【 CASE REPORT 】

Bisoprolol Successfully Improved the Intraventricular Pressure Gradient in a Patient with Midventricular Obstructive Hypertrophic Cardiomyopathy with an Apex Aneurysm due to Apical Myocardial Damage

Ayano Tezuka [1], Kenjuro Higo [1], Yuta Nakamukae [2], Sanae Nishihara [2], Masaki Kamikawa [2], Chihiro Shimofuku [2], Kazumasa Kawazoe [3] and Mitsuru Ohishi [4]

Abstract:

Midventricular obstructive hypertrophic cardiomyopathy (MVOHCM) is a rare form of hypertrophic cardiomyopathy (HCM). An 80-year-old man was administered bisoprolol and warfarin therapies as treatment for MVOHCM with an apex aneurysm due to myocardial damage and intra-aneurysmal thrombus not complicated by atrial fibrillation. The pressure gradient in the midventricle successfully improved from 53.9 to 21.8 mmHg, and the intra-aneurysmal thrombus disappeared.

Key words: midventricular obstructive hypertrophic cardiomyopathy, bisoprolol, beta-blocker

Introduction

Midventricular obstructive hypertrophic cardiomyopathy (MVOHCM) is a rare form of hypertrophic cardiomyopathy (HCM), occurring in 1-9.4% of patients with HCM (1-4). However, MVOHCM is also easily overlooked because the degree of murmur is often mild. This suggests that the diagnosis of HCM patients with MVO seems greatly influenced by the physician's diagnostic ability (5). This subgroup of patients with HCM is still poorly characterized. Minami et al. (3) reported that the prognosis of MVOHCM might be poorer than that of HCM and that appropriate treatment strategies must be established for patients with MVOHCM.

Many cases of HCM including MVOHCM are treated with beta-blockers, but the effectiveness of beta-blockers for improving the pressure gradient in the midventricle in patients with MVOHCM is unclear. While reports of patients with MVOHCM complicated by apex aneurysmal and intra-aneurysmal thromboses with atrial fibrillation are common, reports of patients with MVOHCM complicated by apex aneurysmal thrombosis with a sinus rhythm are few.

We herein report the case of an 80-year-old man who received bisoprolol and warfarin as a treatment for MVOHCM with apex aneurysm due to myocardial damage and intra-aneurysmal thrombus not complicated by atrial fibrillation.

