CASE REPORT

Dobutamine Stress Echocardiography Unmasks Acute Worsening of Mitral Regurgitation with Latent Left Ventricular Outflow Tract Obstruction Behind Diastolic Heart Failure in Hypertensive Heart Disease

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Abstract

In a 57-year-old woman who was referred as refractory diastolic heart failure, dobutamine stress echocardiography facilitated the diagnosis of acute worsening of mitral regurgitation accompanied with latent left ventricular outflow tract obstruction as a cause of recurrent flash pulmonary edema. Echocardiography revealed the presence of sigmoid septum and concentric left ventricular hypertrophy, being consistent with hypertensive heart disease. Dobutamine induced systolic anterior motion of the mitral valve (SAM) with massive mitral regurgitation, resulting in sudden hypotension with dyspnea. The class Ia antiarrhythmic drug, cibenzoline, reduced the SAM during a dobutamine stress test, followed by no recurrence of flash pulmonary edema.

Key words: echocardiography, latent left ventricular outflow tract obstruction, diastolic heart failure, hypertensive heart disease

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Introduction

The most well-known etiology of dynamic left ventricular (LV) outflow tract (LVOT) obstruction is considered to be hypertrophic obstructive cardiomyopathy. The presence and magnitude of the LVOT pressure gradient can be affected by several morphological and hemodynamic factors of the heart (1-6), and latent LVOT obstruction can be non-invasively detected by dobutamine stress echocardiography (DSE) (7, 8). Here, we report a patient with latent LVOT obstruction which was the cause of refractory heart failure.

Case Report

A 57-year-old woman with a history of essential hypertension had recurrent chest pain irrespective of effort and unresponsive to sublingual nitroglycerin for two years. The chest pain usually lasted 5-10 minutes but sometimes persisted for up to 24 hours. Doppler-derived LVOT pressure gradient of 57 mmHg had been documented once by echocardiography. However, cardiac catheterization revealed no significant difference in peak systolic pressure between the LV apex and aorta, no significant coronary artery stenosis, and LV ejection fraction of 76% without mitral regurgitation (MR). Treadmill stress echocardiography showed no significant LVOT pressure gradient during exercise. She was diagnosed as diastolic heart failure when she was admitted six month later because of the increase in incidence of dyspnea along with chest pain. Despite pharmacological treatment with a beta-blocker (metoprolol 40 mg) and an ACE inhibitor (enalapril 2.5 mg), she had experienced two episodes of...
Figure 1. Chest radiograph shows flash pulmonary edema on admission for acute chest pain and dyspnea (Left). When she was transferred to our hospital, the condition of heart failure was compensated. The cardiothoracic ratio is 50.0% (Right).

Figure 2. (A) Electrocardiogram (ECG) shows sinus rhythm and the negative T wave in leads II, III, aVf, and V3-6, and the ECG changes persisted until the discharge of our hospital. (B) Negative T waves disappeared 3 weeks after adding cibenzoline and discontinuing enalapril. The ECG change using neither nitrates nor calcium antagonists was likely the result of the stabilization of hemodynamic status.

flash pulmonary edema in the previous two months (Fig. 1) and negative T waves appeared on electrocardiogram (ECG). Thus, she was transferred to our hospital.

Heart failure in the present patient was compensated on admission (Fig. 1) but she still suffered from dyspnea on exertion. The blood pressure was 120/54 mmHg and the pulse 60/min. The ECG showed sinus rhythm and negative T waves (Fig. 2A). The echocardiography demonstrated concentric LV hypertrophy with wall thickness of 13 mm, the sigmoid septum, the angle between the ascending aorta and the LV long-axis of 60 degrees, and normal systolic function of the left ventricle with no asynergy (Fig. 3). The color Doppler echocardiography showed moderate MR and acceleration flow at the LVOT, but the peak velocity of the flow was up to 2.2 m/s (pressure gradient: 19 mmHg) by Doppler measurement.

DSE was performed to evaluate the latent LVOT obstruction. After the dobutamine infusion rate was increased to 10 μg/kg/min, the severity of MR worsened to severe with the development of systolic anterior motion of the mitral valve (SAM). The peak velocity became 6.0 m/s at 30 μg/kg/min of dobutamine (Fig. 4). At 40 μg/kg/min, systemic blood pressure suddenly dropped from 100/54 mmHg to 60/28 mmHg with dyspnea, and quickly recovered by interruption
Echocardiography demonstrated concentric left ventricular hypertrophy (wall thickness=13 mm), the narrow LVOT (16 mm), the sigmoid septum, the angled ejection flow direction (angle between the ascending aorta and the left ventricular long-axis=66 degrees, diastolic aorto-septal angle=115 degrees), and small cavity size (left ventricular end-diastolic/end-systolic diameter=45/31 mm).

Dobutamine stress echocardiography showed that moderate MR (A) with LVOT acceleration flow of 2.2 m/s at rest (B) and massive MR (D) and LVOT late-peaking Doppler velocity profile reaching 6.0 m/s at 30 μg/kg/min of dobutamine infusion (E). From the M-mode images at rest (C) and dobutamine stress (F), the development of systolic anterior movement of the mitral leaflet is noted (▼).

