CASE REPORT

Spontaneous Reduction in Abnormal Myocardial Uptake of Fluorine-18 Fluorodeoxyglucose in a Patient with Cardiac Sarcoidosis

Fumio Terasaki,1,2 MD, Shu-ichi Fujita,2 MD, Yumiko Kanzaki,2 MD, Yoshinobu Hirose,3 MD and Nobukazu Ishizaka,3 MD

Summary
Fluorine-18 fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) is a useful tool for evaluating disease activity in sarcoidosis including cardiac involvement. A 67-year-old patient who developed atrioventricular block requiring permanent pacemaker implantation was diagnosed with cardiac sarcoidosis. The patient did not undergo steroid or immunosuppressive therapy but underwent serial 18F-FDG PET examination, which showed spontaneous reduction in the myocardial FDG uptake, indicating the remission of immune-inflammatory activity. Although the global systolic function remained preserved, thinning of the septal wall emerged during the clinical course of follow-up, which is characteristic for cardiac sarcoidosis.

Key words: Natural history, Prognosis, Diagnostic imaging, Disease activity

The immune-inflammatory response for some kinds of antigens, mainly helper T-cell type 1 processes, is the underlying pathologies of sarcoidosis.1 Steroid treatment is thus considered to be the first-line therapy for sarcoidosis-associated immune inflammation, and, with the dysfunction of organs including the heart, the delay in the initiation of steroid or other immunosuppressive therapy can lead to the life-threatening consequences.2 For the assessment of immune-inflammatory activity of cardiac sarcoidosis, increase in the uptake of fluorodeoxyglucose (FDG), illustrated by fluorine-18 FDG (18F-FDG) PET, is currently gathering attention owing to its high sensitivity and abnormal cardiac FDG uptake; in fact, uptake of FDG represents one of the hallmarks of cardiac sarcoidosis, especially isolated ones.3 On the other hand, little information is available on what abnormal FDG uptake would become if steroid or other immunosuppressive therapies were not initiated. We herein demonstrate the tread of FDG uptake in the heart in a patient with cardiac sarcoidosis who was not treated with steroid therapy.

Case Report
A 67-year-old woman was admitted to our hospital in 2012 due to floating sensation and general fatigue. On admission, chest X-ray showed mild cardiomegaly with bilateral hilar lymphadenopathy (Figure 1), and electrocardiogram showed the complete atrioventricular block with ventricular escape beats (Figure 2). On admission, the patient’s consciousness was clear, and height was 146.5 cm and weight was 70 kg. Her body temperature was 36.7 degrees, respiratory rate was 18 breaths per min, blood pressure was 130/80 mmHg. Her heart sounds were normal and no abnormal heart murmurs were audible. No ab-

Figure 1. Chest X-ray shows cardiomegaly with bilateral hilar lymphadenopathy.
normal neurological findings were noted. Electrocardiogram presented left ventricular hypertrophy with normal systolic function (left ventricular ejection fraction of 69%) (Figure 3).

The laboratory data showed elevation in the brain natriuretic peptide (109 pg/mL), myocardial troponin T (0.023 ng/mL), C-reactive protein (0.57 mg/dL) and soluble interleukin-2 receptor (sIL-2R: 688 U/mL). Permanent pacemaker implantation was performed along with the search for the underlying cause of atrioventricular block. Histologic assessment of the biopsy sample of mediastinal lymph nodes obtained via mediastinoscopy revealed the noncaseating epithelioid cell granulomas (Figure 4), leading to the diagnosis of sarcoidosis. Coronary angiography showed normal coronary arteries, and endomyocardial biopsy showed interstitial fibrosis but not apparent granulomas (Figure 5).

$^{18}$F-FDG positron emission tomography (PET) showed increased uptake of FDG in the mediastinal as well as hilar lymph nodes, and abnormal focal uptake at

Figure 2. Electrocardiogram shows the third degree (complete) atrioventricular block.

Figure 3. Echocardiogram on admission presents left ventricular hypertrophy with normal systolic function (left ventricular ejection fraction of 69%). (A: end-diastole, B: end-systole.)

