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【 CASE REPORT 】

"Incompatible Housemates": Hypertrophic Obstructive Cardiomyopathy and Takotsubo Syndrome

Yasue Sato, Kensuke Matsumoto, Jun Sakai, Toshihiro Nakamura, Hidekazu Tanaka and Kenichi Hirata

Abstract:
This case report concerns an 81-year-old woman with previously well-controlled hypertrophic obstructive cardiomyopathy (HOCM). She was referred to our hospital because of the acute onset of takotsubo syndrome. Echocardiography revealed basal hyperkinesis due to takotsubo syndrome superimposed on septal hypertrophy, which resulted in the reappearance of prominent left ventricular outflow tract obstruction (LVOTO). Although she developed cardiogenic shock triggered by atrial fibrillation, LVOTO was successfully mitigated by aggressive fluid resuscitation, rhythm control, and the administration of β-blocker. We herein report a rare case with catastrophic hemodynamics due to the incidental combination of HOCM and takotsubo syndrome.

Key words: takotsubo syndrome, left ventricular outflow tract obstruction, hypertrophic obstructive cardiomyopathy, cardiogenic shock

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Introduction

Hypertrophic cardiomyopathy (HCM) is caused by the mutation of genes encoding the proteins of the cardiac sarcomere. Furthermore, from a morphological stand point, HCM generally presents with anteroseptal-dominant asymmetrical hypertrophy and often shows dynamic left ventricular (LV) outflow tract obstruction (LVOTO) due to the combination of hypertrophied ventricular septum and systolic anterior motion (SAM) of the mitral leaflet, which is specifically referred to as hypertrophic obstructive cardiomyopathy (HOCM). On the HCM spectrum, significant LVOTO is known to adversely affect its morbidity and mortality (1).

Takotsubo syndrome is a relatively rare myocardial disease of unknown etiology. It is known to exhibit sudden and reversible akinesis or even dyskinesis of the broad LV apical segments and hyperkinetic motion of the basal segments, often triggered by emotional or physical stressors. Notably, previous studies have reported that 10% to 25% of patients with takotsubo syndrome transiently develop LVOT obstruction (2-4). Therefore, special care should be practiced during the assessment and during the treatment of takotsubo syndrome at in the acute phase, especially in cases that develop LVOTO.

We herein report an extremely rare case in which takotsubo syndrome developed in a patient with HOCM previously been well controlled by medication. However, the patient presented with cardiogenic shock as a result of the reappearance of severe LVOTO induced by the onset of takotsubo syndrome.

Case Report

An 81-year-old woman visited a hospital with shortness of breath and was diagnosed with HOCM 2 years ago. Transthoracic echocardiography demonstrated moderate mitral regurgitation and LVOTO with a peak velocity of 4.1 m/sec (Fig. 1A, E). As a treatment, she was prescribed bisoprolol (5 mg/day). Subsequently, 1 year later, the LVOT obstruction had significantly improved (Fig. 1B, F), and her exertional dyspnea had completely disappeared.

However, she presented to the emergency department

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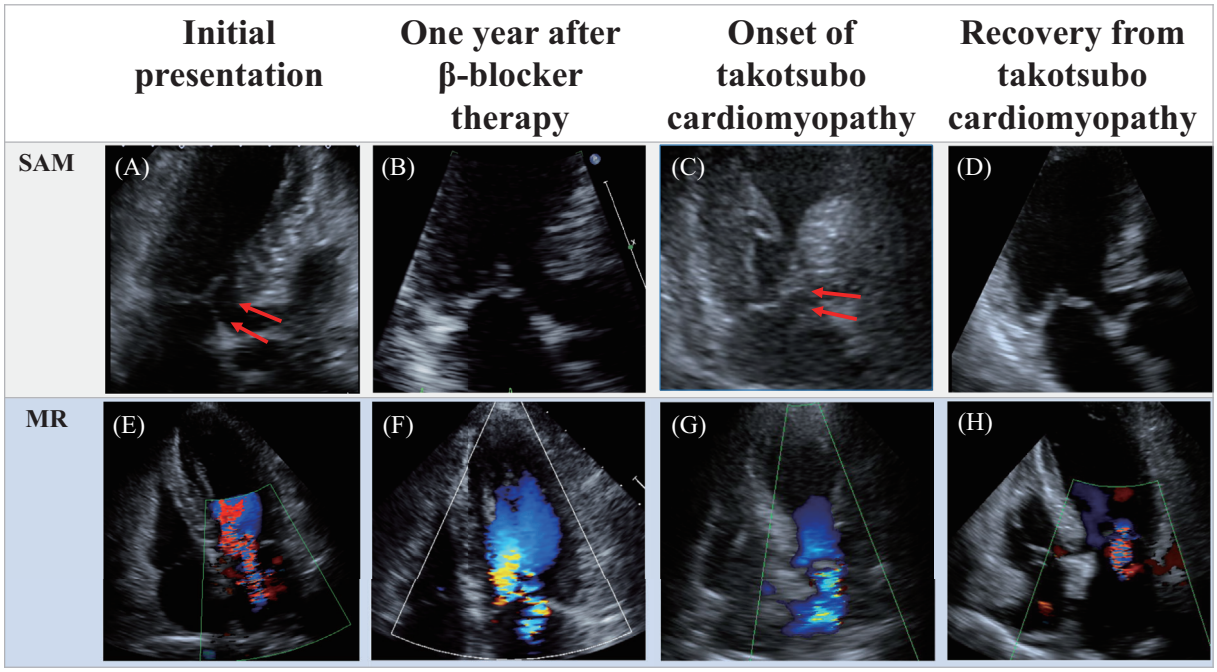

