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【 CASE REPORT 】

Isolated Right Ventricular Stress (Takotsubo) Cardiomyopathy

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Abstract:
A 79-year-old woman was admitted with a left femoral neck fracture and she immediately developed circulatory shock. Echocardiography showed a markedly enlarged right ventricle (RV) with systolic ballooning of the mid-ventricular wall and preserved contractility of the apex. The left ventricular (LV) motion was normal. Multi-detector-row computed tomography showed severe congestion of the contrast media in the right atrium with no forward flow to RV, but no pulmonary embolism. She was successfully treated with percutaneous veno-arterial extracorporeal membrane oxygenation. This case presented with acute, profound, but reversible RV dysfunction triggered by acute stress in a manner similar to that seen in LV stress cardiomyopathy.

Key words: circulatory shock, right heart failure, stress (takotsubo) cardiomyopathy, cardiac magnetic resonance, echocardiography, mechanical support

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Introduction

Stress cardiomyopathy, first reported in Japan as takotstubo, is characterized by transient systolic and diastolic left ventricle (LV) dysfunction with a variety of wall-motion abnormalities (1-5). It predominantly affects elderly women and is often preceded by an emotional or physical trigger. We herein describe a patient who presented with serious, but reversible acute right ventricle (RV) failure and shock without LV dysfunction that was triggered by acute stress in a manner similar to that seen in LV stress cardiomyopathy. She was successfully treated with percutaneous veno-arterial extracorporeal membrane oxygenation (ECMO) (6-8).

Case Report

A 79-year-old woman was admitted to the emergency department with a left femoral neck fracture. She had undergone low anterior resection for rectal cancer 2 months previously. Immediately after admission, she presented with severe upper abdominal pain, fatigue, and confusion. Her heart rate was 80 beats/min, systolic blood pressure was 70 mmHg, respiratory rate was 30 breaths/min, and oxygen saturation was 98% on oxygen (2 L/min). Physical examination revealed no apparent traumatic bruising, but the patient demonstrated cold and clammy skin without any rashes and jugular venous distension and clear lungs with an S_3 cardiac gallop at the left-lower sternal border without peripheral edema; moreover, the edge of the liver was tender on palpation. Electrocardiography showed a sinus rhythm and T-wave inversion in leads V_1-V_4 without ST elevation (Fig. 1A). Echocardiography showed no regional LV motion abnormalities. The RV was markedly enlarged, with systolic ballooning of the mid-ventricular wall and hypercontractility of the apex (Fig. 2A, Supplementary material 1). The interventricular septum (IVS) was flattened during diastole, but not during systole (Fig. 2B, Supplementary material 2). Moderate tricuspid regurgitation with a pressure gradient of 21 mmHg was observed, and this was considered to have developed secondary to RV dysfunction with leaflet tether-

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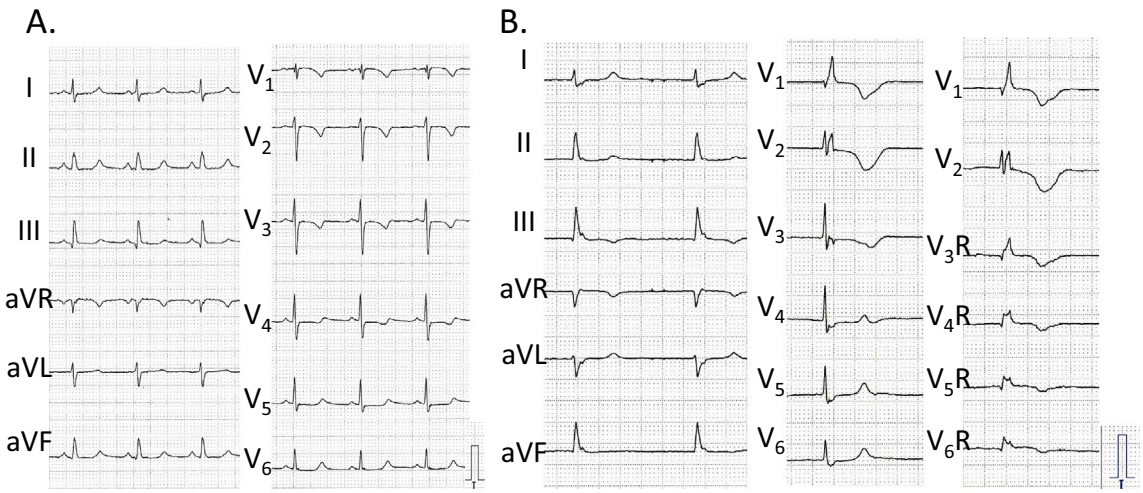

