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CASE REPORT

Case of isolated cardiac sarcoidosis diagnosed by newly developed abnormal uptake during serial follow-up fluorine-18 fluorodeoxyglucose positron emission tomography

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Abstract

Cardiac sarcoidosis (CS) causes lethal arrhythmia and heart failure and has a poor prognosis; therefore, early detection and early stage treatment are important. However, diagnosis of isolated CS may be difficult in some cases owing to the low sensitivity of myocardial biopsy. Herein, we describe the case of a patient with isolated CS, showing change from negative to positive fluorine-18 fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) uptake results within 9 months. The patient showed rapid reduction in left ventricular systolic function with sustained ventricular tachycardia. The diagnosis of isolated CS is often under-recognized in clinical practice because it commonly requires the diagnosis of extracardiac disease in the absence of a positive endomyocardial biopsy. The Japanese Circulation Society recently published guidelines for CS diagnosis stating that isolated CS can be clinically diagnosed with positive ^{18}F-FDG PET or ^{67}Gallium result. In this case, serial follow-up ^{18}F-FDG PET was useful for diagnosing isolated CS.

Keywords Isolated cardiac sarcoidosis; FDG-PET; MRI

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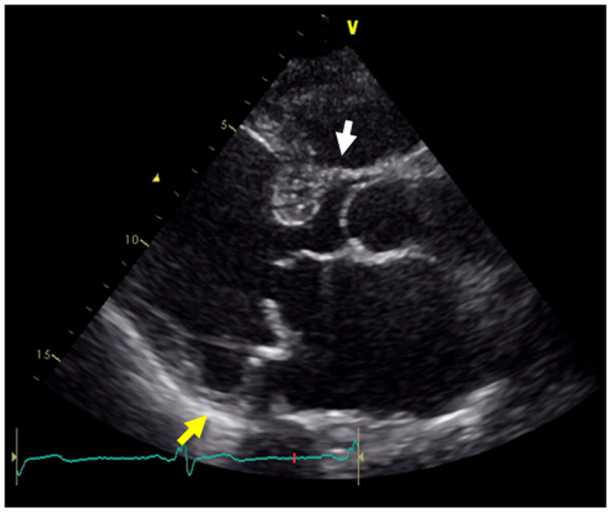
Introduction

Sarcoidosis is a systematic non-caseating granulomatous disease of unknown aetiology that involves multiple organs, including the heart. Cardiac sarcoidosis (CS) can cause lethal arrhythmia and heart failure, resulting in poor prognosis.[1,2] The diagnostic criteria for CS include the presence of extracardiac sarcoidosis or histological diagnosis using myocardial tissue.[3–5] Several recent reports have focused on isolated CS,[6,7] which is difficult to detect because of the poor sensitivity of myocardial biopsy.[8–10] The new guidelines for diagnosing CS were reported in Japan,[11,12] emphasizing the use of fluorine-18 fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) for diagnose of isolated CS. Herein, we describe the case of a patient with suspected CS presenting with rapid left ventricular (LV) function deterioration and sustained ventricular tachycardia (VT). The patient was diagnosed with isolated CS following newly developed myocardial focal uptake in repeated ^{18}F-FDG PET images 9 months after revealing no myocardial uptake of ^{18}F-FDG.

Case report

A 68-year-old woman was treated for hypertension and diabetes mellitus at our hospital as an outpatient for 30 years. Screening using transthoracic echocardiography displayed basal thinning of the interventricular septum and aneurysm of the posterior and lateral wall of left ventricle (*Figure 1*), as well as dilated LV dimension (LVDd; 68 mm) with

Figure 1 First screening echocardiography of parasternal long axis view. Basal thinning of interventricular septum (white arrow) and aneurysm of posterior (yellow arrow) are shown. Cardiomegaly with preserved left ventricular ejection fraction (56%) was observed.



