Cardiac Sarcoidosis Mimicking Septal Tumor with Intermittent Complete Atrioventricular Block

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Summary

A 52-year-old woman with intermittent complete atrioventricular (AV) block detected on exercise was admitted to the hospital. Echocardiography revealed lesions on the right ventricular side of the interventricular septum and free wall of the basal inferolateral area. Gadolinium-enhanced cardiovascular magnetic resonance (CMR) imaging revealed the mass and wall thickening at the same locations with late gadolinium enhancement (LGE). Focal uptake at the septal lesion was detected using 67Ga scintigraphy. Focal on diffuse intense uptake in the lesions was observed on Fluorine-18 fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) imaging. Whole-body CT and laboratory evaluations uncovered no signs of malignant tumors in other organs. Ophthalmologic evaluation revealed ophthalmologic sarcoidosis. Although the result of endomyocardial biopsy was negative, the presence of cardiac sarcoidosis was strongly suggested on the basis of the new Japanese guidelines published in 2017. AV conduction disturbance and tracer accumulation on 67Ga scintigraphy completely disappeared after 2 weeks of steroid therapy. The size of mass, inferolateral wall thickness in echocardiography and CMR, and standardized uptake value (SUV) of the masses on 18F-FDG PET also decreased over time.

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Key words: Cardiac tumor

Sarcoidosis is a granulomatous disease of unknown etiology that involves multiple organs. A definite diagnosis of cardiac sarcoidosis is often difficult to achieve because of the low histological diagnostic rate of endomyocardial biopsy.¹⁻⁴⁾ On the contrary, early intervention is critical for preventing the progression of tissue inflammation and worsening of cardiac function and arrhythmia.^{2,3)} Timely corticosteroid therapy can improve cardiac function and reverse arrhythmia.

Regarding diagnostic guidelines for cardiac sarcoidosis, recommendations from the World Association of Sarcoidosis and Other Granulomatous Disorder (published in 1999) and A Case Control Etiology of Sarcoidosis Study (updated in 2014) have generally been followed.⁵⁾ Guidelines from the Heart Rhythm Society have also been published.⁶⁾ In Japan, guidelines for diagnosing and treating cardiac sarcoidosis were published by the Japan Circulation Society in February 2017.^{7,8)}

In the report, we present a case of cardiac sarcoidosis with intermittent complete AV block and intra-cardiac mass lesions for which clinical diagnosis was made using the new guidelines. Immediate corticosteroid therapy resulted in significant improvement in the patient's symptoms and multimodality imaging findings.

Case Report

A 52-year-old woman without prior cardiac disease presented with dyspnea on exertion. Initial 12-lead electrocardiography (ECG, Figure 1) revealed a first-degree atrioventricular (AV) delay, complete right bundle branch block, and posterior fascicular block. Intermittent complete atrioventricular block during exercise was detected on a 24-hour Holter ECG with the symptom of dyspnea (Figure 2).

Calcium channel blockers and β -blockers had never been used before admission and no significant electrolyte abnormality was detected in laboratory test results (Table).

Transthoracic echocardiography (TTE) revealed a mass lesion on the right side of the ventricular septum and the thickening of the basal inferolateral wall of the left ventricle (Figure 3). Cardiac chamber size and left and right ventricular wall motion were within normal ranges. 67Ga citrate scintigraphy revealed tracer accumulation in the interventricular septum (Figure 4A). Cardiovascular magnetic resonance (CMR) imaging revealed the septal mass and thickening of basal inferolateral wall with high intensity on T2-weighted black blood images and late gadolinium enhancement (LGE) in the same region (Figure 5A, B, C). Focal on diffuse Fluorine-18 fluorode-

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Figure 1. The chest X-ray on admission showed no abnormal findings. Twelve-lead electrocardiography on admission demonstrated first-degree atrioventricular block, complete right bundle branch block, and posterior fascicular block.

