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-echocardiography was performed, which reproduced 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 hypertrophic cardiomyopathy 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/V 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...
was carried out. Although a baseline echocardiogram
tensity and no gadolinium enhancement (Fig. 2A-D).

thickened apical wall with a greater T2-weighted signal in-
demonstrated the complete recovery of the LV function, a
6, the cardiac magnetic resonance imaging (MRI) findings
motion (SAM) of the mitral valve (Fig. 1E-H).

vealed severe MR that was secondary to the systolic anterior
TCM. Echocardiography performed after catheterization re-
gradient was noted (Fig. 1D). She was diagnosed with
the left ventricular apex to the outflow tract, a 50-mmHg
of the LV (Fig. 1B and C). On pullback of the catheter from
showed no significant stenosis. Left ventriculography
as well tolerated. Since then, the patient

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-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).

shock (blood pressure: 48/24 mmHg) and lost conscious-
ess, which necessitated intubation and continuous intrave-
nous noradrenaline infusion. Coronary angiography was per-
formed 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 and C). On pullback of the catheter from
the left ventricular apex to the outflow tract, a 50-mmHg
gradient was noted (Fig. 1D). She was diagnosed with
TCM. Echocardiography performed after catheterization re-
vealed severe MR that was secondary to the systolic anterior
motion (SAM) of the mitral valve (Fig. 1E-H).

The patient was stabilized with intensive therapy. On day
6, the cardiac magnetic resonance imaging (MRI) findings
demonstrated the complete recovery of the LV function, a
thickened apical wall with a greater T2-weighted signal in-
tensity and no gadolinium enhancement (Fig. 2A-D).

On day 13, dobutamine stress-echocardiography (DSE)
was carried out. Although a baseline echocardiogram
showed mild hypertrophy of the LV (the diameters of the in-
traventricular septum and posterior wall were both 12 mm)
and only a modest septal bulge without any intraventricular
pressure gradient, a dynamic LVOT gradient of 250 mmHg
with a late peaking developed during stress, which was ac-
companied by severe MR due to SAM (Fig. 2E-H). The sys-
tolic blood pressure decreased from 120 mmHg to 74
mmHg at peak stress. The impaired wall motion with a di-
lated 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 myo-
cyte disarray, in addition to the multiple foci of contraction-
band myocyte necrosis, which is often documented in pa-
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 symp-
toms.
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).
Figure 3. The histological appearance. The histological appearance of the RV septum demonstrating hypertrophied and bizarre myocytes with myocyte disarray (A: Hematoxylin and Eosin staining), in addition to multiple foci of contraction-band myocyte necrosis (B: PTAH stain; C and D: luxol fast blue staining).

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.

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

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