INTERNAL MEDICINE

□ CASE REPORT □

Cardiogenic Shock due to Left Ventricular Outflow Obstruction and Complete Atrioventricular Block in a Patient with Hypertrophic Cardiomyopathy with Acute Myocarditis

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Abstract

A 67-year-old woman was referred to our hospital with a sudden syncopal attack. She suffered from cardiogenic shock due to left ventricular (LV) outflow stenosis with simultaneous complete atrioventricular (AV) block. An endomyocardial biopsy of the left ventricle demonstrated myocardial disarray and myocardial fibrous and edematous tissue with infiltration of mononuclear cells. Cardiac magnetic resonance imaging (cMRI) detected a damaged septal area that was likely associated with the conduction disturbance. The diagnosis was hypertrophic cardiomyopathy accompanied by acute myocarditis. Although the LV outflow stenosis was transient, the complete AV block was persistent, thus requiring permanent pacemaker implantation.

Key words: acute myocarditis, hypertrophic cardiomyopathy, complete atrioventricular block, cardiogenic shock, MRI

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Introduction

In patients with acute myocarditis, myocardial injury leads to transient interstitial edema, which induces thickening of the ventricular wall (1, 2), occasionally also causing asymmetrical septal hypertrophy (ASH) and narrowing of the cavity of the left ventricle (LV), producing hypertrophic obstructive cardiomyopathy (HOCM) (3). Patients with acute myocarditis may also present with complete atrioventricular (AV) block. Moreover, its clinical features vary, ranging from asymptomatic to fulminant forms, with cardiogenic shock due to severe left ventricular dysfunction. There are, however, no previous reports of patients presenting with hypertrophic cardiomyopathy (HCM) and cardiogenic shock due to LV outflow obstruction and complete AV block in association with acute myocarditis.

In this report, we present a case of HCM with cardiogenic shock due to LV outflow obstruction with simultaneous complete AV block associated with acute myocarditis.

Case Report

A 67-year-old woman was urgently referred to our hospital for a sudden syncopal attack. Although she had been suffering from mild dyspnea on effort since the age of 30, she had neither previously undergone a precise medical examination nor was she on any medication. Her family history was unremarkable.

On admission, the patient was hemodynamically unstable, with a blood pressure of 63/39 mmHg, pulse rate of 43 bpm and body temperature of 36.7℃. A physical examination revealed a Levine IV/VI systolic murmur in the area of the cardiac apex and coarse crackles in almost all lung fields. A chest X-ray in the supine position revealed cardiomegaly and pulmonary congestion (Fig. 1A). An electrocardiogram (ECG) showed complete AV block with atrioventricular junctional rhythm, and ST segment depression in leads I, II,

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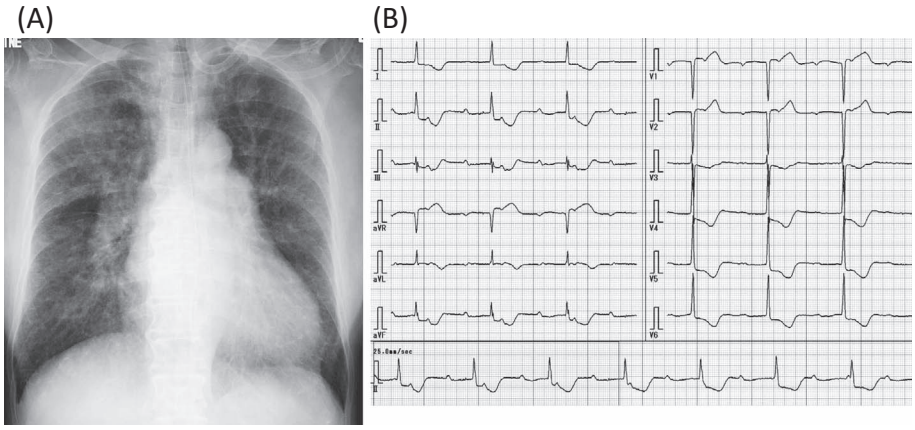