Figure 1. **Electrocardiogram on admission showing sinus rhythm as well as S1 and T-wave inversion in leads V_1-V_4 (A). Electrocardiogram obtained after the detection of changes in the heart rate and a QRS complex pattern. The electrocardiograms displaying progressive changes in the heart rate followed by sinus arrest, complete right bundle-branch block pattern escape beats, T-wave inversion in leads III, V_1-V_3, and V_4R, and no significant ST elevation, including inferior and V_4R leads (B).**

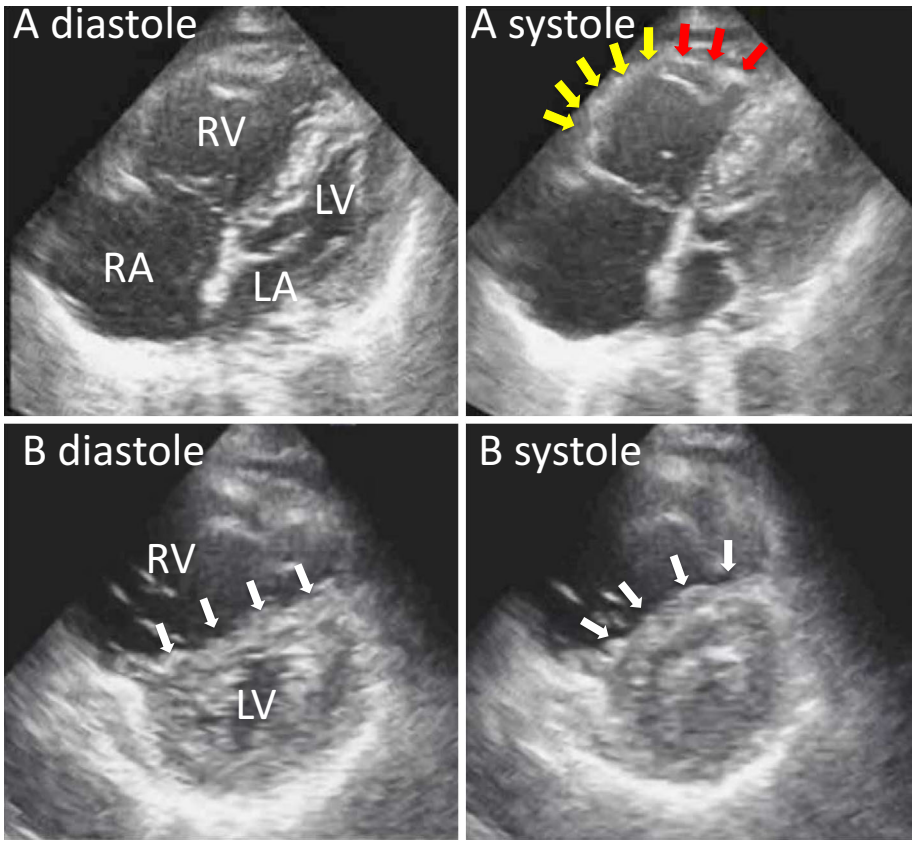

Figure 2. **Echocardiography images obtained on admission. Apical four-chamber view of the heart during diastole and systole indicates right ventricular (RV) enlargement and free-wall systolic ballooning (yellow arrow) with apical motion sparing (red arrow). The left ventricle (LV) is small and no regional wall motion abnormalities are apparent (A). Parasternal short axis view of the heart during diastole and systole reveals RV enlargement. The interventricular septum (IVS) is flattened during diastole (white arrow), but not during systole, indicating a change in the volume without any superimposed pressure overload (B). LA: left atrium, LV: left ventricle, RA: right atrium, RV: right ventricle**

