Mitral Regurgitation Disappearance after Cibenzoline Treatment in a Patient with Hypertrophic Obstructive Cardiomyopathy

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Abstract

Hypertrophic obstructive cardiomyopathy (HOCM), which shows left ventricular outflow pressure gradient (LVPG), is often complicated with mitral regurgitation (MR). We examined a 62-year-old Japanese female with HOCM and MR. Ultrasound echocardiography showed severe MR, asymmetrical septal hypertrophy, systolic anterior movement of the mitral valve anterior leaflet, and left ventricular outflow stenosis. Her LVPG, measured using continuous wave Doppler recording, was 118 mmHg. During heart catheterization, the aortic pressure and left ventricular pressure were simultaneously measured. An intravenous injection of 70 mg cibenzoline decreased the LVPG from 110 mmHg to 16 mmHg. Left ventriculography was performed immediately after the injection and did not show MR. This clearly demonstrates that cibenzoline decreases LVPG in patients with HOCM and also improves the MR that arises from LVPG.

Case Report

A 62-year-old Japanese woman, who had been suffering from chest discomfort on effort for 2 years, was referred from an affiliate clinic. She did not have any history of hypertension. Her chest X-ray revealed mild cardiomegaly while her electrocardiogram displayed the voltage criteria for left ventricular hypertrophy (Fig. 1). Her ultrasound echocardiography showed severe MR, asymmetrical septal hypertrophy, and left ventricular outflow stenosis (Fig. 2). Septal hypertrophy involved the proximal portion (dimension, 17 mm) and the middle portion (dimension, 15 mm) of the septum. The dimension of left ventricular posterior wall was 10 mm. Left ventricular systolic and diastolic dimension was 47 mm and 32 mm, respectively. Abnormal anterior movement of the mitral valve anterior leaflet during systole was also observed. Her LVPG, measured using continuous wave Doppler recording, was 118 mmHg. In elderly patients, especially women, sigmoid septum sometimes causes LVPG and subsequent MR. However, considering the extent of septal hypertrophy, absence of a history of hypertension, and the ratio of septal wall to left ventricular posterior wall, this case could be clearly differentiated from sigmoid septum.

She was admitted to our hospital for heart catheterization to assess the severity of her HOCM. A physical examination revealed that her blood pressure was 148/74 mmHg and her heart rate was 82 bpm and regular. A Levine IV/VI systolic
murmur at 4L and a Levine III/VI systolic murmur at apex were heard. Hematological tests and urinalysis were within normal limits. Simultaneous invasive measurement of the left ventricular pressure and aortic pressure showed an LVPG of 110 mmHg (Fig. 3). We also confirmed that there was no stenosis of the aortic valve. After an injection of 70 mg cibenzoline, her LVPG decreased immediately. Three minutes after the end of the injection, her LVPG had almost disappeared (Fig. 3). Left ventriculography, performed immediately after the injection of cibenzoline, showed no mitral regurgitation (Fig. 4). Coronary angiography showed normal coronary arteries. Her heart murmur at the apex almost disappeared while the systolic murmur at 4L decreased significantly to Levine I/VI. The LVPG was well controlled by cibenzoline (300 mg/day, given orally). Due to the decrease in the LVPG, however, the patient’s blood pressure increased to 180/88 mmHg, therefore amlodipine was also administered.

**Discussion**

Cibenzoline clearly reduced both the LVPG and the MR in this patient with HOCM.

Ca antagonists or beta-blockers have been used to decrease LVPG, but in most cases, these types of drugs cannot effectively decrease LVPG. Recently, a class 1a antiarrhythmic drug, disopyramide, has been proven to decrease LVPG in patients with HOCM. However, disopyramide has several adverse effects (including an anticholinergic effect). Hamada

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**Figure 1.** Electrocardiogram shows the voltage criteria for left ventricular hypertrophy.

**Figure 2.** Ultrasound echocardiography shows left ventricular pressure gradient (A) and severe mitral regurgitation (B) before cibenzoline treatment.

**Figure 3.** Simultaneous measurement of aortic pressure and left ventricular pressure before and after an injection of cibenzoline.
et al (1) first showed that another class Ia antiarrhythmic drug, cibenzoline, is more effective in decreasing LVPG in patients with HOCM. In the present case, cibenzoline almost completely eliminated LVPG.

The mechanism by which class Ia antiarrhythmic drugs decrease LVPG is unknown at present. Hamada et al (1) speculate that the mechanism might be the negative inotropic effect of class Ia antiarrhythmic drugs. Some class Ia drugs have a Ca channel blocking effect, although the Ca channel blocking effect of cibenzoline is 50 times smaller than that of
During Na\(^+\) influx, a focal increase in the Na\(^+\) concentration could accelerate Ca\(^{2+}\) influx via a reversal of Na\(^+\)/Ca\(^{2+}\) exchange. Therefore, inhibiting the Ca\(^{2+}\) influx that is induced by the Na\(^+\)-current might influence the negative inotropic effect of class Ia antiarrhythmic drugs. However, the negative inotropic effect of class Ia antiarrhythmic drugs is much smaller than that of beta-blockers or Ca antagonists. Thus, the negative inotropic effect cannot fully account for the mechanism by which class Ia antiarrhythmic drugs decrease LVPG. Hamada et al (3) recently showed that cibenzoline improves diastolic function. This is another possible mechanism by which cibenzoline decreases LVPG in patients with HOCM.

The patient in this case did not have organic mitral disease, and cibenzoline completely eliminated MR. When HOCM is treated surgically through myotomy-myectomy, MR disappears in some patients (4). Yu et al (4) also suggested that the severity of the MR is directly related to the magnitude of the LVPG. Thus, it is highly likely that cibenzoline treatment decreases MR in patients with HOCM. The mechanism by which LVPG induces MR is thought to be a Venturi force. A decrease in the left ventricular pressure (Fig. 3) might be another factor in the decrease in MR. Careful attention should be paid, however, because 10 to 20% of patients with HOCM also have an independent mitral disease. In these cases, additional mitral valve surgery might be necessary.

References