Takotsubo Cardiomyopathy in a Patient with Previously Undiagnosed Hypertrophic Cardiomyopathy with Latent Obstruction

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Abstract:
A 62-year-old woman with takotsubo cardiomyopathy (TCM) accompanied by cardiogenic shock due to the obstruction of left ventricular outflow tract (LVOT) and massive mitral regurgitation (MR) was admitted to the emergency department. After successful treatment with intensive care, dobutamine stress-echo-cardiography (DSE) was performed, which showed a dynamic LVOT gradient, severe MR and cardiogenic shock. A histological examination obtained from the right ventricular septum demonstrated hypertrophied and bizarre myocytes, with myocyte disarray. Besides TCM, a diagnosis of preexisting HCM with latent obstruction was made. She was discharged with medical therapy including a beta-blocker, which would not be routinely employed in the treatment of a patient with TCM.

Key words: takotsubo cardiomyopathy, hypertrophic cardiomyopathy, endomyocardial biopsy, dobutamine stress-echocardiography

Introduction
Hypertrophic cardiomyopathy (HCM), defined by a characteristic histopathological appearance called myocyte disarray, is caused by a multitude of mutations of genes encoding proteins of cardiac sarcomeres (1), which may result in asymmetric septal hypertrophy (ASH) of the left ventricle (LV) and a dynamic gradient of the LV outflow tract (LVOT). Even in patients without this gradient at rest, LVOT obstruction can often be provoked by several hemodynamic factors or a hyperadrenergic state called “latent obstruction”. It sometimes leads to dynamic deterioration and catastrophic outcomes, such as cardiogenic shock. Besides HCM with obstruction (HOCM), latent obstruction of the LVOT is also frequently identified in patients with takotsubo cardiomyopathy (TCM).

We report a unique case of TCM in a patient with previously undiagnosed HCM with latent obstruction, who presented with cardiogenic shock.

Case Report
A 62-year-old woman, with no history of cardiovascular disease was admitted to the emergency department with an acute onset of chest pain and faintness with antecedent severe emotional stress. She had been given medication to treat anxiety neurosis (etizolam [0.5 mg daily]) and had a family history of HOCM. A physical examination suggested hypotension (78/50 mmHg) and Grade IV/VI systolic murmur at the apex. Her initial laboratory data showed no remarkable abnormalities with the exception of troponin I (1.53 ng/ml). Electrocardiography showed ST-segment elevation in I, aVL and V3-V6, which led to the suspicion of acute myocardial infarction (Fig. 1A). Immediately before emergent cardiac catheterization, she went into cardiogenic

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shock (blood pressure: 48/24 mmHg) and lost consciousness, which necessitated intubation and continuous intravenous noradrenaline infusion. Coronary angiography was performed under the support of an intra-aortic balloon pump, which showed no significant stenosis. Left ventriculography demonstrated extensive akinesis of the apical, anteroapical, and inferoapical walls with massive mitral regurgitation (MR) and the hyperdynamic function of the basal segments of the LV (Fig. 1B, 1C). On pullback of the catheter from the left ventricular apex to the outflow tract, a 50-mmHg pressure gradient, a dynamic LVOT gradient of 250 mmHg with a late peaking developed during stress, which was accompanied by severe MR due to SAM (Fig. 2E-2H). The systolic blood pressure decreased from 120 mmHg to 74 mmHg at peak stress. The impaired wall motion with a dilated akinetic apex was not reproduced by DSE.

On the next day, she underwent endomyocardial biopsy of the right ventricular septum. A histological examination demonstrated hypertrophied and bizarre myocytes with myocyte disarray, in addition to the multiple foci of contraction-band myocyte necrosis, which is often documented in patients with TCM (2) (Fig. 3).

Besides TCM, a diagnosis of preexisting HCM with latent obstruction was made. She was discharged with medical therapy, including a beta-blocker (bisoprolol [2.5 mg daily]), which has been well tolerated. Since then, the patient (NYHA functional class I) has not complained of any symptoms.

Figure 1. Electrocardiography. Left ventriculograms with pressure tracing and echocardiograms obtained on admission. A: A 12-lead electrocardiogram showing marked ST-segment elevation in I, aVL, and V3 through V6. B and C: End-systolic and end-diastolic ventriculograms showing basal hyperkinesis and apical akinesis with massive mitral regurgitation. D: A pressure tracing on pullback through the left ventricular outflow tract demonstrating the pressure gradient of 50 mmHg. E through H: Echocardiograms showing the increased contraction of the base and systolic anterior motion of the mitral valve (white arrows), with secondary eccentric severe mitral regurgitation directed anteriorly (E: M-mode at the level of mitral valve; F and G: long-axis view of the diastolic (F) and systolic (G) phases; H: color flow Doppler).
Figure 2. Cardiac magnetic resonance imaging (CMR) on day 6 and dobutamin stress-echocardiography (DSE) on day 13. A through C: T2-weighted signal intensity revealing a thickened apical wall with circumferential myocardial edema (white arrows) in the apex (B: apical level; C: basal level), without gadolinium enhancement (D). E through H: Echocardiograms at baseline (E-d: end-diastole and E-s: end-systole) and during dobutamine stress (F-d: end-diastole and F-s: end-systole). The latter demonstrated systolic anterior movement of the mitral valve (yellow arrow), a dynamic LVOT gradient of 250 mmHg with a late peak developed during stress (G) and severe mitral regurgitation (H).

Discussion

LVOT obstruction is identified in 15% of patients with HCM and 33% of patients with TCM (3, 4). Several cases of TCM have been previously described in patients with HOCM. In these cases, a persistent gradient across the LVOT and ASH was demonstrated by echocardiography, even after the normalization of the LV function in the stable period (5, 6). In the present case, in which the thickening of the septum or LVOT gradient were not so pronounced at rest, HCM with latent obstruction was diagnosed based on the histopathological and DSE findings, and the patient’s family history. During DSE, although no regional wall motion abnormalities appeared, LVOT obstruction and massive MR were reproduced, followed by cardiogenic shock.

The LVOT gradient in HCM patients fluctuates during their daily life activities. Even in patients without outflow obstruction at rest, LVOT gradients can be provoked by physiological and pharmacological interventions that augment left ventricular contractility (7). However, not every patient with dynamic LVOT obstruction has HCM. Some other structural or functional features of the LV may play important roles in the development of LVOT obstruction (8, 9). Indeed, patients with TCM complicated by LVOT obstruction have been reported to frequently present a sigmoid septum (10). However, the underlying mechanisms and features of recurrence of labile LVOT obstruction in TCM patients have not been fully elucidated (11). Latent obstruction can be non-invasively detected by DSE. Thus, in cases that include TCM, DSE could be a useful tool for assessing the presence and significance of LV dynamic obstruction and for clinical decision-making, similarly to cases of HCM (12).
Furthermore, endomyocardial biopsy and cardiac MRI are valuable for further delineating the morphology and characteristics of the LV in order to clarify the underlying disease of the LVH with latent obstruction.

The identification of HCM with latent obstruction should prompt more vigorous pharmacological therapy, including beta-blocker treatment, which would not be routinely employed in the treatment of TCM.

The present report suggests that acute-phase patients with TCM complicated by LVOT obstruction should be considered to have DSE and endomyocardial biopsy to detect the anatomical and physiological substrate for the development of LVOT obstruction in the setting of catecholamine surge.

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References


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