Figure 1. **Serial changes in the systolic anterior motion of the mitral leaflet and mitral regurgitation. Echocardiograms at the initial presentation (panels A and E), one year after β-blocker therapy (panels B and F), acute phase (panels C and G), and recovery phases of takotsubo syndrome (panels D and H) are shown. Significant systolic anterior motion of the mitral leaflet was observed at the initial presentation and reappeared at the onset of takotsubo syndrome (red arrows, respectively). SAM: systolic anterior motion, MR: mitral regurgitation**

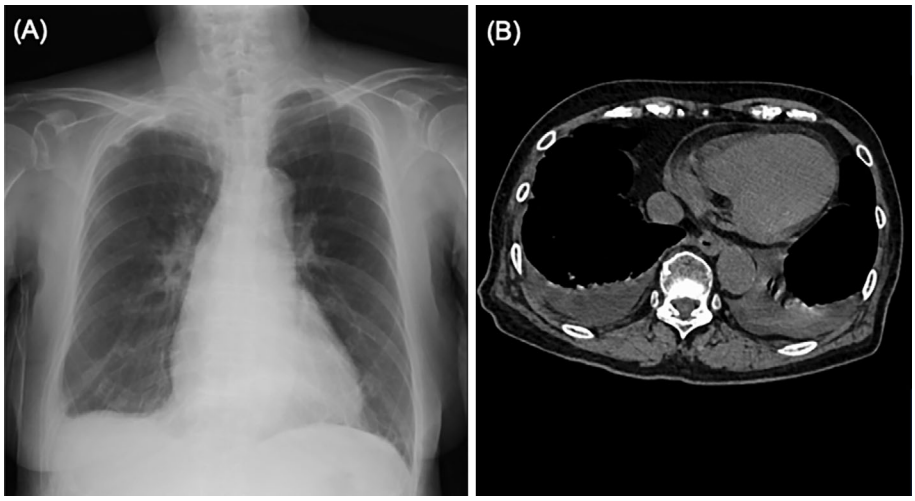

Figure 2. **Chest radiograph and computed tomography on admission. A chest radiograph on admission (A) shows cardiomegaly concomitant with pleural effusion, and computed tomography confirms bilateral pleural effusion, which is consistent with acute decompensated heart failure.**

again complaining of the sudden onset of shortness of breath. At her initial presentation, the patient's blood pressure was 132/96 mmHg, resting heart rate at 112 beats/min, oxygen saturation of 96% (room air), and body temperature 38.6°C. Cardiac auscultation revealed Levine III/VI harsh and late peaking systolic ejection murmur at the fourth left intercostal space. Chest radiography revealed cardiomegaly concomitant with pleural effusion, and computed tomography confirmed bilateral pleural effusion (Fig. 2). Electrocardiography on admission showed ST segment elevation and the disappearance of the R wave in the precordial leads compared to the previous electrocardiography (Fig. 3). Although the blood count and biochemical findings were almost within normal limits (Table), the troponin I and brain natriuretic peptide concentration were found to be significantly elevated to 8.86 ng/mL (normal range 0-0.014 ng/

