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CASE SERIES
Heart failure

Takotsubo syndrome complicated by cardiogenic shock due to left ventricular outflow tract obstruction, acute mitral regurgitation, and atrial fibrillation: a case report

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Background Although Takotsubo syndrome (TTS) is generally considered a benign disease, recent reports showed the incidence of cardiogenic shock due to left ventricular outflow tract obstruction (LVOTO), mitral regurgitation (MR), and primary pump failure was estimated to be 6–20%.

Case summary A 78-year-old woman presented with chest pain and cold sweats 2 days after surgery for lung cancer. Acute coronary syndrome was suspected based on her symptoms, electrocardiography, transthoracic echocardiography (TTE), and laboratory data; thus, emergency catheterization was performed. Normal coronaries were observed, with hyperkinesis at the base of the left ventricle and akinesis at its apex, leading to the diagnosis of the apical ballooning type of TTS. Pressure differences between the apex of the left ventricle (168/8/28 mmHg) and aorta (94/50/64 mmHg) indicated the presence of LVOTO. Two days after TTS onset, she developed cardiogenic shock (blood pressure was 54/38 mmHg). Transthoracic echocardiography showed acute MR due to systolic anterior motion of the mitral valve caused by LVOTO, which was further exacerbated by paroxysmal atrial fibrillation. Fluid resuscitation, intravenous β-blockers, and amiodarone were administered for reduction of the pressure gradient in the left ventricular outflow, rate control, and sinus rhythm maintenance. Her condition improved along with the MR, thereby improving LVOTO and maintaining sinus rhythm.

Discussion Takotsubo syndrome should be kept in mind as a potential cause of acute MR due to LVOTO. Catheterization and multiple follow-up TTE play a major role in early detection for this condition.

Keywords Takotsubo syndrome • Cardiogenic shock • Left ventricular outflow tract obstruction • Acute mitral regurgitation • Paroxysmal atrial fibrillation • Case report

ESC curriculum 2.2 Echocardiography • 4.3 Mitral regurgitation • 6.4 Acute heart failure

Learning points

- This case demonstrates the exacerbating factors and the management of cardiogenic shock in Takotsubo syndrome.
- This case highlights the role of catheterization and echocardiography in detecting and managing mitral regurgitation and left ventricular outflow tract obstruction in Takotsubo syndrome.

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Introduction

Takotsubo syndrome (TTS), a relatively rare disease, occurs in ~2–3% of patients with suspected acute coronary syndrome[1–3] and is often preceded by emotional and physical stress, such as in the post-surgical period.[4] Takotsubo syndrome is often thought to have a good prognosis because the wall motion naturally improves in most cases within days to weeks after onset.[5] However, recent reports show some cardiac complications during the acute phase after onset of TTS,[4,6] while cardiogenic shock and mortality rates are no different than when occurring in the context of acute coronary syndromes.[7] Based on the International Expert Consensus Document on TTS, acute heart failure (12–45%), left ventricular outflow tract obstruction (LVOTO) (10–25%), mitral regurgitation (MR) (14–25%), cardiogenic shock (6–20%), and atrial fibrillation (AF) (5–15%) occurred during the acute phase.[8] In this case, transthoracic echocardiography (TTE) identified complications of TTS such as LVOTO and MR and enabled real-time documentation of MR deterioration at the onset of paroxysmal AF (PAF).

Summary figure

Time	Events
On the day of operation	Thoracoscopic right lung upper lobectomy for lung cancer.
Post-operative Day 2	Patient complained of chest pain and cold sweats and was suspected to have acute coronary syndrome based on electrocardiography and TTE findings.
	TTS onset was confirmed by coronary angiography and left ventriculography.
	The patient's BP dropped from 140/90 to 94/50 mmHg.
Post-operative Day 4	TTE demonstrated moderate MR and left ventricular ejection fraction (LVEF) of 58%.
	During the TTE procedure, PAF occurred and MR was further worsened.
	The patient's haemodynamics then collapsed, leading to shock (BP, 54/38 mmHg).
	Fluid resuscitation and intravenous β-blocker were administered for reduction of the pressure gradient in the left ventricular outflow. Furthermore, sinus rhythm was successfully maintained with the administration of amiodarone in addition to the intravenous β-blocker.
Post-operative Days 5–7	The patient's haemodynamics gradually stabilized through the use of fluid resuscitation, intravenous β-blocker, and amiodarone.
Post-operative Day 10	TTE demonstrated left ventricular outflow tract gradient (21 mmHg), mild MR, and improved LVEF (68%).
Post-operative Day 15	Discharge
Post-operative Day 84	TTE demonstrated LVOT gradient (16 mmHg), trivial MR, and improved LVEF (76%).