preserved LV ejection fraction (LVEF) of 56%. The echocardiography conducted 5 years previously revealed normal LV wall motion without the aneurysm. Three-Tesla cardiac magnetic resonance imaging showed midwall late gadolinium enhancement (LGE) of the basal interventricular septum, subendocardial LGE in the posterior and lateral wall of the left ventricle, and 19% LGE area (*Figure 2*). High-contrast coronary computed tomography showed no significant stenosis of the coronary arteries. Isolated CS was suspected because the heart delineates regional structure (new development of LV aneurysm and septal thinning of basal LV) as well as no sign of sarcoidosis of other organs. However, after an 18 h fast and 15 min after administration of heparin, ^{18}F-FDG PET identified no areas showing abnormal uptake, including the heart [*Figure 3A–C*]. Therefore, isolated CS could not be diagnosed at the time. We speculated that either there was no inflammatory disease activity or that it had subsided. At follow-up, the patient did not require steroid and immunosuppressive therapy because the LV systolic function was preserved, and there were no symptoms.

The patient was admitted to our hospital presenting with palpitations after 9 months. Electrocardiography showed sustained VT (*Figure 4*). Consciousness was clear, and her vital signs were as follows: body temperature, 37.4°C; respiratory rate, 18 breaths per min; blood pressure, 135/87 mmHg; and heart rate, 156 beats per min. Her heart sounds were normal, and no abnormal heart murmur was audible. Chest X-ray showed cardiomegaly with no hilar lymphadenopathy. Echocardiogram revealed progressing enlargement of LVDd (78 mm) and reduction of LVEF (39%). Laboratory analysis showed normal levels of angiotensin-converting enzyme activity (10.6 U/L) and soluble interleukin-2 receptor (276 U/mL), as well as elevated brain natriuretic peptide level (390 ng/L). We began continuous infusion of lidocaine and amiodarone to treat the VT; then, once stabilized, amiodarone was changed to an oral regimen with oral carvedilol. Cardiac magnetic resonance imaging revealed reduced LVEF (37%) and increased LGE area percentage (25%) (*Figure 2*).

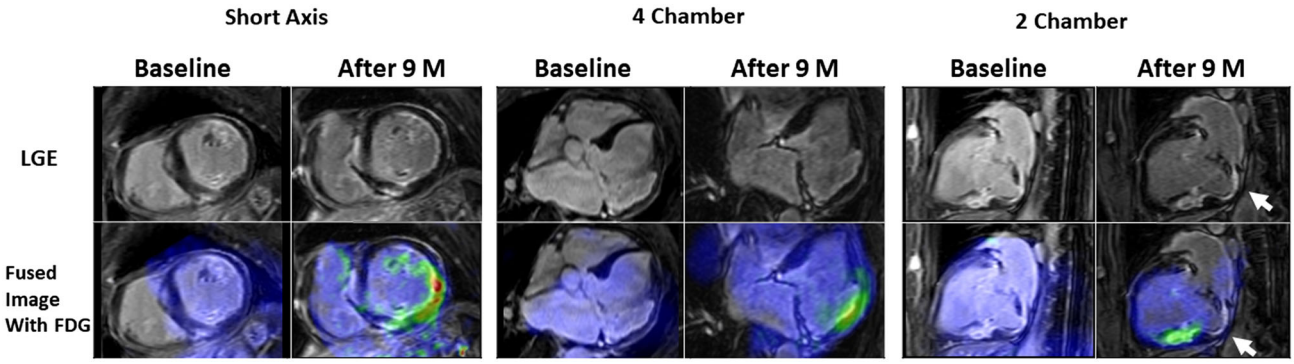
A previous examination of the same condition using ^{18}F-FDG PET showed abnormal focal uptake at the inferior and lateral walls of the left ventricle (*Figure 3D–F*); therefore, we made a clinical diagnosis of active isolated CS according to the new guideline for CS.[11,12] Invasive procedures, including cardiac biopsy, catheter ablation, and implantable cardioverter defibrillator, were considered; however, informed consent could not be obtained. Prednisolone (30 mg/day) was started, and the remainder of the patient's hospital course was uncomplicated. Prednisolone was gradually tapered to 5 mg/day for a 6 month follow-up. Brain natriuretic peptide levels decreased to 45 ng/L, LV function had gradually improved (LVDd, 67 mm and LVEF, 52%), and sustained VT was not reported. The patient's clinical course was stable at 1 year follow-up.