Figure 1. **(A) A chest X-ray revealed cardiomegaly and pulmonary congestion. (B) An ECG on admission showed complete atrioventricular (AV) block with AV junctional rhythm, and ST segment depression in leads I, II, III, aVL, aVF and V3-6.**

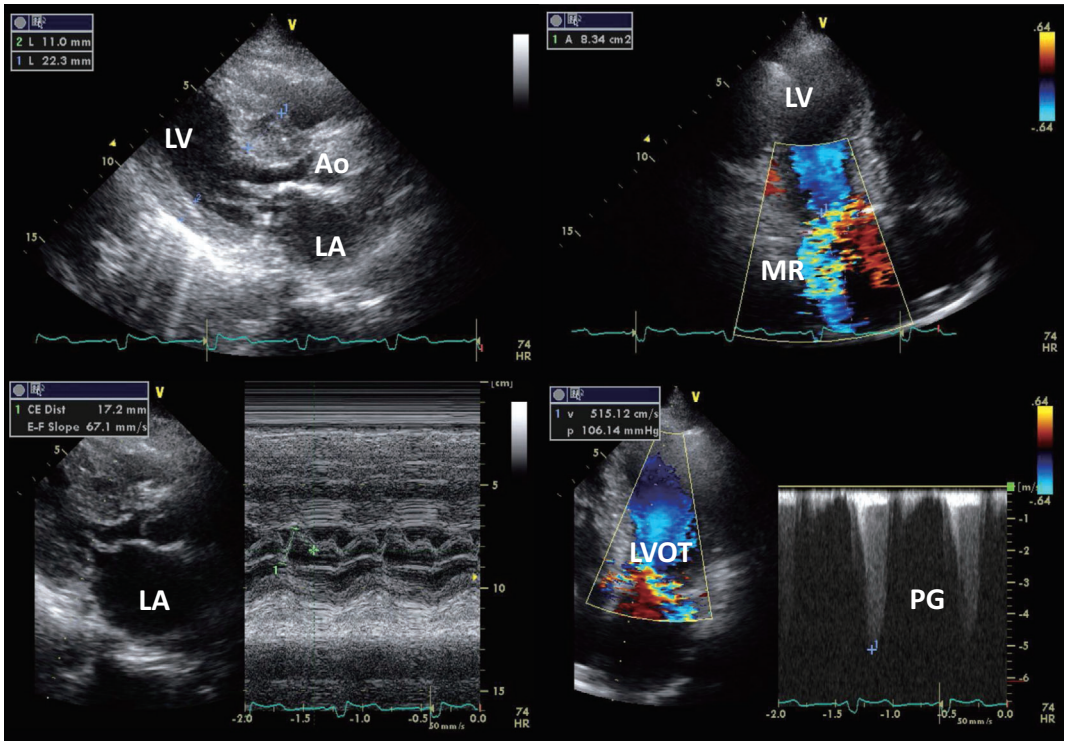

Figure 2. **Cardiac ultrasonography (UCG) showed normal LV systolic function with asymmetric septal hypertrophy (ASH). LV outflow tract obstruction with a pressure gradient of 106 mmHg was also seen. Severe mitral regurgitation (MR) occurred as a consequence of systolic anterior movement (SAM) of the mitral leaflets (arrow).**

III, aVL, aVF and V3-6 (Fig. 1B). Ultrasonic echocardiography (UCG) showed normal LV systolic function with asymmetrical septal hypertrophy (ASH) (thickness of the interventricular septum (IVS): 22 mm, and thickness of the posterior wall (PW): 11 mm), an end-diastolic diameter of 34 mm, end-systolic diameter of 22 mm and ejection fraction of 65%. LV outflow tract obstruction was seen with a pressure gradient of 106 mmHg. Severe mitral regurgitation (MR) also occurred as a consequence of the systolic anterior movement (SAM) of the mitral valve leaflets (Fig. 2).