The detailed time course of the acute phase of TTS is shown in *Figure 1*.

Case presentation

A 78-year-old woman with prior history of hypertension was admitted due to thoracoscopic right lung upper lobectomy for lung cancer. She received a digoxin (0.25 mg) intravenous drip, which is occasionally used for post-operative management of respiratory surgery, on post-operative day (POD) 1 to treat her sinus tachycardia. On POD 2, she presented with chest pain and cold sweats [blood pressure (BP), 94/50 mmHg; heart rate (HR), 93 b.p.m.; and oxygen saturation, 98% under nasal mask 3 L/min). Physical examination revealed a Grade Ⅱ/Ⅵ systolic murmur at the apex and coarse crackles. Electrocardiography showed a sinus rhythm with ST segment elevation in V3–6 and negative T waves in Ⅰ, Ⅱ, aVL, and V3–6, suggesting acute coronary syndrome (*Figure 2A*). Chest X-rays showed slight congestion of the lung fields and atelectasis and bronchial deviation due to lung cancer surgery (*Figure 2D*). White blood cell counts (14 800 cells/μ) (normal range: 3300–8600), creatinine kinase (335 IU/L) (normal range: 59–248), creatinine kinase-MB (45 IU/L) (normal range: <25), and highly sensitive troponin I (916 pg/mL) (normal range: <16) were increased. Emergency catheterization was performed, revealing normal coronaries (*Figure 2B* and *C*) with hyperkinesis at the base of the left ventricle and akinesis at its apex (*Figure 2E* and *F*). Thus, we diagnosed the patient with the apical ballooning type of TTS. In addition, we confirmed the pressure difference between the apex of the left ventricle (168/8/28 mmHg) and aorta (94/50/64 mmHg), which indicated the presence of LVOTO.

The time course of the acute phase of TTS is shown in *Figure 1*. Low-dose 0.1 μg/kg/min noradrenaline for mild hypotension and 20 mg/day furosemide intravenous drip was initiated for heart failure because of high end-diastolic pressure in the left ventricle and slight congestion. However, both BP and urine volume dropped further after initiation of treatment.

On POD 4 (2 days after TTS onset), a Grade Ⅳ/Ⅵ systolic murmur at the apex was auscultated and TTE revealed MR due to systolic anterior motion (SAM) of the mitral valve caused by LVOTO during sinus rhythm (*Figure 3*; Supplementary material online, *Video S1*). During the TTE procedure, PAF occurred and MR was further worsened due to significant deterioration of SAM (*Figure 4*; Supplementary material online, *Video S2*). The patient's haemodynamics then collapsed, leading to shock (BP, 54/38 mmHg; HR,114 b.p.m.). Due to sudden onset of shock, we could not measure the left ventricular outflow gradient. Lactate levels (17 mg/dL) (normal range: 4.5–14.4) were increased. A change in treatment strategy was required since preload reduction using diuretics can worsen LVOTO and induce acute MR. Therefore, we stopped the administration of diuretics and started fluid resuscitation. Intravenous β-blocker (landiolol hydrochloride, 3 μg/1 kg/min) was