Case Report

An 80-year-old man presented to the Department of Neurosurgery of the Japanese Red Cross Kagoshima Hospital with a complaint of dizziness. As magnetic resonance imaging of the head revealed a high-density area in the pons, the neurosurgeon made a diagnosis of cerebral infarction. The patient was admitted to the Department of Neurosurgery and administered antiplatelet therapy with ozagrel sodium and clopidogrel sulfate. The dizziness improved after the antiplatelet therapy. Due to the differential diagnosis of cardiogenic cerebral infarction with atrial fibrillation, the patient underwent electrocardiographic monitoring continuously. As a result, electrocardiographic monitoring documented frequent nonsustained ventricular tachycardia (NSVT) with no
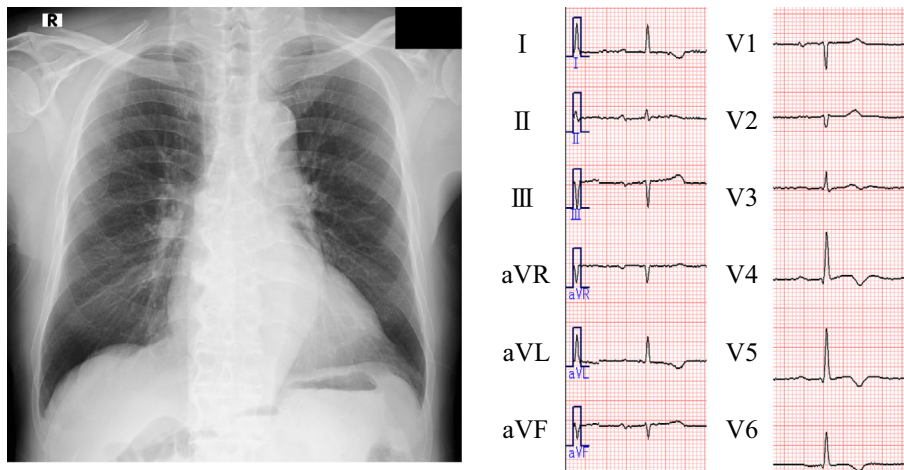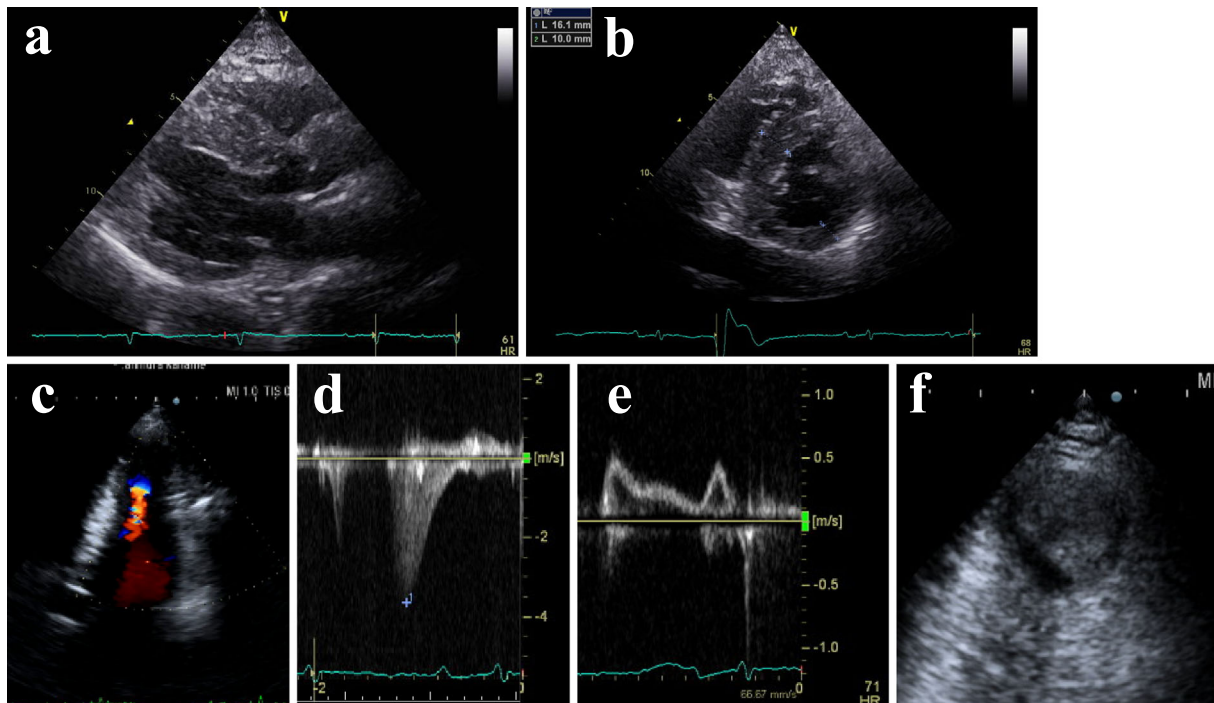
Figure 1. No pulmonary congestion was observed on the chest radiograph. An electrocardiogram showed ST elevation in V5 and V6 and negative T in I, aVL, and V4-V6.


Figure 2. The echocardiogram obtained at admission is shown. The echocardiogram in the parasternal long-axis view (a) and short-axis view (b) showed asymmetric septal hypertrophy. A paradoxical jet flow from the apex toward the base of the left ventricle was observed during early diastole (c). This accelerated flow in the midventricle showed a peak velocity of 2.00 m/s at systole and 3.67 m/s at diastole (d). The E/A velocity ratio was 1.12, showing a pseudonormal transmitral flow pattern (e). Furthermore, echocardiogram revealed an apex aneurysm and thrombosis measuring 21×14 mm (f).

symptoms. An asymptomatic premature ventricular contraction (PVC) of 7,888 beats/day was also documented. Therefore, the patient was referred to our Department of Cardiology for a further evaluation regarding cardiovascular diseases.

The patient's vital signs were as follows: heart rate 71 beats/min and blood pressure 109/72 mmHg. The lungs were clear. We heard a fourth heart sound on auscultation.

