Hypertrophic Cardiomyopathy Complicated by Cardiac Sarcoidosis Diagnosed by Both the Morphological Abnormalities and the Time Course of the Disease

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Summary

The definite diagnosis of cardiac sarcoidosis (CS) can be difficult because it mimics other cardiomyopathies and morphological abnormalities during its time course. Distinguishing CS isolated cardiac sarcoidosis from other cardiomyopathies is very important for the introduction of immunosuppressive therapy.

In this study, we report a patient who had initially been diagnosed with hypertrophic obstructive cardiomyopathy (HOCM). The patient developed complete atrioventricular block (CAVB) and morphological abnormalities, which led to his primary diagnosis being re-conducted. Moreover, we made a definite diagnose of isolated CS (ICS) based on the guideline for the diagnosis and treatment using 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/CT)1) and performed tailor-made treatment including immunosuppressive therapy.

Key words: Isolated cardiac sarcoidosis, Hypertrophic obstructive cardiomyopathy

Sarcoidosis is a systemic granulomatous disease of unknown cause. CS characterized by granulomas in the myocardium presents with various pathologies, e.g., atrioventricular block, ventricular arrhythmias, and a reduced ventricular function. Furthermore, many different morphological abnormalities, such as localized myocardial thickening, ventricular aneurysm, diffuse myocardial thinning, and left ventricular dilatation, can also be seen in CS. Therefore, CS can mimic other cardiomyopathies and can be difficult to diagnose definitively.

Case Report

The patient was a 69-year-old man with a history of HOCM and pacemaker implantation. He was referred to our hospital for worsening heart failure due to the onset of atrial fibrillation. He had been diagnosed with HOCM five years previously and had received DDD pacemaker implantation for CAVB four years previously. At the same time, intracardiac thrombus at the left ventricular apical aneurysm was observed despite no significant stenosis of the coronary artery. He had started to take warfarin as an anticoagulant. A year later, he had developed myocardial infarction showing total occlusion of the right coronary artery (RCA) due to apical thrombus, and reperfusion of the RCA was attained using intravenous heparin.

On admission, a chest X-ray showed slight cardiomegaly with a cardiothoracic ratio (CTR) of 61.2%, mild bilateral congestion, and a small amount of pleural effusion (Figure 1). A 12-lead electrocardiogram (ECG) showed paced-QRS morphology at the right ventricular apex with a QRS width of 208 ms (Figure 1). Transthoracic echocardiography showed a reduced left ventricular ejection fraction (LVEF; 30%), local hypertrophy of the base to mid-interventricular septum, local thinning of the apex and inferior and posterior LV wall, and LV apical aneurysm (Figure 2). Obstruction of the left ventricular outflow tract was not observed. Given his medical history of CAVB and echography findings, a diagnosis of sarcoidosis was suspected.

18F-FDG-PET/CT demonstrated a high FDG uptake in the basal interventricular septum and basal inferior wall of the heart, but nowhere else in other organs (Figure 3). His blood tests indicated that his angiotensin-converting enzyme and serum interleukin-2 receptor levels were within the normal range (18.8 U/L and 276 U/mL, respectively). A definitive diagnosis of ICS was made, even though an endomyocardial biopsy was not performed.1)

Stepwise treatment was performed. First, radiofrequency catheter ablation for atrial fibrillation, such as pulmonary vein isolation, roof line ablation, and cavotricuspid isthmus ablation using a 3.5-mm-tip externally irrigated ablation catheter, was performed (Figure 4). His blood tests indicated that his angiotensin-converting enzyme and serum interleukin-2 receptor levels were within the normal range (18.8 U/L and 276 U/mL, respectively). A definitive diagnosis of ICS was made, even though an endomyocardial biopsy was not performed.1)

Stepwise treatment was performed. First, radiofrequency catheter ablation for atrial fibrillation, such as pulmonary vein isolation, roof line ablation, and cavotricuspid isthmus ablation using a 3.5-mm-tip externally irrigated ablation catheter, was performed (Figure 4). The DDD pacemaker was then upgraded to a cardiac resynchronization therapy defibrillator (CRT-D) with extraction of the right ventricular (RV) lead (Figures 5, 6). Biven-
Figure 1. Chest X-ray and 12-lead ECG findings on admission. A: Chest X-ray showed slight cardiomegaly with a cardiothoracic ratio of 61.2%, mild bilateral congestion, and a small amount of pleural effusion. B: An electrocardiogram showed the paced-QRS morphology at the right ventricular apex with QRS width of 208 ms.