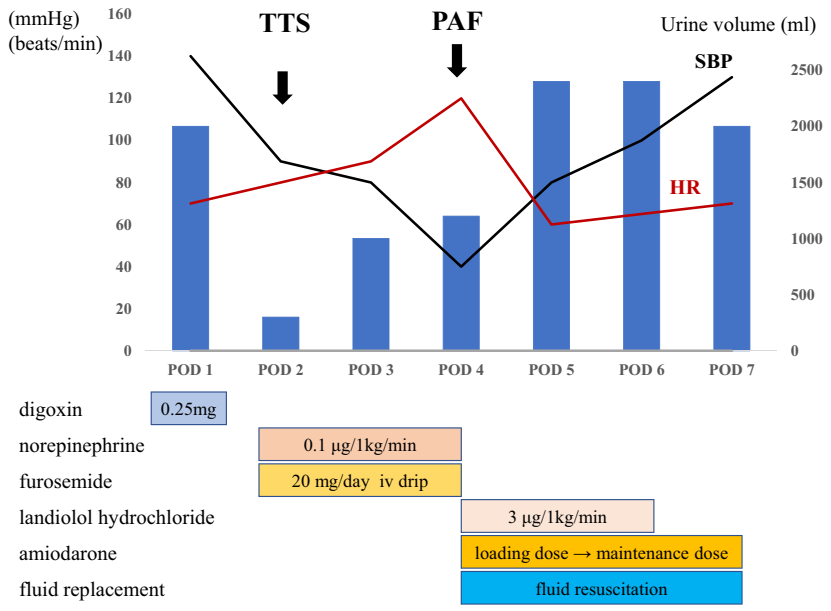

Figure 1 Time course of acute phase. HR, heart rate; iv, intravenous; PAF, paroxysmal atrial fibrillation; POD, post-operative day; SBP, systolic blood pressure; TTS, takotsubo syndrome.

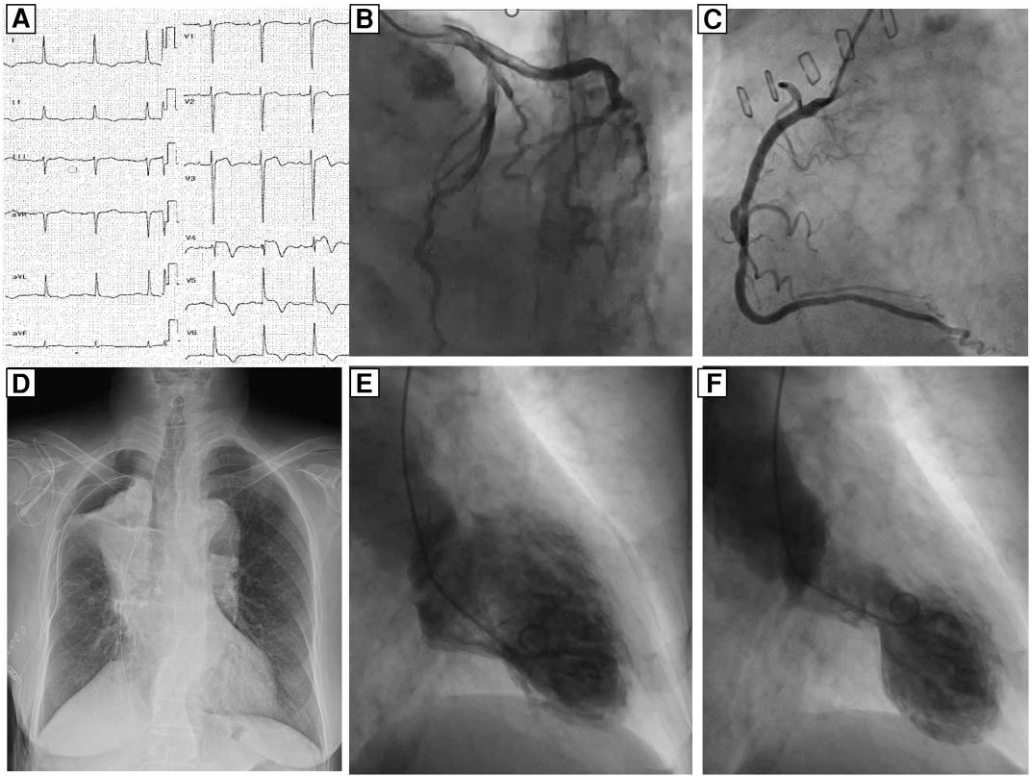

Figure 2 Electrocardiogram, X-rays, coronary angiography, and left ventriculography. (*A*) Electrocardiogram showing ST segment elevation in V3–6 and negative T waves in Ⅰ, Ⅱ, aVL, and V3–6. (*B*) Left coronary artery showing no significant stenosis. (*C*) Right coronary artery showing no significant stenosis. (*D*) X-rays showing slight congestion of the lung fields. (*E*) Left ventriculography at diastolic phase. (*F*) Left ventriculography at systolic phase shows hyperkinesis at the base of the left ventricle and akinesis at its apex.