The dobutamine-induced LVOT pressure gradient was also confirmed at cardiac catheterization. The difference in peak systolic pressure between the LV apex and aorta increased from 20 mmHg at baseline to 94 mmHg at dobutamine infusion of 30 μg/kg/min. Myocardial biopsy revealed moderately hypertrophic cardiomyocytes without disarray, being consistent with hypertensive heart disease rather than hypertrophic cardiomyopathy (Fig. 5).

According to the treatment regimen of hypertrophic obstructive cardiomyopathy (HOCM), the patient was given 300 mg/day of the class Ia antiarrhythmic drug cibenzoline. At the follow-up DSE, the peak velocity at the LVOT was attenuated up to 3.4 m/s at dobutamine 30 μg/kg/min infusion. SAM and the related MR were clearly suppressed as compared to them in the previous DSE. Before hospital discharge we discontinued the ACE inhibitor which has vasodilator action. Since then, small doses of diuretics (furosemide 10 mg and spironolactone 10 mg) were needed for volume control, and no recurrence of flash pulmonary edema has been observed for more than 12 months. Negative T wave disappeared 3 weeks after alteration of the treatment (Fig. 2B).

Discussion

Dynamic LVOT obstruction can be induced by nitrate (2), hypovolemia, vasodilation (3), exercise (4), and catecholamine excess (5-8) in HOCM and it is observed also in hypertensive patients with preserved left ventricular function (9). According to the past reports, echocardiographic findings such as anterior displacement of the papillary muscle (1), the sigmoid septum or subaortic septal bulge with the narrow LVOT (≤20 mm) (10), and angled ejection flow direction [large angle between the ascending aorta and the LV long-axis ≥35 degrees (10) or the decreased aorto-septal angle ≤100 degrees (8)] suggest development of SAM and LVOT obstruction. In the present case, the history of the pressure gradient >30 mmHg also made us consider latent or labile LVOT obstruction.

The results of DSE suggest that the ejection blood flow accelerated by the inotropic action can be responsible for lifting up and sucking the anterior leaflet of the mitral valve when the flow passing by the subaortic septal bulge. In addition, the acutely increased MR caused elevation of left
atrial pressure when considerable LVOT pressure gradient developed with SAM and the decrease of forward stroke volume resulted in the fall of blood pressure. The worsening of MR accompanied with dynamic LVOT obstruction is thought to be a kind of acute MR; left atrial pressure can rise quickly above the limit of compensation of the left atrium, possibly causing rapid onset pulmonary edema. In patients with hypertrophic cardiomyopathy, LVOT obstruction is a strong predictor of death (11). Among patients with diastolic heart failure, a group of patients with acute MR related to latent LVOT obstruction may mediate poor prognosis despite the standard pharmacological therapy including diuretics, aldosterone receptor blockers, ACE inhibitors, and angiotensin II receptor blockers. Although a situational trigger for the provocation of increased LVOT pressure gradient was unknown in the present case, the fact that the combination of SAM and MR induced such a situation during low-dose dobutamine stress implies that the physical and mental activities in ordinary life easily provoke the vicious circle between enhanced sympathetic nerve activation followed by endogenous catecholamine release and worsening of MR. Since the addition of cibenzoline that reduced latent LVOT obstruction was effective for the discontinuation of recurrence of the flash pulmonary edema, the latent LVOT obstruction can be a potential cause of the acute transition to the decompensated condition.  

Class Ia antiarrhythmic drugs can reduce LVOT pressure gradient (12-17). The effects have been explained by the negative inotropic action, resulting in ventricular afterload reduction and deceleration of the LV ejection acceleration (13). Hamada et al (16, 17) reported on the prominent effect of cibenzoline on LV diastolic function which is due to the marked attenuation of intracellular Ca²⁺ overload produced by antagonization of Ca²⁺- and Na⁺-channels, despite less potent anticholinergic effects than disopyramide. In the present case, atrial fibrillation has never been documented even in the acute decompensated status, thus being unlikely as a direct cause of the congestive heart failure. The antiarrhythmic action of cibenzoline is probably a potential benefit. Here, after the addition of cibenzoline and discontinuation of enalapril, the negative T waves of ECG disappeared gradually. Although coronary artery spasm provocation test was not performed, the normalization of negative T waves using neither nitrates nor calcium antagonists is attributable to the stabilization of hemodynamic status rather than the spontaneous abatement of severe coronary artery spasm.  

## Conclusion

This report shows that the class Ia antiarrhythmic drug, cibenzoline, was effective to prevent the recurrence of flash pulmonary edema in a patient who had been treated as diastolic heart failure. Acute worsening of MR accompanied with latent LVOT obstruction is a plausible mechanism for acute decompensated heart failure in patients with preserved LV systolic function, not HCM, diagnosed by histopathology. Since acute MR related to latent LVOT obstruction may produce a poor prognosis in a group of patients with diastolic heart failure, active challenge tests using DSE are recommended for its diagnosis.  

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## References

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