Blood tests showed an increased D-dimer level of 5.70 μg/mL and a plasma B-type natriuretic peptide (BNP) level of 525.7 pg/dL. No pulmonary congestion was seen on a chest radiograph (Fig. 1). Electrocardiogram showed the following: an ST elevation in V5 and V6 and a negative T in I, aVL, and V4-V6 (Fig. 1). Echocardiogram revealed asymmetric hypertrophy of the left ventricle (Fig. 2a and b). Doppler echocardiography revealed a paradoxical jet flow
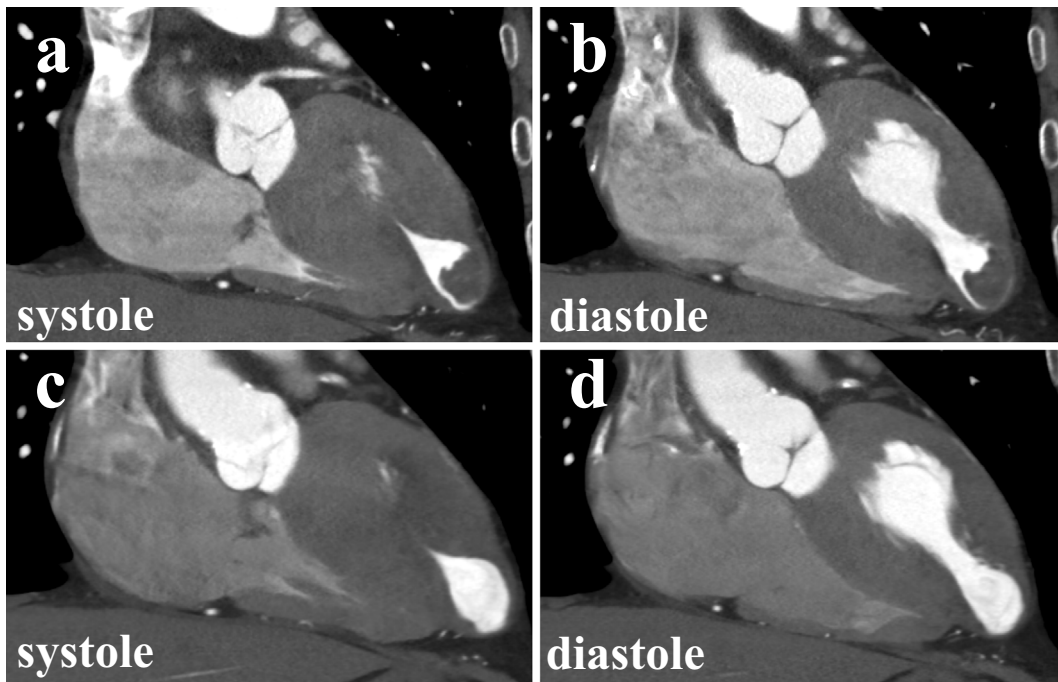
Figure 3. Enhanced computed tomography revealed an apex aneurysm and thrombosis (a and b). After anticoagulation therapy with warfarin, the apex thrombosis disappeared (c and d).

from the apical aneurysm to the left ventricular outflow during early diastole (6) (Fig. 2c). This accelerated flow in the midventricle showed a peak velocity of 2.00 m/s at systole and 3.67 m/s at diastole, respectively (Fig. 2d). Doppler echocardiography also showed an E-wave velocity of 0.54 m/s, an A-wave velocity of 0.48 m/s, and an E/A velocity ratio of 1.12, indicating a pseudonormal transmitral flow pattern (Fig. 2e). The early-diastolic mitral annular velocity (Ea) was 3.4 cm/s, and the E/Ea ratio was 19.2. Furthermore, both the echocardiogram and enhanced computed tomography (CT) revealed an apex aneurysm and a thrombosis measuring 21×14 mm (Fig. 2f, 3a and b). Coronary CT showed that there was no significant stenosis in the left or right coronary arteries, suggesting that ischemic cardiac disease was not the cause of the apex aneurysm. The serum levels of amyloid A protein, angiotensin-converting enzyme, and α-galactosidase A were normal, which suggested the absence of amyloidosis, sarcoidosis, and Fabry disease. Therefore, we made a diagnosis of MVOHCM with complications of apex aneurysm and thrombosis. The patient had no family history of hypertrophic cardiomyopathy.