The patient's laboratory data on admission are shown in Table. Her hemoglobin level and white blood cell count were normal. The serum levels of creatine phosphokinase (CK), CK-MB and C-reactive protein were normal on admission, but on day one after admission, the CK, CK-MB and high sensitive troponin T levels had increased to 3,027 U/L, 266 U/L and 4.760 ng/mL, respectively. The N-terminal pro-brain natriuretic peptide was also elevated. Her serum level of angiotensin-converting enzyme, a marker of sarcoidosis, was normal. Because she had severe hypoxia

Table. Laboratory Data on Admission

WBC	8,300 /μL	BUN	14 mg/dL	Arterial blood gas	
RBC	419×10^4 /μL	Cre	0.96 mg/dL	PH	7.279
Hb	13.4 g/dL	Na	141 mEq/L	PCO2	34.8 torr
Hct	39%	K	4.2 mEq/L	PO2	62.9 torr
PLT	16.2×10^4 /μL	Cl	107 mEq/L	HCO3	15 mEq/L
TP	7.2 g/dL	BS	128 mg/dL	BE	9.7mmol/L
T-Bil	1.0 mg/dL	CRP	0.03 mg/dL	O_2SAT	86.8%
AST	22 IU/L	CK	69 IU/L		(room air)
ALT	15 IU/L	CK-MB	7 IU/L		
LDH	275 IU/L	NT-pro BNP	6847 pg/mL		

WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, Hct: hematocrit, PLT: platelets, TP: total protein, T-bil: total bilirubin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, BUN: blood urea nitrogen, Cre: creatinine, BS: blood sugar, CRP: C-reactive protein, CK: creatine kinase, NT-pro BNP: N-Terminal pro-brain natriuretic peptide (normal <131 pg/mL)

due to acute heart failure, she was intubated for mechanical ventilation. Temporary pacing was introduced for the complete AV block and cardiac catheterization was performed to examine the cause of the cardiogenic shock. Coronary angiography showed no significant coronary artery stenosis, and left ventriculography demonstrated normal LV systolic function with narrowing of the LV cavity. Cardiac catheterization showed that the pressure gradient across the LV outflow tract was 120 mmHg. As these findings indicated HOCM or acute myocarditis, an endomyocardial biopsy of the LV was performed. A histological examination demonstrated a hypertrophic myocardium with myocardial disarray, replacement interstitial fibrosis and interstitial edema with obvious infiltration of mononuclear cells. These mononuclear cells were positive for anti-human leukocyte common antigen (Fig. 3). All of these findings collectively indicated a diagnosis of HCM with acute myocarditis.

After temporary pacing was performed, bisoprolol and cibenzoline were started for treatment of the LV outflow obstruction. As a result, the pressure gradient across the LV outflow tract gradually decreased from 106 mmHg to 20 mmHg, the mitral regurgitation almost disappeared within nine days, and the complete AV block had disappeared by two weeks after admission. The thickness of the IVS wall also decreased from 22 mm to 16 mm (Fig. 4). The patient gradually recovered from the critical phase of acute myocarditis, and her complete AV block reverted to normal sinus rhythm. Following this recovery, the patient could be successfully weaned from temporary pacing and the ventilator. Anti-viral antibody examinations for the coxsackie A and B virus, enterovirus, echovirus, and parainfluenza and adenoviruses that were performed on admission and three weeks later were all negative.