Figure 2. A 24-hour Holter electrocardiogram for dyspnea during dancing revealed advanced atrioventricular block with 3:1 conduction followed by intermittent complete atrioventricular block. The longest RR was 4.5 seconds.

oxyglucose (18F-FDG) uptake was observed at the mass and thickening lesions on positron emission tomography (PET) imaging (Figure 6A).

The presence of primary and secondary cardiac tumors was considered in the differential diagnosis. However, no abnormal findings were detected in other organs on whole-body CT, and laboratory tests, including the measurements of several common tumor markers, were all within normal ranges. The levels of interleukin-2 receptor, angiotensin-converting enzyme, and lysozyme were also normal (Table).

Coronary angiography findings showed no significant stenosis and anatomical abnormality.

The patient had a history of uveitis 3 months previ-

ously, and the presence of ocular sarcoidosis was strongly suggested by an ophthalmologic examination performed after admission. The patient underwent TTE and intra-cardiac echocardiography-guided endomyocardial biopsy of the septal mass lesion, though only mild hypertrophy of cardiac muscle cells without disarray and mild vessel wall thickening of small arteries were detected on pathological examination.

The cardiac findings of the patient fulfilled the 4 major criteria of cardiac involvement of sarcoidosis on the basis of the new guidelines for diagnosing cardiac sarcoidosis in Japan (high-grade atrioventricular block, regional ventricular wall thickening, abnormally high tracer accumulation on 67Ga citrate scintigraphy and 18F-FDG PET,

Table. Laboratory Data on Admission

Analyte	
TP	7.5 g/dL
Alb	4.5 g/dL
BUN	10 mg/dL
UA	4.6 mg/dL
Cre	0.60 mg/dL
Na	144 mEq/L
K	4.0 mEq/L
Cl	102 mEq/L
Ca	9.7 mg/dL
IP	3.6 mg/dL
Mg	2.4 mg/dL
T-Bil	0.5 mg/dL
AST	37 IU/L
ALT	74 IU/L ↑
LDH	192 U/L
CK	113 U/L
CRP	0.1 mg/dL
IgG	1092 mg/dL
BNP	61.2 pg/mL ↑
WBC	5000 /uL
RBC	13.2 × 10 ⁴ /uL
Hb	13.2 g/dL
Hct	40.1 %
Plt	22.9 × 10 ⁴ /uL
ACE	17.3 IU/L
Lysozyme	5.2 µg/mL
sIL-2R	289 U/mL
SCC	0.5 µg/mL
SLX	31 U/mL
PIVKA2	2.6 mAU/mL
AFP	7.5 ng/mL
CA125	< 1.2 U/mL
CA19-9	10.2 U/mL
NSE	1.4 ng/mL
CEA	8.7 ng/mL
CA15-3	2.6 U/mL
NCC-ST-439	< 1.0 U/mL

TP indicates total protein; Alb, albumin; BUN, blood urea nitrogen; UA uric acid; Cre, creatinine; Na, sodium; K, potassium; Cl, chloride; Ca, calcium; IP, inorganic phosphate; T-Bil, total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; CK, creatine phosphokinase; CRP, C-reactive protein; IgG, immunoglobulin G; BNP, brain natriuretic peptide; WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; Hct, hematocrit; Plt, platelet; ACE, angiotensin converting enzyme; sIL2-R, Interleukin-2 Receptor; SCC, squamous cell carcinoma antigen; SLX, sialyl Lewis X-1; PIVKA2, protein induced by vitamin K absence or antagonist-II; AFP, alpha-fetoprotein; CA125, carbohydrate antigen 125; CA19-9, carbohydrate antigen 19-9; NSE, neuron-specific enolase; CEA, carcinoembryonic antigen; CA15-3, carbohydrate antigen, and NCC-ST-439, Nation Cancer Center-Stomach-439