Discussion

Herein, we describe a case of a patient with isolated CS showing change from negative to positive ^{18}F-FDG PET uptake within 9 months. The patient showed rapid reduction of LV systolic function with sustained VT. Serial follow-up ^{18}F-FDG PET was useful to the diagnosis of isolated CS. In addition, steroid therapy for CS led to compensation of heart failure, and LV systolic function subsequently improved. To the best of our knowledge, there are few reports of cases with clinically diagnosed isolated CS using the new guideline.[11,12]

Diagnosis of isolated CS is difficult, and as a result, this condition is often under-recognized in clinical practice[6,7] because commonly used clinical criteria require the diagnosis of extracardiac disease in order to establish a clinical diagnosis of CS in the absence of a positive endomyocardial biopsy.[3–5] Cardiac biopsy is an invasive procedure with a low diagnostic rate[8–10]; therefore, histological diagnosis of CS is challenging. Recently, the Japanese Circulation Society published the guidelines for the diagnosis of CS, stating that isolated CS can be clinically diagnosed without extracardiac sarcoidosis; clinical diagnosis of isolated CS is supported when at least four of the five characteristics findings [high-grade atrioventricular block or fatal ventricular arrhythmia, basal thinning of the ventricular septum or abnormal ventricular wall anatomy, LV contractile dysfunction (EF $<$ 50%), and gadolinium-enhancement MRI reveals contrast enhancement of the myocardium], including positive ^{18}F-FDG PET or

Figure 2 Cardiac magnetic resonance imaging showing midwall late gadolinium enhancement (LGE) of basal interventricular septum and subendocardial LGE in the posterior and lateral wall of the left ventricle. Fused images clearly show an overlap of ^{18}F-FDG uptake and LGE in most myocardial regions. Follow-up ^{18}F-FDG PET showed increased ^{18}F-FDG uptake in most myocardial regions, but LGE positive regions remained unchanged. However, there was a discrepancy among the areas of ^{18}F-FDG uptake and LGE in the basal inferior wall (white head arrows). ^{18}F-FDG PET, fluorine-18 fluorodeoxyglucose positron emission tomography.



^{67}Gallium scintigraphy, for the diagnosis of isolated CS are observed.[11,12] The present case could be diagnosed according to this guideline.

Fluorodeoxyglucose, a glucose analogue, is useful for highlighting distinct inflammatory lesions wherein activated proinflammatory macrophages show a high metabolic rate and glucose utilization. ^{18}F-FDG PET is a useful modality to evaluate disease severity and activity in patients with CS.[13–15] Moreover, previous reports showed serial ^{18}F-FDG PET scanning was useful for evaluating therapeutic response and effect, believed to be associated with active inflammation.[16–18] However, the usefulness of serial ^{18}F-FDG PET scans for the diagnosis of isolated CS remains unknown. In the present case, the reason for the change from negative to positive in ^{18}F-FDG PET is unclear. The natural history of systemic sarcoidosis is self-limiting and reactivating.[19] It is speculated that the inflammation grade was too low to clinically detect or had subsided at the time of the first ^{18}F-FDG PET scan and/or was performed after completion of the acute inflammatory phase that left scar areas on the initial scan; however, the later scan picked up the reactivation of CS. The prevalence of CS among patients with systemic sarcoidosis is believed to be 27% to 54%.[7] Nevertheless, autopsy studies indicated that subclinical cardiac involvement may be present in up to 70% of cases.[8] Approximately 13% to 75% of deaths from sarcoidosis have been attributed to CS.[20] Therefore,

Figure 3 Chronological changes of ^{18}F-FDG PET findings and biomarkers in baseline and after 9 months (A and D, full body; B and E, enlarged view of the thorax; and C and F, transaxial fusion PET/computed tomography findings). Baseline images revealed no abnormal ^{18}F-FDG uptake including the heart. However, follow-up ^{18}F-FDG PET demonstrated focal ^{18}F-FDG uptake (red arrows) in the posterior and lateral wall of the left ventricle. ^{18}F-FDG PET, fluorine-18 fluorodeoxyglucose positron emission tomography; SUV, standardized uptake value.