Figure 2. Transthoracic echocardiography showed a reduced left ventricular ejection fraction (LVEF: 30%), local hypertrophy of the base to mid-interventricular septum, LV apical aneurysm, and local thickness of the apex and inferior and posterior LV wall. LV indicates left ventricle; and RV, right ventricle.
Cardiac sarcoidosis mimics HCM

Figure 3. A: 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/CT) imaging demonstrated a high FDG uptake in the basal interventricular septum and the basal inferior wall of the heart. B: One year after steroid introduction, the 18F-FDG uptake in the heart had diminished.

Figure 4. Radiofrequency catheter ablation for atrial fibrillation, pulmonary vein isolation, roof line ablation, and cavitricuspid isthmus ablation were performed. A: Catheter position in the left anterior oblique (LAO) view. B: The red circles on the CARTO (Biosense Webster Inc., Diamond Bar, California) image indicate the point of ablation.

Tricuspid pacing resulted in a QRS width of 148 ms than a QRS width of 208 ms by RV apex pacing and corrected the left ventricular (LV) dyssynchrony caused by RV pacing (Figure 7). Finally, immunosuppressive therapy using steroids was introduced. Prednisolone was gradually decreased from 30 mg to 10 mg daily over 4 months.

At follow-up PET/CT one year after steroid introduction, the 18F-FDG uptake in the heart had decreased (Figure 3). The thickness of the interventricular septum at 3 and 15 months after using steroid was 18 mm and 19 mm, respectively. At the 15-month follow-up, a chest X-ray demonstrated a decrease in the CTR without pulmonary congestion, and a 12-lead ECG showed paced-QRS morphology at biventricular pacing with a QRS width of
Figure 5. Upgraded to CRTD with the extraction of the RV lead from the DDD pacemaker. The right ventricular apical lead was extracted via a femoral approach/snare technique. RAO indicates right anterior oblique.

Figure 6. Upgraded to CRTD with the extraction of the RV lead from the DDD pacemaker. A: A right ventricular (RV) defibrillator lead was placed at the RV apex. A left ventricular lead was placed at the lateral vein. B: Biventricular pacing resulted in a QRS width of 148 ms.
156 ms (Figure 7). The LV end-systolic volume index had decreased by over 30%, and the LVEF had increased at 3 and 15 months after therapeutic intervention (Figure 8).

He has not been hospitalized for heart failure in the 2-year follow-up period under sinus rhythm, biventricular pacing, and a maintenance dose of prednisolone (10 mg daily).

Discussion

In some cases, CS manifests hypertrophy and mimics HCM.2,3) Saito et al. reported a drastic structural transition of the basal interventricular septum from “hypertrophic” to the thin stage in ICS masquerading as HCM.4) At the first visit to our hospital, 5 years after his diagnosis with HOCM at another hospital, the thickness of the interventricular septum was 21 mm, although the obstruction of the LV outflow tract was not observed. No interventricular thinning—a characteristic finding of CS—was observed. Both the morphological abnormalities, namely, the echocardiography findings of the LV apical aneurysm,5) which did not correspond to the normal flow of the coronary artery, local hypertrophy and thinning, and the time course of the disease that means the occurrence of thromboembolism induced by the thrombus at the apical aneurysm were compatible with a history of HCM. His medical history of CAVB was the decisive reason for the differential diagnosis of CS for us.

Very little information is available on atrioventricular block associated with HCM,6-7) and the occurrence of CAVB in HCM patients is rare.8-12) Among HOCM patients who underwent septal reduction, AV block requiring permanent pacing occurred in approximately 2%-3% of patients after septal myectomy and 10%-15% of patients...
after alcohol septal ablation. However, this patient had not undergone septal reduction. The utility of delayed contrast enhancement of the myocardium on gadolinium-enhanced magnetic resonance imaging (MRI) for the diagnosis of CS has been reported; however, MRI is contraindicated for patients with non-MRI-conditional cardiac implantable electronic devices, like the present case. The $^{18}$F-FDG-PET uptake was useful for prompting a diagnosis of ICS. CRTD implantation was selected out of consideration of the future potential of ventricular arrhythmias associated with CS, despite no documentation of ventricular tachycardia in this patient. The occurrence of ventricular arrhythmias is also common in HCM.