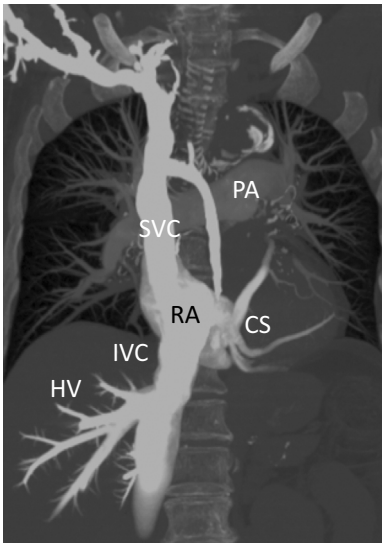

Figure 3. Maximum intensity projection (MIP) image of multi-detector row computed tomography shows excessive contrast in the systemic venous system, including the superior vena cava, inferior vena cava, hepatic vein, and coronary sinus, but faint contrast in the pulmonary circulation and no pulmonary embolism. These findings indicate severe right ventricular dysfunction; the majority of the contrast did not flow into the pulmonary circulation, but instead spilled over into the systemic venous system. CS: coronary sinus, HV: hepatic vein, IVC: inferior vena cava, PA: pulmonary artery, RA: right atrium, RV: right ventricle, SVC: superior vena cava

ing. The inferior vena cava was dilated without any respiratory changes. No evidence of any other valvular insufficiency, intracardiac shunting, pericardial effusion, or venous clot was observed. Multi-detector row computed tomography (MDCT) revealed a left femoral neck fracture without multiple traumas. Pericardial effusion, pneumothorax, pleural effusion, or ascites was not apparent. Enhanced MDCT images showed that most of the contrast medium did not flow into the RV, but instead spilled over into the systemic venous system (Fig. 3). Moreover, MDCT pulmonary arteriography did not show any evidence of pulmonary embolism (PE) or pulmonary arterial dilatation. Furthermore, no apparent deep vein thrombosis, aortic dissection, or active bleeding was observed.

Arterial blood gas measurements performed while the patient breathed 3 L/min of oxygen were as follows: pH 7.12; partial pressure of carbon dioxide in arterial blood ($PaCO_2$), 21 mmHg; partial pressure of oxygen in arterial blood (PaO_2), 133 mmHg; HCO_3^-, 6.8 mmol/L; BE, -20.8 mmol/L; lactate, 12.2 mmol/L; and oxygen saturation, 96.9%. The levels of white blood cells, C-reactive protein, D-dimer, B-type natriuretic peptide, and troponin I were 18,900/μL, 0.58 mg/dL, 59.9 μg/mL, 185 pg/mL, and 1.23 ng/mL, respectively.

In addition to the diagnostic procedures, hemodynamic support, including inotropic drugs, was initiated. Electrocardiographic monitoring demonstrated rhythm changes. A subsequent electrocardiogram showed sinus arrest, a complete right bundle-branch block escape beat pattern, and T-wave inversion in leads III, $V_{1\text{-}3}$, and V_4R (Fig. 1B). The electrocardiogram did not show any ST-segment elevation, including right precordial leads. Treatment with escalating doses of inotropes did not improve the circulation, and she developed pulseless electrical activity. After short and successful cardiopulmonary resuscitation and tracheal intubation was achieved, we decided to perform percutaneous veno-arterial extracorporeal membrane oxygenation (V-A ECMO). V-A ECMO improved the hemodynamics, and the patient was successfully weaned from V-A ECMO on the next day. Oxygenation was relatively well preserved, mechanical ventilation was performed with an FiO_2<0.35, and the endotracheal tube was removed on day 3. Inotropic drugs were discontinued within 3 days.