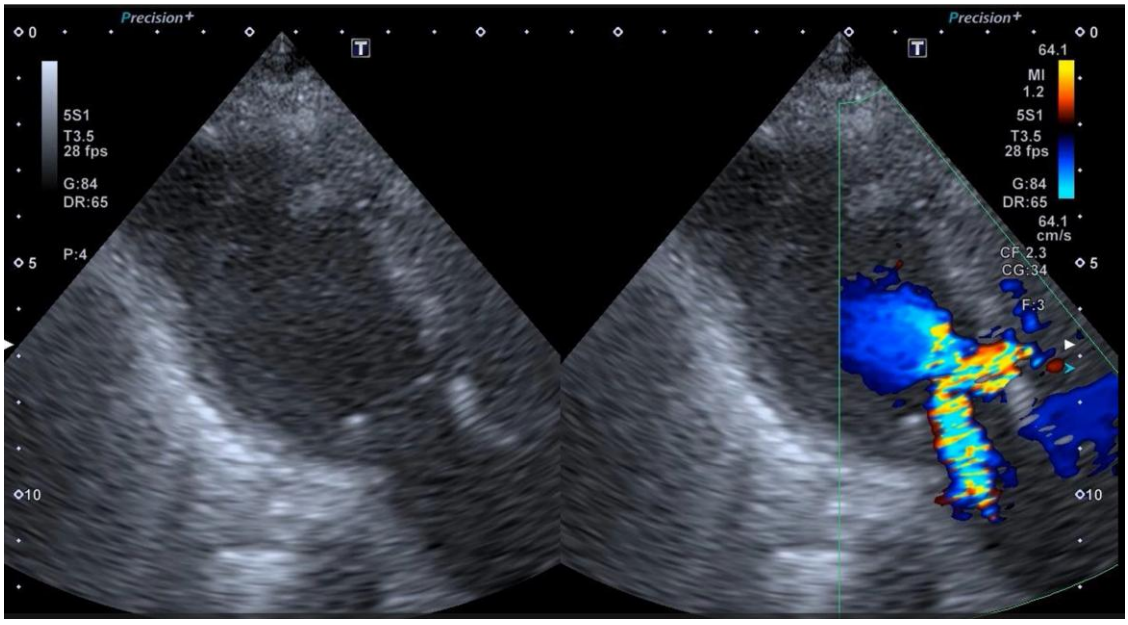

Figure 3 Transthoracic echocardiography performed 2 days after takotsubo syndrome onset at sinus rhythm. Three-chamber view at systolic phase showing left ventricular outflow tract obstruction and mitral regurgitation.