We decided to immediately start anticoagulant therapy with heparin and warfarin. Based on the head magnetic resonance angiography finding of arteriosclerosis in cerebral arteries, the oral administration of clopidogrel was continued. To prevent NSVT and PVC and decrease the pressure gradient in the midventricle, we initiated oral bisoprolol treatment.

Bisoprolol treatment was started at 0.625 mg/day, with the dosage gradually increased. At a dose of 1.875 mg/day, the patient showed bradycardia during sleep. Although the patient did not exhibit hypotension with bradycardia during sleep and did not show persistent bradycardia during the daytime, we did not increase the dose of bisoprolol to more than 1.875 mg/day, given that the patient was elderly.

Three months after the initiation of bisoprolol treatment, the peak velocity of the accelerated flow in the midventricle decreased from 3.67 to 2.34 m/s at diastole and from 2.00 to 1.67 m/s at systole, respectively (Fig. 4). The pressure gradient in the midventricle decreased from 53.9 to 21.8 mmHg at diastole and from 15.9 to 11.1 mmHg at systole (Fig. 4). The E/A velocity ratio was 0.92, showing an abnormal relaxation transmitral flow pattern. The Ea improved from 3.4 cm/s to 4.73 cm/s, and the E/Ea ratio improved from 19.2 to 16.5. The BNP level decreased from 525.7 to 322.4 pg/mL. NSVT disappeared, and PVC decreased from 7,888 to 2,409 beats/day. Furthermore, the thrombus in the apex aneurysm disappeared (Fig. 3c and d).

Even at eight months after the initiation of bisoprolol treatment, no progression was noted in either the peak velocity or the pressure gradient of the accelerated flow in the midventricle (Fig. 4). The E/A velocity ratio was still 0.92, showing an abnormal relaxation transmitral flow pattern. The E/Ea also was not worsened compared with the value before the administration of bisoprolol.

Throughout the clinical course, the patient did not complain of specific chest symptoms. Furthermore, the NSVT and VPC were asymptomatic. Therefore, we believe that none of the symptoms in this patient were directly related to MVOHCM and that the present case is one of incidentally diagnosed MVOHCM.
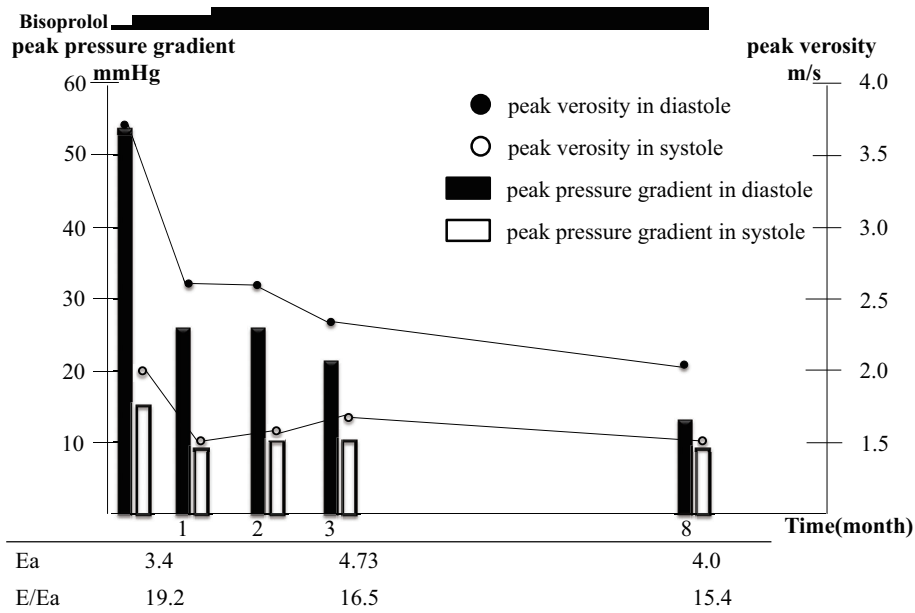
Figure 4.   **The time course of the treatment is shown. Three months after the initiation of bisoprolol, the peak velocity of the accelerated flow in the midventricle decreased from 3.67 to 2.34 m/s at diastole and from 2.00 to 1.67 m/s at systole. The pressure gradient of the midventricle decreased from 53.9 to 21.8 mmHg at diastole and from 15.9 to 11.1 mmHg at systole. The Ea improved from 3.4 cm/s to 4.73 cm/s, and the E/Ea ratio improved from 19.2 to 16.5. Even after eight months, there was no progression in either the peak velocity of the accelerated flow or the pressure gradient. The E/Ea also was not worsened compared with the value before the administration of bisoprolol.**