Pulmonary perfusion scintigraphy performed on day 3 did not show any significant pulmonary perfusion defect. Cardiac magnetic resonance (CMR) was performed on day 5 and showed RV enlargement with systolic ballooning of the mid-ventricular wall and relatively preserved motion of the apex (Fig. 4A). CMR did not detect LV dysfunction, short-T1 inversion recovery (Fig. 4B), and late gadolinium enhancement (Fig. 4C). CMR angiography revealed that several non-obstructive RV branches diverged from the right coronary artery perfused inferior LV wall (Fig. 4D).

Her clinical course was good, and the electrocardiographic and echocardiographic findings were almost normal after 1 month (Fig. 5). Hip arthroplasty was performed, and the patient was subsequently discharged without any ambulatory support.

Discussion

In the present case, the acute, profound, but reversible RV shock originated from the RV myocardium due to an unknown cause. The salient features of RV shock are RV dysfunction and dilatation accompanied with a high right-atrial pressure, without LV dysfunction and pulmonary congestion. The two categories and related causes of RV shock are as follows: an acute increase in RV afterload caused by the pulmonary vascular bed (acute cor pulmonale) and disease of the RV myocardium (9).

Initially, a massive PE was considered to be the most likely cause of RV shock based on the presence of multiple predisposing factors for venous thrombosis (10, 11); however, MDCT did not show any evidence of massive PE. Severe peripheral PE, especially a fat embolism, should be considered in the differential diagnosis, as this condition could develop after long-bone fractures, and microembolisms cannot be detected on MDCT pulmonary arteriography (11). The clinical manifestations of the present case were related to shock rather than respiratory distress. The IVS flattening during diastole, and the appearance of a resolved shape at end-systole, indicated a change in the RV volume without a superimposed pressure overload (12, 13);