Figure 4. The biopsy of mediastinal lymph nodes using a mediastinoscopy. Presence of noncaseating epithelioid cell granulomas with multinucleated giant cells (arrow) was shown. Hematoxylin eosin (H&E) staining, magnification: ×200.
basal lesion of interventricular septum, anterior wall, and inferior-posterior wall of left ventricle (Figure 6, arrows). Taking these findings together, diagnosis of sarcoidosis with cardiac involvement was made.

Then the initiation of steroid therapy was considered; however, informed consent could not be obtained mainly owing to anxiety regarding its side effects. Consequently, the patient underwent periodical follow-up on an outpatient basis. During the 5-year follow-up period, 18F-FDG PET was periodically performed that showed, unexpectedly, decreasing grade of FDG uptake in the myocardium (Figure 6). On the other hand, increased FDG uptake in mediastinal, hilar and para-abdominal aortic lymph nodes was continued. Serum sIL-2R level was also persistently elevated (Figure 7). On echocardiography, the thinning of the basal part of the interventricular septum may have progressed in five years (Figure 8), although the global left ventricular systolic function was maintained. By periodical check-up of the permanent pacemaker record, no life-threatening ventricular arrhythmia was found.

Discussion

The clinical expression, natural history, and prognosis of sarcoidosis are highly variable. It is known that sarcoidosis occasionally shows spontaneous recovery, as well as having a self-limiting course. Approximately two-thirds of pulmonary sarcoidosis subjects spontaneously resolve their disease, whereas the remaining third have progressive pulmonary decompensation.

On the other hand, it is not well known whether cardiac sarcoidosis has a spontaneous recovery and/or a self-limiting course, and if so, what the rate is of spontaneously recovering patients. Few reports, to our knowledge, have shown the appearance of FDG uptake in the self-limiting condition of cardiac sarcoidosis.

The present case has clearly demonstrated the improvement of 18F-FDG PET findings in five years, without steroid or any other immunosuppressive therapy. Although local myocardial fibrosis in the basal part of the interventricular septum may have been suggested as the healing process, it is considered that, at least, active inflammation...
Figure 7. Chronological changes of $^{18}$F-FDG PET findings and biomarkers. $^{18}$F-FDG PET and laboratory data at July 2012 (A), August 2014 (B), and May 2017 (C). Maximum intensity projection images of $^{18}$F-FDG PET showed that enhanced FDG uptake remained present in the mediastinal, hilar and para-abdominal aortic lymph nodes (arrows), but not in the heart in May 2017 (C). Serum sIL-2R concentrations continued to elevate during the 5-year period shown in this figure.

Figure 8. Echocardiogram five years after the diagnosis of sarcoidosis. Thinning of the basal part of interventricular septum (arrow) became apparent. (A: end-diastole. B: end-systole.)

may have achieved spontaneous remission and left ventricular systolic function preserved.

In sarcoidosis, lymph nodes are one of the major and fundamental organs affected. The lymph nodes’ involvement is often associated with cardiac sarcoidosis that sometimes is an important indication in diagnosing this disease.\textsuperscript{10,11} It is notable in this case that the FDG uptake was reduced only in the heart, but not in the lymph nodes, indicating that reduction in the disease activity occurred exclusively in the cardiac tissue. Clarification of the mechanisms underlying such heart-specific remission in
sarcoidosis-related immune-inflammatory process may shed light on and help to understand the pathogenesis of so-called “isolated cardiac sarcoidosis.”

With current therapy, the prognosis of cardiac sarcoidosis appears better than generally considered, but patients presenting with heart failure still have poor long-term outcome. Furthermore, relatively rapid deterioration of left ventricular function may not infrequently occur; therefore, early diagnosis and non-delayed initiations of appropriate treatment are essential for the management of cardiac sarcoidosis. The present case may develop recurrence in the future, and there is no doubt that continuous observation is essential.

Clinical outcomes of cardiac sarcoidosis are quite diverse, including improvement with steroid treatment, relapse/recurrence, and deterioration. The present case notifies us that spontaneous remission of cardiac sarcoidosis might not be rare, and factors affecting the clinical phenotypes remain to be elucidated.

Disclosures

Conflicts of interest: None.

References