Discussion

In the present case, bisoprolol successfully improved the pressure gradient in the midventricle. The paradoxical jet flow (6) from the apex toward the base of the left ventricle was observed in early diastole. Nakamura et al. reported that the paradoxical jet flow in patients with MVOHCM is due to the coexistence of mid-chamber obliteration and segmental wall motion abnormalities of the apex (6). In our case, both of these phenomena were observed. Nishikawa et al. reported that the pressure gradient of the midventricle in a patient with MVOHCM who exhibited both mid-chamber obliteration and segmental wall motion abnormalities of the apex was reduced by propranolol during both diastole and systole (7). Similarly, in the present case, the pressure gradient in the midventricle was reduced by bisoprolol during both diastole and systole. Furthermore, Doppler echocardiography on admission showed a restrictive transmitral flow pattern, but three months later, the abnormal relaxation pattern was observed, indicating that the relaxation ability had improved. The Ea was also improved. These findings suggest that bisoprolol might be able to improve the pressure gradient of the midventricle in some patients with MVOHCM.

Recently, although beta-blockers have been effective in relieving clinical symptoms, especially in patients with hypertrophic obstructive cardiomyopathy (HOCM), it has generally been acknowledged that beta-blockers cannot dramatically improve the pressure gradient in patients with HCM (8-10). In patients with HOCM, several factors affecting the pressure gradient in the outflow tract of the left ventricle, such as septal hypertrophy, anterior deposition of papillary muscle, or systolic anterior movement of the mitral valve, are recognized (8). Therefore, in general, patients with HOCM are treated with not only beta-blockers but also calcium antagonists, type 1A antiarrhythmic drugs, pacemaker therapy, or surgical therapy (8). In our case, we did not note any other causes of midventricular obliteration, such as systolic anterior movement of the mitral valve. We believe that, in our case, the pressure gradient of the midventricle was simply caused by chamber obliteration, which explains the effectiveness of bisoprolol. Furthermore, we speculate that the response to beta-blockers may differ between patients with HOCM and those with MVOHCM.

Several case reports on patients with MVOHCM have been published (11-19), but few reports have described the effectiveness of beta-blockers on improving the pressure gradient in the midventricle. Recently, two single-center cohort studies on patients with MVOHCM in Japan (3) and Greece (4) were published. In these studies, although medical treatments including beta-blockers and the prognosis of patients with MVOHCM were reported, the effectiveness of each medication on the pressure gradient in patients with MVOHCM was unclear. Aoki et al. classified patients with MVOHCM into three groups based on the morphological cardiac imaging characteristics of the left ventricle to investigate for complications and treatment (20). Although the ef-

fectiveness of beta-blockers was not discussed in that study, we agree with their suggestion that the response to therapy in patients with MVOHCM may depend on the type of obliteration in the midventricle. In the cohort study reports of Minami et al. (3) and Efthimiadis et al. (4), the relationship between the type of obliteration in the midventricle and the response to the medical treatments was unclear. In addition, the presence of a paradoxical jet flow in each patient, which we believe may indicate the type of obliteration in the midventricle, was also unclear. The relationship between the type of obliteration characterized by the paradoxical jet flow and the response to medical treatments, including beta-blockers, should therefore be clarified in future studies.

Regarding the mechanism underlying aneurysm formation in patients with MVOHCM, Fighali et al. suggested that midventricular obstruction and pressure overload lead to myocardial dysfunction with dilatation of the apical chamber (21). We believe that this mechanism may underlie the aneurysm formation in our case, as the apical aneurysmal thrombosis in our patient occurred with a sinus rhythm, suggesting that apical myocardial damage led to the thrombosis. We speculate that MVOHCM with an apex aneurysm, which was reported by Fighali et al., may be one type of MVOHCM that is responsive to beta-blockers.

Needless to say, we believe that MVOHCM may not be a contraindication for surgical therapy (15), dual-chamber pacing (18), or percutaneous myocardial ablation (19) if medical therapies, including beta-blockers, are insufficient to improve the pressure gradient of the midventricle in patients with MVOHCM (15) or if the use of beta-blockers is contraindicated, such as in patients with vasospastic angina (16).

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

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