An electrophysiological study (EPS) was performed three weeks after admission, which showed normal cardiac conduction without infra-hisian block as follows: the AH time was 132 ms and HV time was 47 ms; the Wenckebach point was on 160 bpm and a 2:1 AH block was at 170 bpm of right atrial (RA) pacing. We therefore decided not to implant a permanent pacemaker and she was discharged on the 40th day after admission. However, gadolinium-enhanced cardiac MRI performed on the 38th day after admission still showed isolated delayed uptake of contrast in the transmural anterior IVS, mid-layer of the middle IVS, and subendomyocardium of the posterior IVS, and edematous changes in the subendomyocardium of the IVS, although the thickness of the IVS had decreased to 16 mm (Fig. 5). Seven days after discharge, the patient was readmitted to our hospital for dizziness. ECG showed an intermittent complete AV block. Her UCG showed left ventricular hypertrophy with ASH (thickness of the IVS: 13 mm, thickness of the PW: 11 mm, end-diastolic diameter: 35 mm and end-systolic diameter: 20 mm), but the pressure gradient across the LV outflow tract was only 15 mmHg. A laboratory examination revealed that the cardiac inflammatory enzyme levels were not elevated. Due to the recurrence of the complete AV block, the patient was treated by dual-chamber permanent pacemaker implantation. After pacemaker implantation, she had no more cardiac symptoms and was once again discharged.

At the time of the pacemaker check about one week after the implantation, we performed RA pacing by the implanted pacemaker, which demonstrated that RA pacing of 90 bpm induced complete AV block, suggesting organic damage of the AV conduction system as a result of the myocarditis, because there was no evidence of recurrence of the myocarditis. Six months after the acute phase, her UCG showed left ventricular hypertrophy with mild LV outflow stenosis, as before.

Discussion

HCM is a relatively common genetic heart disease diagnosed clinically by the presence of unexplained cardiac hypertrophy. However, there have been several reports about patients with acute myocarditis mimicking HCM, with reversible ASH producing transient LV outflow stenosis (4-9). Histopathological studies have suggested that the transient ventricular wall thickening in acute myocarditis is induced