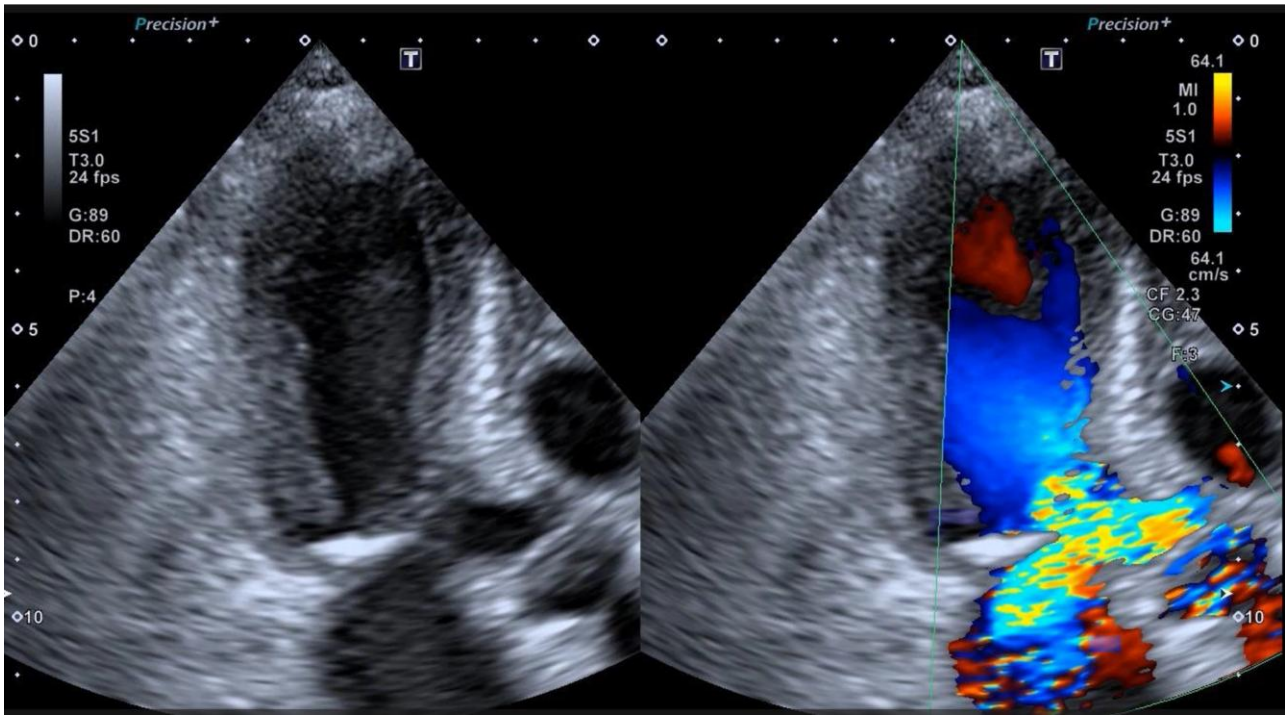

Figure 4 Transthoracic echocardiography performed 2 days after takotsubo syndrome onset at paroxysmal atrial fibrillation. Three-chamber view at systolic phase showing deterioration of left ventricular outflow tract obstruction and worsening mitral regurgitation.

administered for reduction of the pressure gradient in the left ventricular outflow and rate control. Finally, with the administration of amiodarone (loading dose was 33 mL/h, and maintenance dose was 17 mL/h after loading 750 mg dissolved in 500 mL glucose solution) in addition to the intravenous β-blocker, sinus rhythm was successfully maintained. The patient's haemodynamics gradually stabilized with fluid resuscitation and maintenance of sinus rhythm. Her urine output increased without the usage of diuretics, and her general condition further improved. Transthoracic echocardiography performed on POD 10 showed that apical akinesis and basal hyperkinesis had improved, and MR had also improved to mild. She was thus discharged 2 weeks after the onset of TTS.

Discussion

Left ventricular outflow tract obstruction and SAM of the mitral valve occurring in the context of the acute phase of TTS can lead to acute MR in some patients.[9] Left ventricular outflow tract obstruction is commonly induced by typical septal hypertrophy of the left ventricle in patients with hypertrophic obstructive cardiomyopathy, but the LVOTO seen in patients with TTS is believed to be related to the apical ballooning type, a hyperdynamic state of the basal segment of the left ventricle.[10]

Left ventricular outflow tract obstruction treatment regimens in TTS should avoid the use of diuretics due to reduction in the preload as well as nitroglycerin and intra-aortic balloon pumping due to reduction in the preload and afterload, since LVOTO can worsen the pressure gradient.[8] On the other hand, therapies for LVOTO of TTS include intravenous fluids (if no heart failure is present), short-acting β-blockers, and alpha-adrenergic agonists such as phenylephrine in TTS cases with shock to prevent inappropriate peripheral vasodilation, which may exacerbate LVOTO.[8,11] Although intravenous administration of β-blockers is not generally recommended during hypotension, the patient in this case required rhythm control, rate control, and the improvement of LVOTO. Therefore, we selected landiolol hydrochloride as the β-blocker, since it is a short-acting selective β1-blocker with rapid onset of effect and a very short biological half-life. If cardiogenic shock is unresponsive to drugs, the possible usage of percutaneous left ventricular assist devices can be considered.[8] Extra-corporeal membrane oxygenation may have some benefit derived from increased afterload, but it should be used as a last resort considering its strong preload reduction. In cases of primary pump failure without LVOTO, intra-aortic balloon pumping may be considered as well as extra-corporeal membrane oxygenation and percutaneous left ventricular assist devices.[8,11]

In this patient, considering the high end-diastolic pressure of the left ventricle and low oxygenation, the diagnosis was determined to be heart failure, and the use of diuretics and positive inotropes further worsened LVOTO, leading to exacerbation of MR. The initial management protocol may have had detrimental effects. In addition, AF led to a reduction in blood flow to the left ventricle due to the lack of atrial kick, diastolic dysfunction, and inadequate diastolic filling time. We therefore considered that LVOTO may have worsened due to decreased preload, leading to further worsening of MR.

The apical ballooning type of TTS should prompt us to check for LVOTO during catheterization and perform follow-up TTE during the acute stage. The treatment of LVOTO also needs to be carefully considered, especially since even PAF can worsen LVOTO and should be prevented. In addition, multiple follow-up TTE procedures may be required to establish an appropriate treatment strategy for patients with this condition.

Lead author biography

Dr Yuya Ishizaki was born in Nagasaki, Japan in 1993. He graduated from Nihon University in 2017. He experienced this case at the Tokai University School of Medicine in 2020.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Conflict of interest: None declared.

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Data availability

The data underlying this article are available in the article and in its online Supplementary material.

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