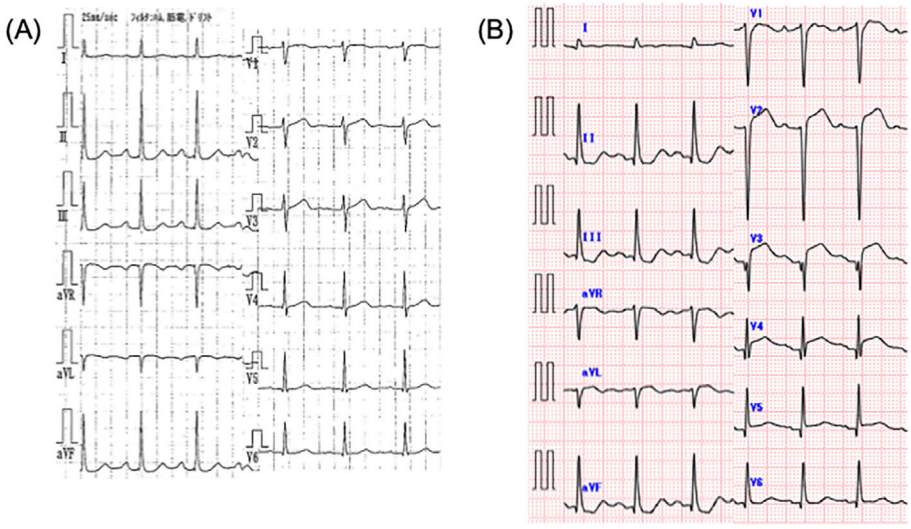

Figure 3. **The previous electrocardiogram and that obtained on admission. The previous electrocardiogram is shown in panel A. Compared to the previous electrocardiogram, the electrocardiogram obtained on admission shows ST segment elevation in leads V1-V4 and the disappearance of the R wave in leads V1-V3 (B).**

Table. **Blood Findings on Admission.**

Peripheral blood		Biochemistry	
White blood cells	6,100 /μL	Total bilirubin	0.9 mg/dL
Neutrophil	53.7 %	Aspartate transaminase	33 U/L
Lymphocyte	38.8 %	Alanine transaminase	14 U/L
Basophil	0.2 %	Lactate dehydrogenase	218 U/L
Eosinophil	0.2 %	Alkaline phosphatase	220 U/L
Monocyte	7.1 %	γ-glutamyl transpeptidase	13 U/L
Hemoglobin	13.1 g/dL	Total protein	0.9 mg/dL
Hematocrit	39.1 %	Albumin	3.4 g/dL
Platelets	143 /μL	Urea nitrogen	14.7 mg/dL
		Creatinine	0.74 mg/dL
		Na	136 mmol/L
		K	3.8 mmol/L
		Cl	105 mmol/L
		Calcium	8.8 mg/dL
		C-reactive protein	0.46 mg/dL
		Creatine kinase	138 U/L
		Creatine kinase-MB	11 U/L
		Troponin I	8.86 ng/mL
		Brain natriuretic peptide	1,307 pg/mL

mL) and 1,307 pg/mL (normal range 0-18.4 pg/mL), respectively. The serum noradrenaline concentration was not assessed on admission. The rapid influenza antigen test was positive for influenza A. Echocardiography showed dyskinesis of the apical segment along with significant basal hyperkinesis with an LV ejection fraction of 50% (Supplementary material 1). Significant SAM of the mitral leaflet and mitral regurgitation relapsed as a result of the combination of septal hypertrophy and hyperkinesis of the basal septum (Fig. 1C, G). The peak velocity of the LVOT was revealed to be 5.2 m/sec; therefore, the pressure gradient at LVOT was estimated to be 107 mmHg. The patient underwent urgent coronary angiography to rule out acute coronary syndrome, which did not show any significant coronary artery stenosis. Subsequently, the diagnosis of takotsubo syndrome triggered by influenza A infection was established.

Thereafter, triggered by the onset of atrial fibrillation, the blood pressure of the patient was found to have critically deteriorated to 74/40 mmHg. She did not adequately respond to judicious fluid resuscitation and eventually suffered hemodynamic collapse. We therefore administered noradrenaline in expectation of its vasoconstrictive effect with a high degree of caution and very close monitoring of her hemodynamics. The patient was then transferred to the intensive-care unit and underwent emergent cardioversion. Notably, the sinus rhythm was restored by cardioversion fol-

