“Incompatible Housemates”: Hypertrophic Obstructive Cardiomyopathy and Takotsubo Syndrome

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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 standpoint, HCM generally presents with antero-ventral-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...
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/
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| Total bilirubin 0.9 mg/dL |
| Neutrophil       | Aspartate transaminase 33 U/L |
| Lymphocyte       | Alanine transaminase 14 U/L |
| Basophil         | Lactate dehydrogenase 218 U/L |
| Eosinophil       | Alkaline phosphatase 220 U/L |
| Monocyte         | γ-glutamyl transpeptidase 13 U/L |
| Hemoglobin       | Total protein 0.9 mg/dL |
| Hematocrit       | Albumin 3.4 g/dL |
| Platelets        | 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-
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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.

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.
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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