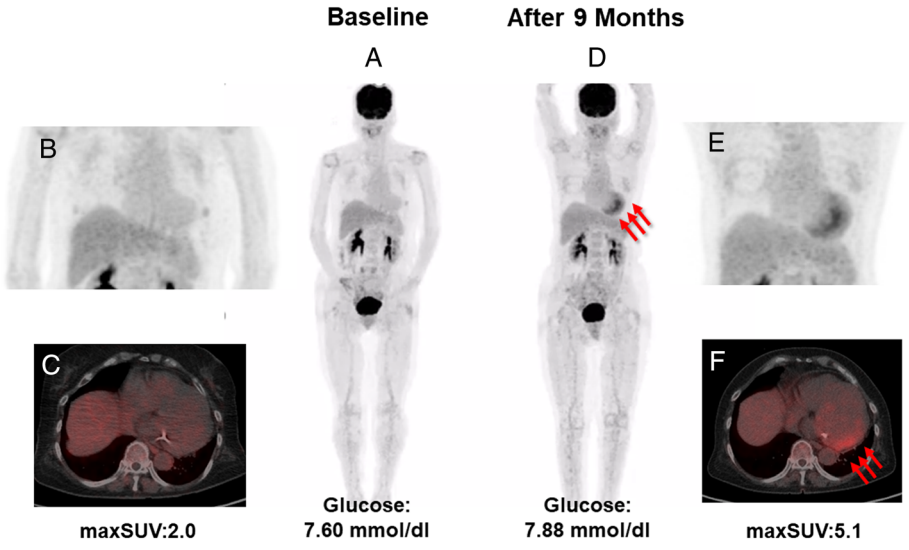


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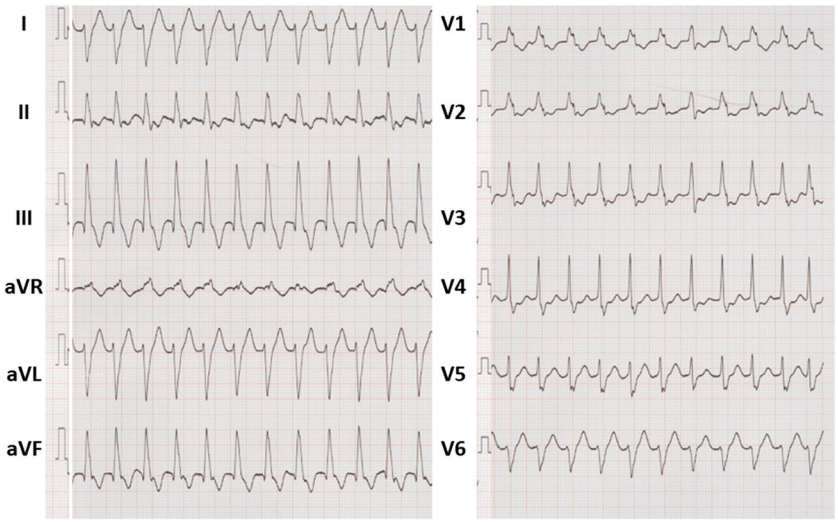
Figure 4 Electrocardiography on admission showing wide QRS tachycardia of 160 beats per min. QRS complex showed a right bundle block pattern and inferior axis, suggesting posterior and lateral wall of left ventricular origin.



early detection and early stage treatment for CS are crucial. However, steroid therapy or any other immunosuppressive therapy may preclude treatment because of their side effects, although there is a lack of evidence or their efficacy without confirming disease activity. In cases of suspected CS, repeated ^{18}F-FDG PET might be useful, even in cases with previously negative ^{18}F-FDG PET to confirm disease activity.

The present case report has some limitations. The other inflammatory disorder could not be excluded because of lack of evidence of organ involvement or tissue diagnosis. Physiological ^{18}F-FDG uptake in the heart sometimes shows false-positive results because normal myocytes utilize glucose as one of their main energy sources. In this case, after an 18 h fast and 15 min after administration of heparin, ^{18}F-FDG PET examinations were performed. The baseline T2 weighted black blood images were of poor quality to detect the area of oedema in LV. The usefulness of ^{67}Gallium scintigraphy, T2 mapping, T1 mapping on MRI, and the other modalities should be investigated for detecting inflammation. It will be necessary to verify the validity of the new guideline with further large-scale clinical investigations.

Conflict of interest

None declared.

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