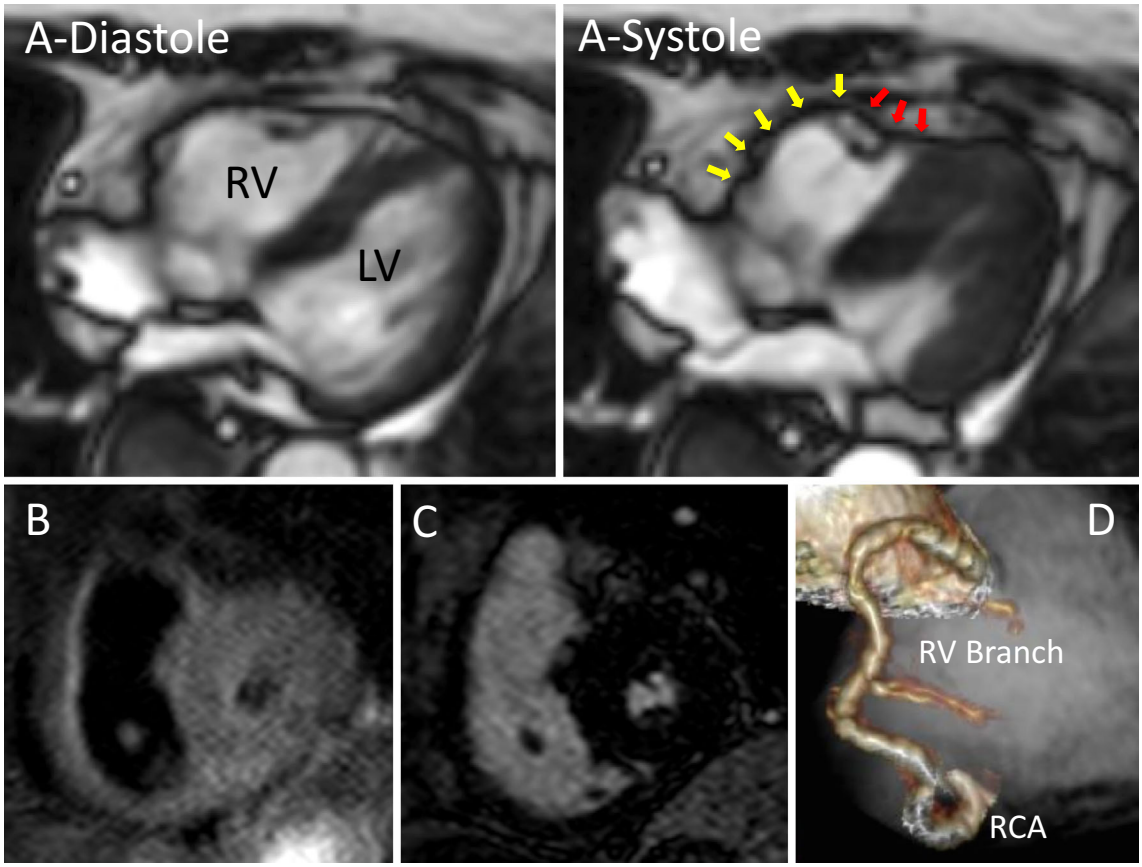

Figure 4. **Cardiac magnetic resonance (CMR) imaging confirmed right ventricular (RV) enlargement and free wall systolic ballooning (yellow arrow) with apical motion sparing (red arrow). No regional left ventricular (LV) wall motion abnormalities are visible (A). CMR demonstrated no abnormalities of short-T1 inversion recovery (B), and late gadolinium enhancement (C). CMR angiography revealed that several non-obstructive RV branches diverged from the right coronary artery (RCA) perfused inferior LV wall (D).**

moreover, pulmonary arterial dilatation was not observed. These findings confirm that acute cor pulmonale did not cause the RV shock in this case.

With regard to RV myocardium, RV infarction is an important cause of RV shock (14). The high levels of troponin I observed in this case upon admission indicate acute ischemic myocardial injury (15). However, we excluded such a possibility in the acute setting according to the electrocardiography and echocardiography findings. Electrocardiography did not detect ST-segment elevation and upright T waves in inferior and V_4R leads (16). Echocardiography showed well-preserved inferior LV and IVS contraction (13). RV infarction is an important cause of RV shock and it is associated with occlusion of the proximal segment of the right coronary artery, which supplies the inferior LV, including the inferior IVS (14). Inferior IVS dysfunction is associated with hemodynamic deterioration in RV infarction (13). The preservation of the inferior LV, including IVS motion, indicates that shock caused by RV infarction is less likely. Moderate tricuspid regurgitation which was considered to be secondary to RV dysfunction and distension with leaflet tethering was not sufficient to account for the patient's shock. After excluding PE and myocardial infarction, we minimized the anticoagulation dose during V-A ECMO and prevented bleeding from the fracture site.

Clearly the demonstration of the non-obstructive RV branches and right coronary artery perfusing the inferior LV wall could not support the causative pathogenesis that an acute coronary event, including coronary spasm, was responsible for the RV shock in this case. CMR findings of lack of short-T1 inversion recovery, or late gadolinium enhancement indicate the absence of significant edema, infarction, fibrosis, or necrosis. The rapid recovery of circulation without coronary revascularization, normal pulmonary perfusion scintigraphy findings, and CMR results helped exclude PE, myocardial infarction, and myocarditis as the causes of RV shock.

The exact etiology of RV dysfunction and shock in the current case could not be determined. The acute, profound, but reversible RV shock originated from the RV myocardium, and it was triggered by acute stress closely resembling that observed in LV stress cardiomyopathy (1, 3). CMR has emerged as a gold standard technique that provides the precise identification of localization, and stress cardiomyopathy is classified into four distinct patterns based on regional ventricular ballooning: apical, biventricular, mid-