and delayed contrast enhancement of the myocardium on gadolinium-enhanced MRI) and one of the characteristic laboratory findings of sarcoidosis.^{5,6)} In addition, the clinical findings strongly suggested the presence of ophthalmic sarcoidosis. We decided to initiate steroid therapy (30 mg

of prednisolone) according to the diagnosis of “strongly suggested cardiac sarcoidosis” in the guidelines.^{5,6)} Following 1 week of steroid therapy, intermittent complete atrioventricular block completely disappeared. The regression of first-degree atrioventricular block was observed after 2 weeks. Tracer accumulation on ⁶⁷Ga citrate scintigraphy also disappeared simultaneously (Figure 4B). The size of the septal mass and thickness of the left ventricular free wall decreased in line with the improvement of clinical symptoms on echocardiographic follow-up. CMR performed after 2 months of therapy also revealed the disappearance of the high-intensity area on T2-weighted images and a decrease of LGE (Figure 5D-F). Exercise ECG after 2 months of therapy confirmed the good heart rate response to 150 bpm without an AV block (Figure 7). The patient has been followed up without symptom under the maintenance dose of prednisone (7.5 mg/day).

Discussion

This case has the following 2 major unique features: 1) tumor-like morphological features, which are unusual for cardiac sarcoidosis and 2) a rapid improvement and excellent clinical course (disappearance of AV block) after steroid therapy on the basis of the clinical diagnosis supported by the new Japanese guidelines for diagnosing cardiac sarcoidosis.^{7,8)}

Tumor-like morphological features: Several reports discussed cardiac sarcoidosis exhibiting myocardial wall thickening^{9,10)} and cardiac tumor-like morphology.

A case of cardiac sarcoidosis mimicking hypertrophic cardiomyopathy was reported by Yazaki, *et al.* in which gallium and technetium tracer accumulation disappeared after 2 months of steroid treatment.¹¹⁾ Recent reports also described tumor-like features of cardiac sarcoidosis in the ventricular septum, right ventricle, and left and right atria.¹²⁻¹⁷⁾

Sarcoidosis is an inflammatory disease, and myocardial tissue involvement progresses with inflammatory cell infiltration, edema, and granuloma formation in the early phase. Focal wall thickening and/or tumor-like morphology should be observed more frequently in the acute phase than previously reported. In most patients, cardiac involvement might progress without symptoms.^{2,3,18)} Although wall thickening and tumor-like morphology are rare findings, these early inflammatory signs should be diagnosed rapidly, as early therapeutic intervention is crucial for the prognosis of cardiac sarcoidosis.^{7,8)}

Rapid improvement of atrioventricular conduction disorder after steroid therapy: The disappearance of AV block after steroid therapy and avoidance of permanent pacemaker implantation have been previously reported.¹⁹⁻²¹⁾ Patients with early treatment, younger age, and preserved left ventricular systolic function are reported to have higher rates of recovery.²²⁻²⁴⁾ Kato, *et al.* reported the recovery of AV block in 4 of 9 patients with normal left ventricular function with steroid therapy at an average of 2.5 months after disease onset.²⁵⁾ Usually, pacemaker implantation has the priority considering the risk of infection and uncertainty of long-term response to steroid therapy.⁷⁾ However, the order should be carefully evaluated in con-

Figure 3. Transthoracic echocardiographic images at admission demonstrating a mass lesion on the right side of the ventricular septum and thickening of the basal inferolateral wall of the left ventricle. **A:** Parasternal long-axis view. **B:** Parasternal short-axis view.

The yellow arrow denotes the septal mass lesion. The red arrow indicates thickening of the basal inferolateral wall. The size of the septal mass lesion was $16.2 \times 24.8 \times 28$ mm, and the maximal thickness of the basal inferolateral wall was 12.4 mm in the peak diastolic phase (**C** and **D**).

Figure 4. ^{67}Ga citrate scintigraphy before and after steroid therapy. **A:** ^{67}Ga citrate scintigraphy revealed tracer accumulation in the interventricular septum (arrow). **B:** Tracer accumulation disappeared completely after corticosteroid therapy.