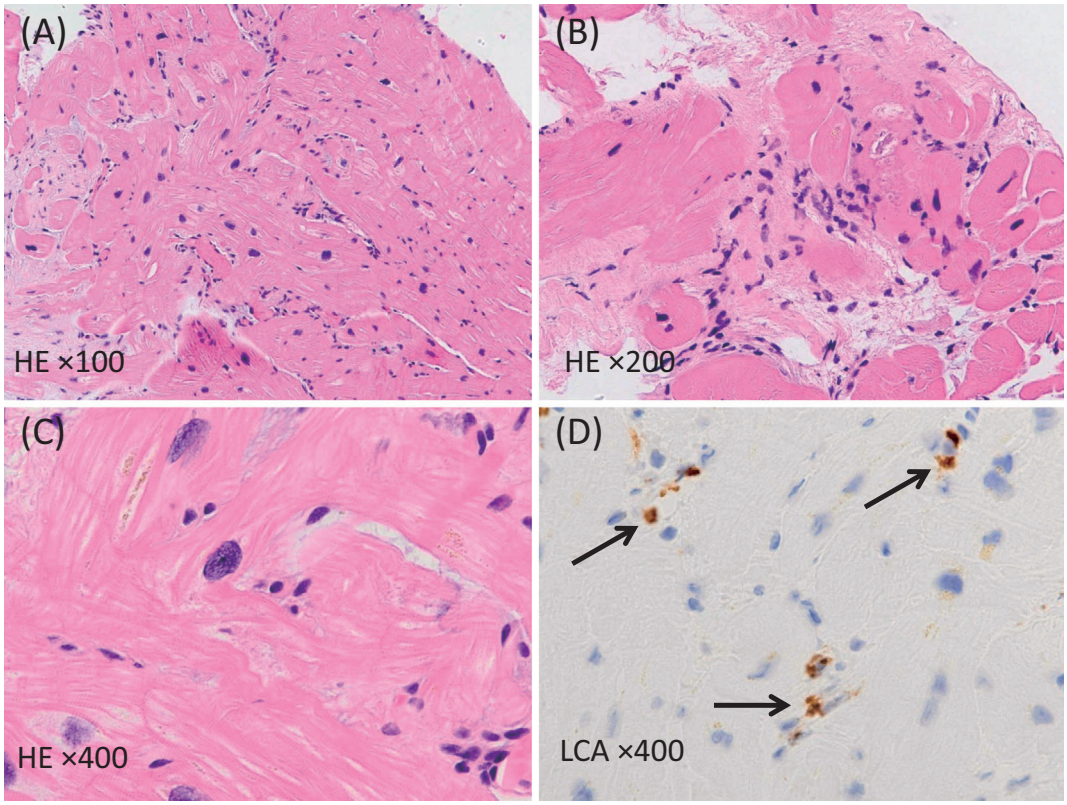

Figure 3. **Representative histological findings in endomyocardial biopsy samples. (A-C) Hypertrophic myocardium with myocardial disarray, and replacement interstitial fibrous and interstitial edema with infiltration of mononuclear round cells was observed (Hematoxylin and Eosin staining, original magnification ×100, A; ×200, B; ×400, C). (D) The mononuclear round cells were positive for anti-human leukocyte common antigen.**

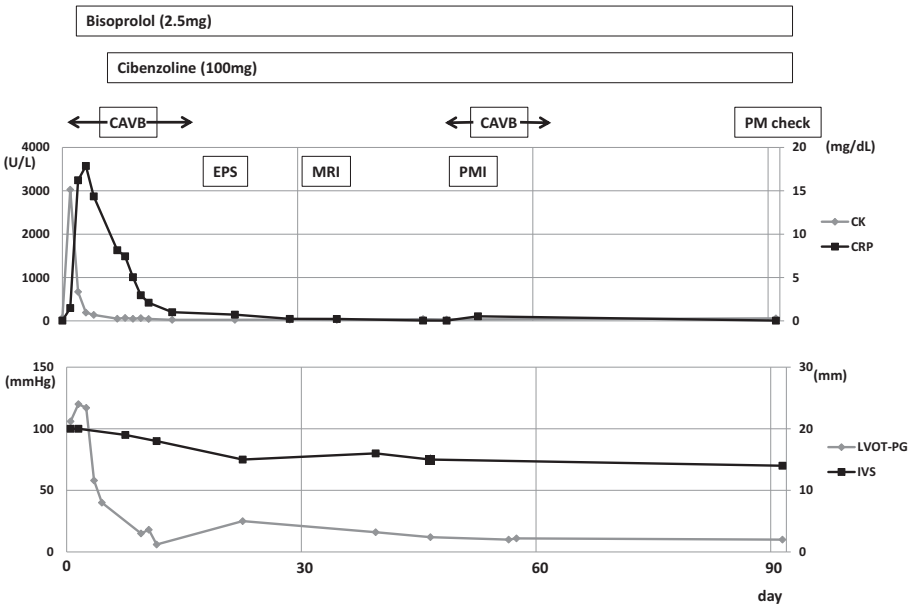

Figure 4. **The patient's clinical course. The C-reactive protein and creatine phosphokinase levels were elevated at the start of therapy, but gradually normalized after several days. After resolution of the acute myocarditis and treatment with medications, the thickness of the IVS decreased and the LV outflow stenosis was ameliorated, although there was still septal hypertrophy and mild LV outflow stenosis. CAVB: complete atrioventricular block, EPS: electrophysiological study, MRI: magnetic resonance imaging, PMI: pacemaker implantation, PG: pressure gradient**