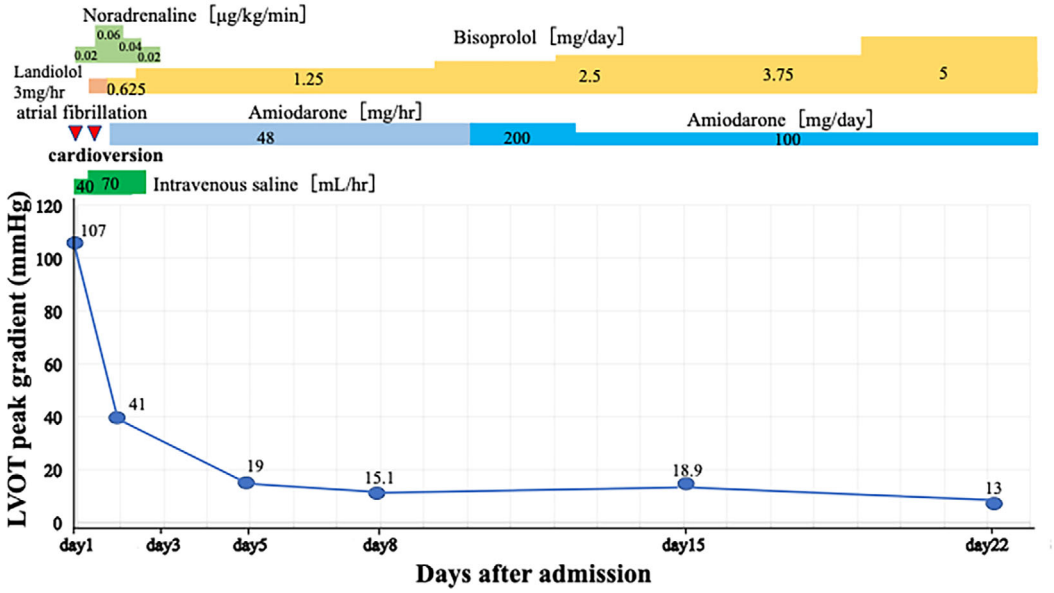

Figure 4. **Clinical course after admission. The clinical course and the treatment process after admission are shown.**

lowed by the administration of intravenous amiodarone. After the successful maintenance of the sinus rhythm, fluid resuscitation, administration of intravenous β-blocker, and the effect of noradrenaline, the hemodynamics were gradually stabilized. The intravenous β-blocker was then switched to oral bisoprolol and up-titrated to the maximally tolerated dose of 5 mg/day.

On day 22, echocardiography showed a normal LV wall motion without apical ballooning or basal hyperkinesis, as had been observed in the acute phase (Supplementary material 2). In addition, the LVOT peak velocity significantly decreased to 1.8 m/sec as a result of the disappearance of basal hyperkinesis and SAM of the mitral leaflet, thereby resulting in the significant improvement of her mitral regurgitation as well (Fig. 1D, H). Along with the hemodynamic improvements, the brain-type natriuretic peptide (BNP) concentration significantly decreased from 1,307 pg/dL to 650 pg/dL at discharge. The patient was discharged on the 23rd hospital day, and her medical course was uneventful throughout the follow-up period.

The clinical course and the treatment process were shown in Fig. 4, and the serial changes in the peak velocity, pressure gradient, and LVOT Doppler wave forms are presented in Fig. 5.

Discussion

HOCM has the unique morphologic characteristic of asymmetrical septal hypertrophy typically including the LVOT, in which the hypertrophied septal muscle often bulges into the LVOT. As a result of this septal bulging and concomitant SAM of the mitral apparatus, LVOT obstruction is reported to be present in approximately one third of the patients with HCM. From a hemodynamic point of view, LVOTO is induced by maneuvers that reduce the cardiac preload, decrease the afterload, and increase the ventricular contractility. Therefore, drugs such as ß-blockers and the expansion of the total blood volume can mitigate the outflow obstruction in cases with LVOTO.

The pathogenesis of takotsubo syndrome is still not completely understood. The suggested mechanisms include catastrophic catecholamine surges induced by psychological or physical stress, estrogen deprivation, multi-vessel coronary artery spasms, micro-vascular dysfunction, and neurogenic stunned myocardium (5). Although takotsubo syndrome generally shows transient akinetic or dyskinetic motion of the apical segments of the LV; conversely, the basal LV segments often show hyperkinetic motion, which can induce LVOTO in some cases. Early studies reported that approximately 10% to 25% of the patients with takotsubo syndrome developed with LVOT obstruction, which can result in cardiogenic shock or even cardiac rupture in serious cases (2-4). In such cases, echocardiography shows a typical septal bulge into the LVOT, severe SAM of the mitral leaflet, and resultant LVOTO, similar to the findings observed in HOCM (6).