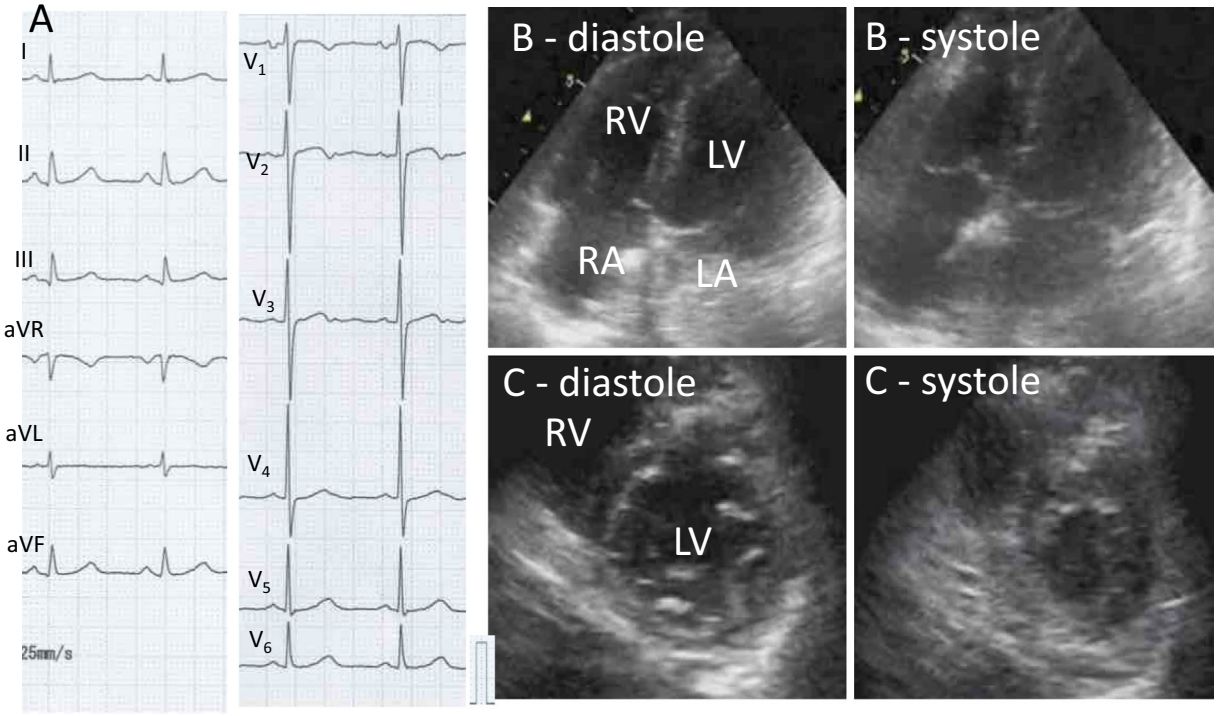

Figure 5. **Electrocardiography traces and echocardiography images obtained at 1 month post admission. A normal sinus rhythm without T-wave inversions is seen (A). Apical 4-chamber view of the heart in diastole and systole reveals right ventricle enlargement; free-wall systolic ballooning is not apparent (B). Parasternal short-axis view of the heart in diastole and systole reveals right ventricle enlargement; flattening of the interventricular septum in diastole is not apparent (C). IVS: interventricular septum, LA: left atrium, LV: left ventricle, RA: right atrium, RV: right ventricle**

ventricular, and basal (2). By extending the concept of stress cardiomyopathy from the LV to the RV, we propose that RV free-wall dysfunction may therefore represent a new pattern of stress cardiomyopathy.

The most common electrocardiographic changes associated with stress cardiomyopathy are ST-segment elevation and negative T waves. Negative T waves appear on initial electrocardiography in many patients with stress cardiomyopathy, and this was found in our patient. If ST-segment elevation was present, then the clinical features might have more closely mimicked pure RV infarction. A complicated differential diagnosis makes it important to select the appropriate treatment strategy. Echocardiography focusing on the motion of the IVS is essential. The "triple rule-out protocol" of MDCT might also be helpful (17). Coronary angiography should not be withheld, and when the RV branch is not occluded, then this pathogenesis should be considered. Studying more cases and understanding the pathogenesis of this condition are necessary to establish the diagnosis and management of patients with RV shock.

We herein described a new variant of stress cardiomyopathy. Kagiyama et al. reported a similar case of transient RV dysfunction by echocardiographic and CMR imaging, but they did not describe the clinical characteristics (18). The accumulation of more cases and elucidation of the pathogenesis of this condition are necessary to establish the optimal treatment strategies.

The authors state that they have no Conflict of Interest (COI).

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