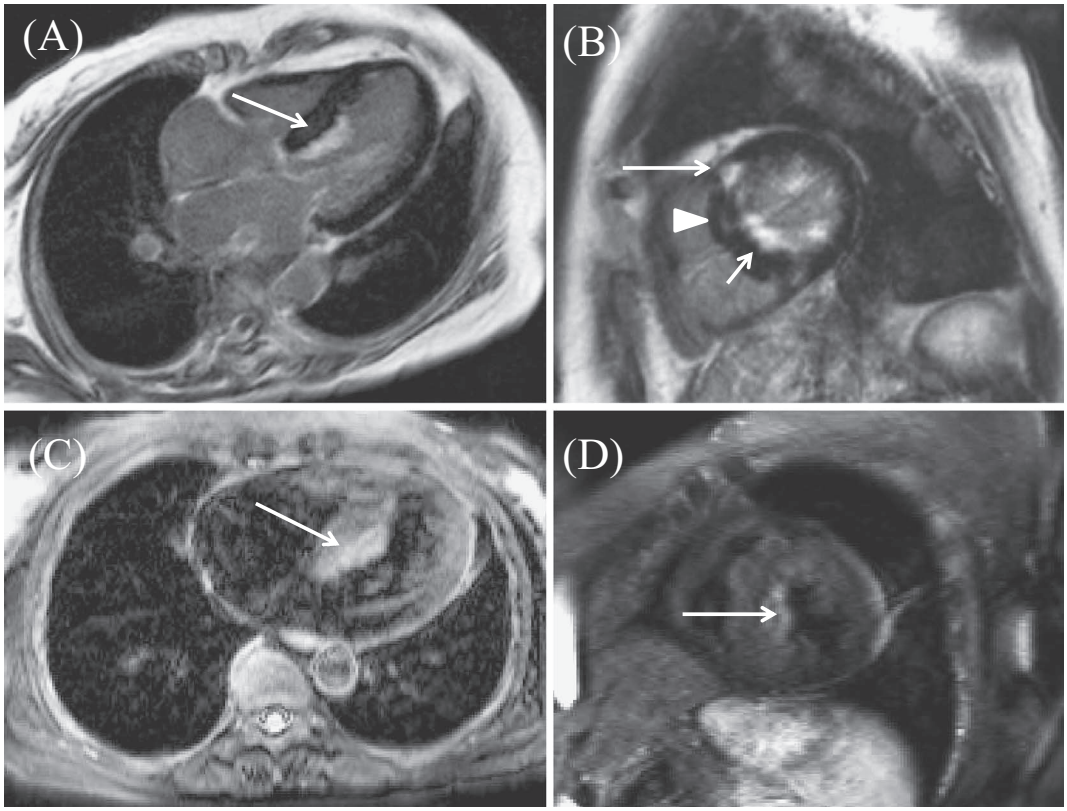

Figure 5. **(A, B) Cardiac MRI with delayed contrast enhancement in the transmural anterior IVS (long arrow), mid-layer of the middle IVS (arrow head), and subendomyocardium of the posterior IVS (small arrow). (C, D) T2-weighted MRI showed edematous changes in the subendomyocardium of the IVS.**

by myocardial interstitial edema (1, 3), which also induces narrowing of the left ventricular cavity at the end-diastolic phase (2). These findings suggest that the diagnosis of HCM may be difficult in cases with acute myocarditis.

There are only two previous reports of acute myocarditis with HCM identified by histological studies (10, 11). One of the patients died of cardiogenic shock due to Fiedler's myocarditis and the other had transient LV outflow obstruction. However, neither of those cases had complete AV block. There seem to be two major mechanisms that induce LV outflow obstruction in the acute myocarditis associated with HCM. One is due to myocardial edema of the basal IVS, and the other involves hyperkinesis of the basal IVS in association with extensive hypokinesis, including of the apical region of the LV. In previous reports, the latter mechanism seemed to induce transient LV outflow stenosis. Therefore, stress cardiomyopathy, i.e., LV apical ballooning with hyperkinesis of LV outflow, has to be considered as a differential diagnosis in such cases.

