure gradients. Intern Med. 2005;44:727–32.