Although case reports describing HOCM accompanied by takotsubo syndrome have been quite rare, two completely distinct phenotypes may exist. The first phenotype is predominantly severe LV systolic dysfunction during the acute phase of takotsubo syndrome, which results in the cardinal symptom of a low cardiac output. As a result, severe LV dysfunction masks preexisting LVOTO (7). In this phenotype, as the LV wall motion restores after the acute phase, previously existing LVOTO recurs again. The second phenotype is the so-called ”catastrophic phenotype”, wherein septal hyperkinesis due to takotsubo syndrome is superimposed on the hypertrophied basal septum of HOCM and preexist-

	Initial presentation	One year after β-blocker therapy	Onset of takotsubo cardiomyopathy	Recovery from takotsubo cardiomyopathy
LVOT Peak velocity	4.1 m/s	2.0 m/sec	5.2 m/sec	1.8 m/sec
LVOT Peak gradient	67 mmHg	16 mmHg	107 mmHg	13 mmHg

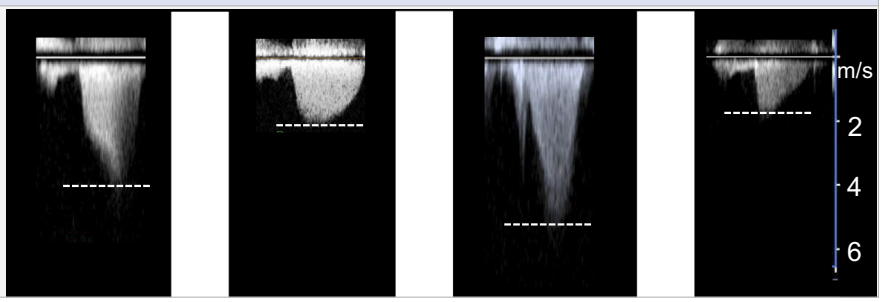

Figure 5. **Serial changes in the peak velocity, peak pressure gradient, and Doppler wave forms from the left ventricular outflow tract. When hypertrophic obstructive cardiomyopathy was first diagnosed, the peak velocity of the left ventricular outflow obstruction was 4.1 m/sec. After the β-blocker therapy was introduced, the peak velocity improved to 2.0 m/sec. However, at the onset of takotsubo syndrome, the peak velocity was re-exacerbated to 5.2 m/sec. After recovery from takotsubo syndrome, the LVOT peak velocity decreased to only 1.8 m/sec. LVOT: left ventricular outflow tract**

ing SAM, which results in profound LVOTO. This superimposed LVOTO leads to significant reduction in the forward cardiac output and the development of severe mitral regurgitation, ultimately resulting in cardiogenic shock (8-10).

This present case appears to correspond to the latter "catastrophic phenotype". In our case, the formerly well controlled LVOTO significantly deteriorated due to the onset of hyperdynamic motion of the basal septum associated with takotsubo syndrome. To make matters worse, the exacerbated SAM aggravated the coaptation of the mitral leaflets, resulting in significant mitral regurgitation. Furthermore, the sudden onset of atrial fibrillation appeared to put an end to the unstable hemodynamics. As a result of these acute hemodynamic derangements, the hemodynamics plummeted and ultimately led to cardiogenic shock.

The management of the "catastrophic phenotype" with the combination of HOCM and takotsubo syndrome is quite challenging. In general, the management of acute decompensated heart failure includes vasodilators, diuretics, and inotropic agents. In addition, deteriorated hemodynamics can be restored with intraaortic balloon pumping in some cases of cardiogenic shock. However, in cases of the "catastrophic phenotype" combined HOCM and takotsubo syndrome, such general management of acute decompensated heart failure will induce opposite hemodynamic effects for this unique hemodynamics; these procedures are therefore strongly discouraged for this phenotype. Instead, the cornerstones of the management are aggressive fluid resuscitation and intensive usage of β-blockers, which can improve the hemodynamics by mitigating LVOTO. Consequently, specific care is required for these patients to mitigate LVOTO, including the aggressive administration of β-blockers and fluid resuscitation, which must never be used for the management of usual acute decompensated heart failure.

Conclusions

The two distinct pathophysiologies of HOCM and takotsubo syndrome usually never get along and rarely share a room. This combination of "incompatible housemates" ultimately can lead to catastrophic hemodynamics as observed in this case. Although the medical treatment in such cases is challenging, combined therapeutic strategies including appropriate volume resuscitation, rhythm control, and the judicious usage of β-blockers are the cornerstones of the treatment for these cases.

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

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