In the present case, cMRI demonstrated that there was myocardial edema mainly in the endomyocardium of the basal IVS. An endomyocardial biopsy of the left ventricle showed myocardial disarray and fibrous and edematous tissue with infiltration of mononuclear cells that were positive for leukocyte common antigen. After resolution of the acute myocarditis, the thickness of the IVS decreased and the LV outflow stenosis was ameliorated, although there was still septal hypertrophy and mild LV outflow stenosis. Taken together, these findings indicated that the myocardial edema due to acute myocarditis induced a transient severe LV outflow obstruction, in addition to the septal hypertrophy due to HCM in the present case.

Drugs with negative inotropic effects are widely used to decrease obstruction in patients with HCM (12, 13). In the present case, beta-blockers and cibenzoline were used, which resulted in a dramatic decrease in the LV outflow obstruction even before the IVS swelling could decrease after the treatment of the acute myocarditis. There is only one previous report describing a disopyramide-induced decrease in LV outflow obstruction resulting from transient LV apical hypokinesis caused by acute myocarditis in a patient with HCM (11). Our case further confirms that drugs with negative inotropic effects are useful for the treatment of LV outflow obstruction in association with acute myocarditis in patients with HCM, as well as HOCM.

Our patient also had persistent AV block. Histopathological studies in previous cases suggested that myocardial edema is mainly responsible for the transient complete AV block in acute myocarditis (14). Although transient complete AV block was often seen in patients with acute myocarditis in previous reports, persistent AV block occurs in only 22-28% of patients with acute myocarditis with complete AV

block (15, 16). In the present case, cMRI demonstrated that there was myocardial damage mainly in the subendomyocardium at the base of the IVS, close to the site of the atrioventricular node. In HCM, scarring occurs mostly in hypertrophied regions and is usually patchy with multiple foci, predominantly affecting the mid-ventricular wall (17). Therefore, acute myocarditis can induce myocardial damage, including in the AV conduction system, resulting in disturbed AV conduction. In the present case, perhaps as a results of the treatment with beta blockers and cibenzoline, EPS showed normal AV conduction. However, the conduction disturbances recurred after regression of the myocarditis. Ohmae et al. (18) reported in their study on murine myocarditis that the appearance of complete AV block in myocarditis may suggest not only significant pathology of the conduction system, but also trivial edematous changes. In the present case, the myocarditis seems to have persisted longer than ordinary cases, because cMRI showed myocardial edema, as well as myocardial damage, at the base of the IVS as severe myocardial inflammation more than one month after admission. Taken together, these findings suggest that there was progression of damage to the AV conduction system near the base of the IVS by the persistent myocarditis, which may have provoked the recurrence of AV block after the disappearance of the initial AV block, and this was mainly induced by the edematous changes that occurred in the acute phase of myocarditis.

The precise reason why myocardial edema and damage due to myocarditis occur mainly in the basal area of the IVS in HCM patients is unknown. However, mechanical stress may enhance the damage to the myocardium caused by myocarditis or may make the myocarditis more persistent, because the basal area of the IVS, especially the endocardial site, is subjected to the stress of turbulent flow and high pressure induced by the LV outflow stenosis associated with HCM. This may also explain why the late gadolinium enhancement and myocardial edema were prominent at the subendocardium in the basal area of the IVS, in addition to focal areas of the mid-layer and transmural IVS, although MRI usually shows a focal area of subepicardial late gadolinium enhancement in patients with myocarditis.

Cardiac sarcoidosis is one of the causes of AV block, which can cause myocardial changes mimicking HCM in the acute phase (19, 20). Previous reports indicate that cardiac sarcoidosis predominantly affects the basal myocardium and the subepicardial layer (21), which is different from the endomyocardial damage seen in our patient. Moreover, in our patient, the IVS wall thickness decreased without steroid therapy within about one month. These differences in the myocardial damage pattern demonstrated by cMRI in our patient, in addition to the differences in the clinical course between acute myocarditis and cardiac sarcoidosis, indicate that cardiac sarcoidosis was not responsible for our patient's disease.

In conclusion, acute myocarditis with HCM should be considered in patients presenting with cardiogenic shock due to LV outflow obstruction and complete AV block.

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

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