Figure 5. Cardiovascular magnetic resonance (CMR) images before and after steroid therapy. **A:** FIESTA images in the end diastolic phase revealed a septal mass lesion (red arrow) and thickening of the basal inferolateral wall (green arrow). **B:** T2-weighted black blood image revealed a high-intensity lesion on the right side of the ventricular septum (red arrow) and basal inferolateral wall (green arrow) of the left ventricle. **C:** Late gadolinium enhancement was observed at the same positions (red and green arrow). CMR after 6 months illustrated decreases in mass size and inferolateral wall thickness, disappearance of the high-intensity area on T2-weighted image, and decreases of the late gadolinium enhancement area (**D-F:** red and green arrow).

Figure 6. Fluorine-18 fluorodeoxyglucose (18F-FDG) PET images before and after steroid therapy. **A:** Strong focal on diffuse accumulation of 18F-FDG PET was observed at the septal mass lesion (maximum standardized uptake value [SUVmax] = 20.1) and inferolateral left ventricular free wall (SUVmax = 13.4). Mild accumulation was observed in the bilateral mediastinal lymph nodes (indicated by arrow, SUVmax = 6.2) and inguinal lymph nodes (SUVmax = 3.4). **B:** 18F-FDG PET imaging after 6 months of corticosteroid therapy revealed the disappearance of accumulation in the lymph nodes and a decreased SUV for the septal and inferolateral lesions (red arrow, SUVmax = 7.7; green arrow, SUVmax = 7.4).

Figure 7. Exercise electrocardiography performed after 2 months of corticosteroid therapy revealed a heart rate response to 150 bpm without any signs of atrioventricular block (**A**: at rest, **B**: at peak exercise).

sideration of the duration of AV block, patient's age, ventricular function, and general status.

In the current case, exercise-induced advanced AV block completely disappeared after steroid therapy initiated 1.2 months after symptom onset. In addition, the first-degree AV block and left posterior hemi-block vanished both at rest and during exercise. Although the electrophysiological examination was not performed, the patient was presumed to have advanced injury in AV node and His and infra-His bundle influenced by septal mass lesion which represent the inflammation and edema in the right side of basal septum. The improvement of inflammation and edema by corticosteroid therapy resulted in the recovery of electrical conduction,²⁶⁾ except the right bundle branch which is frequently damaged in patients with sarcoidosis.⁷⁾

In the present case, the clinical diagnosis based on the new Japanese guidelines supported the rapid initiation of steroid therapy. The multimodality images, especially 18F-FDG PET and CMR, played a critical role in the diagnosis and follow-up management. 18F-FDG PET has been demonstrated to be sensitive for detecting disease activity and useful both for the diagnosis and determination of therapeutic efficacy,^{27,28)} although several circumferential conditions should be ensured for eliminating physiological accumulation.²⁹⁾ Quantitative evaluation using the standardized uptake value (SUV) enabled a more precise evaluation of disease activity and the effects of treatment. In addition to the disappearance of tracer accumulation on 67Ga scintigraphy, the absence of a high-intensity area on T2-weighted black blood images during follow-up clearly revealed the disappearance of tissue edema and reduced disease activity, thus confirming the effect of treatment.

The proper time interval and interpretation of the findings of 18F-FDG PET and MRI after steroid therapy have not been determined. One report identified a maximum SUV of 2.5 on PET as a useful threshold for disease

activity.³⁰⁾

Studies for clarifying the adequate SUV for dose titration or cessation of steroid are necessary in the future. Residual LGE on CMR might illustrate the progression of fibrosis in the affected region, although the prognostic value of LGE for acute-phase sarcoidosis is unclear. The value of new imaging modalities in the treatment of sarcoidosis should be evaluated in the future.

Disclosures

Conflicts of interest: None.

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