As previously mentioned, both the time course of the disease and morphological abnormalities in this case were compatible with HCM. We suspected CS based on his history of CAVB and were ultimately able to diagnose him with ICS using $^{18}$F-FDG PET/CT. In addition, the dilated phase of HCM and pacing-induced cardiomyopathy were proposed as possible reasons for the reduced LVEF. Local hypertrophy of the base to mid-interventricular septum was observed after using steroid; we diagnosed him with HCM complicated by CS. We should have performed endomyocardial biopsy to confirm the diagnosis of HCM and other secondary cardiomyopathies, including sarcoidosis. Distinguishing CS from other cardiomyopathies is crucial for determining treatment strategies, especially immunosuppressive therapy. We should recall that CS can mimic HCM in both morphological abnormalities of local hypertrophy in the ventricular wall and the time course of the disease, e.g., the presence of ventricular arrhythmias, thromboembolic events, and heart failure.

Disclosure

Conflicts of interest: None.

References

1. Terasaki F, Azuma A, Anzai T, et al. JCS 2016 guideline on diagnosis and treatment of cardiac sarcoidosis - Digest version. Circ J 2019; 83: 2329-88.
2. Matsumori A, Hara M, Nagai S, et al. Hypertrophic cardiomyopathy as a manifestation of cardiac sarcoidosis. Jpn Circ J 2000; 64: 679-83.
3. Yazaki Y, Isobe M, Hayasaka M, Tanaka M, Fujii T, Sekiguchi M. Cardiac sarcoidosis mimicking hypertrophic cardiomyopathy: Clinical utility of radionuclide imaging for differential diagnosis. Jpn Circ J 1998; 62: 465-8.
4. Saitou T, Nagai T, Kanda S, Yoshioka K, Ikari Y. A 30-day drastic thinning of the basal interventricular septum in isolated cardiac sarcoidosis masquerading as a hypertrophic cardiomyopathy. Eur Heart J Cardiovasc Imaging 2019; 20: 65.
5. Maron MS, Finley JJ, Bos JM, et al. Prevalence, clinical significance, and natural history of left ventricular apical aneurysms in hypertrophic cardiomyopathy. Circulation 2008; 118: 1541-9.
6. Williams L, Frenneaux M. Syncope in hypertrophic cardiomyopathy: Mechanisms and consequences for treatment. Europace 2007; 9: 817-22.
7. Fananapazir L, Tracy CM, Leon MB, et al. Electrophysiologic abnormalities in patients with hypertrophic cardiomyopathy. A consecutive analysis in 155 patients. Circulation 1989; 80: 1259-68.
8. Rosen KL, Cameron RW, Bigham PJ, Neish SR. Hypertrophic cardiomyopathy presenting with 3rd-degree atrioventricular block. Tex Heart Inst J 1997; 24: 372-5.
9. Przybojewski JZ, van der, Walt JJ, Ellis GC, Tiedt FA. Hypertrophic cardiomyopathy complicated by complete heart block. Case report and review of the literature. S Afr Med J 1984; 66: 847-55.
10. Thongtong V, Panchavinin P, Chaithiraphan S. Familial hypertrophic cardiomyopathy associated with spontaneous complete heart block. J Med Assoc Thai 1991; 74: 301-5.
11. Tamura M, Harada K, Ito T, Enoki M, Takada G. Abrupt aggravation of atrioventricular block and syncope in hypertrophic cardiomyopathy. Arch Dis Child 1995; 73: 536-7.
12. Desai DM, Bhat GS, Daxini BV, Sharma S. Complete heart block as a cause of syncope in hypertrophic cardiomyopathy. J Assoc Phys India 1991; 39: 965-6.
13. Fitzgerald P, Kusumoto F. The effects of septal myectomy and alcohol septal ablation for hypertrophic cardiomyopathy on the cardiac conduction system. J Interv Card Electrophysiol 2018; 52: 403-8.
14. Shimada T, Shimada K, Sakane T, et al. Diagnosis of cardiac sarcoidosis and evaluation of the effects of steroid therapy by gadolinium-DTPA-enhanced magnetic resonance imaging. Am J Med 2001; 110: 520-7.
15. Kramer CM, Barkhausen J, Buccioni-Ducci C, Flamm SD, Kim RJ, Nagel E. Standardized cardiovascular magnetic resonance imaging (CMR) protocals: 2020 Update. J Cardiovasc Magn Reson 2020; 22: 17.
16. Ishida Y, Yoshinaga K, Miyagawa M, et al. Recommendations for (18)F-fluorodeoxyglucose positron emission tomography imaging for cardiac sarcoidosis: Japanese Society of Nuclear Cardiology recommendations. Ann Nucl Med 2014; 28: 393-403.
17. Kumita S, Yoshinaga K, Miyagawa M, et al. Recommendations for (18)F-fluorodeoxyglucose positron emission tomography imaging for diagnosis of cardiac sarcoidosis-2018 update: Japanese Society of Nuclear Cardiology recommendations. J Nucl Cardiol 2019; 26: 1414-33.