Early Detection of Cardiac Sarcoid Lesions with $^{18}$F-fluoro-2-deoxyglucose Positron Emission Tomography

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Abstract

In April 2005, a 72-year-old woman with pulmonary sarcoidosis exhibited focal $^{18}$F-fluoro-2-deoxyglucose ($^{18}$F-FDG) uptake in her heart on $^{18}$F-FDG positron emission tomography (PET). Although Japanese guidelines for diagnosing cardiac sarcoidosis were not met at this point, electrocardiography, echocardiography, and magnetic resonance imaging became diagnostic for cardiac sarcoidosis 1 year later. In the present case report, the potential of $^{18}$F-FDG PET in the early recognition of cardiac sarcoidosis in comparison with other imaging modalities is discussed.

Key words: cardiac sarcoidosis, $^{18}$F-FDG PET, MRI


Introduction

Recent studies have demonstrated promising potential for $^{18}$F-fluoro-2-deoxyglucose ($^{18}$F-FDG) positron emission tomography (PET) in the diagnosis and assessment of cardiac sarcoidosis (CS). This imaging modality reportedly provides equivalent or better sensitivity for diagnosing CS than magnetic resonance imaging (MRI) and other imaging modalities (1-5). The specificity, however, is relatively low and often cases are encountered in which the interpretation of myocardial $^{18}$F-FDG uptake remains inconclusive.

We present herein the case of a patient with pulmonary sarcoidosis who had focal $^{18}$F-FDG uptake in the heart on fasting $^{18}$F-FDG PET. CS was diagnosed 1 year later, when findings from electrocardiography (ECG), echocardiography, and MRI proved sufficiently diagnostic. The potential ability and limitations of $^{18}$F-FDG PET for early detection of CS are discussed with reference to this case.

Case Report

In May 2002, a 72-year-old woman with uveitis was referred to our department and was clinically diagnosed with pulmonary sarcoidosis based on bilateral hilar lymphadenopathy on chest radiography, accumulation of $^{67}$Ga-citrate in mediastinal and hilar lymph nodes (“$\lambda$ pattern”), negative results from the tuberculin skin test, and a high CD4/8 ratio for lymphocytes from bronchoalveolar lavage. In April 2005, complete right bundle-branch block developed on ECG, and $^{18}$F-FDG PET showed focal $^{18}$F-FDG uptake in anteroseptal, anterolateral, and inferior walls of the left ventricle (Fig. 1a). Serum levels of angiotensin-converting enzyme were elevated to 25.0 IU/L (normal range, 8.3-21.5 IU/L). CS was suspected, but echocardiography, $^{99m}$Tc-sestamibi (MIBI) scintigraphy and cardiac MRI revealed no abnormalities (Fig. 1b). Left ventricular (LV) ejection fraction (LVEF) and LV end-diastolic dimension (LVDd) were both within normal ranges (LVEF, 67%; LVDd, 49 mm). At this point, the criteria of the Japanese Ministry of Health and Welfare Guidelines for Diagnosing Cardiac Sarcoidosis (6) were not met and the patient was followed closely without medical treatment.

In May 2006, she was readmitted to our hospital for new-onset left axis deviation. Compared with the previous studies, echocardiography showed thickening and high echo-
genicity in the interventricular septum (IVS). LVEF was 65% and LVDD was 45 mm. Focal uptake of 18F-FDG on LV walls and IVS became slightly more prominent compared with previous findings (Fig. 1c). Furthermore, cardiac MRI revealed late gadolinium enhancement (LGE) in the anteroseptal and inferior LV walls (Fig. 1d). LGE in the anteroseptal LV wall showed a mid-layer pattern, which is reportedly specific to CS. Coronary heart disease was excluded based on coronary angiography. Pathological examination of mandibular lymph nodes showed non-caseating granulomas, consistent with sarcoidosis. We therefore diagnosed CS based on the Japanese guidelines, and started treatment with 30 mg/day of prednisolone acetate in July 2006. Follow-up 18F-FDG PET performed 1 month later showed obviously reduced 18F-FDG uptake in the heart (Fig. 1e).

Discussion

Whether myocardial 18F-FDG uptake reflects cardiac sarcoid lesions in patients with sarcoidosis remains to be debated. Indeed, whether cardiac 18F-FDG uptake in the first evaluation for the present case represented a “true-positive” was uncertain, as echocardiography, 99mTc-MIBI and MRI showed no abnormalities at that time. The Japanese criteria for diagnosing CS were thus not met at that point. However, abnormal findings were evident 1 year later on ECG, echocardiography and MRI, and 18F-FDG PET also showed progressed 18F-FDG uptake in the heart. Reductions in myocardial 18F-FDG uptake after steroid therapy provided further support to the notion that 18F-FDG PET at the first work-up had detected early cardiac sarcoid lesions.

A series of case reports have suggested the value of 18F-FDG PET in detecting cardiac sarcoid lesions (7, 8), and have indicated favorable capability of 18F-FDG PET to monitor disease activity of CS during steroid therapy (9-11). For example, Koiwa et al reported an autopsy case demonstrating that 18F-FDG uptake in the heart corresponds well with pathologically confirmed sarcoid lesions (8). Tadamura et al also documented reduced regional 18F-FDG uptake in the heart after steroid therapy. In that case report, myocardial 18F-FDG uptake decreased together with reductions in serum angiotensin-converting enzyme level, as one of the biomarkers reflecting disease activity of sarcoidosis (10).

Prior studies have shown that the specificity of 18F-FDG PET for detecting CS (31-91%) is relatively low compared
with the sensitivity (82-100%) (1-5). Possible explanations include nonspecific myocardial uptake of $^{18}$F-FDG in the normal heart. Indeed, physiological $^{18}$F-FDG uptake has been reported in the lateral wall of the left ventricle in healthy individuals under fasting conditions (12, 13). Another possibility is early-stage sarcoid lesions that might be present in the heart even in patients who do not meet the diagnostic criteria for CS. This latter possibility might have been applicable to the present case.

Causes of sarcoidosis remain unclear, although several possibilities have been raised (14, 15). Pathology findings seen in CS range from inflammatory cell infiltration, edema, noncaseating granuloma formation and fibrotic changes to scarring. Among these, $^{18}$F-FDG PET theoretically identifies active lesions. Although $^{67}$Ga scintigraphy and MRI can also theoretically detect inflamed lesions, it is not surprising that imaging modalities based on different rationales provide different cardiac images with a varied pattern. The microangiopathy that commonly develops in sarcoidosis (16) could also augment cardiac $^{18}$F-FDG uptake, particularly when myocardial cells are exposed to ischemia. In the present study, $^{18}$F-FDG PET, but not MRI, demonstrated positive findings at the first hospitalization. This is probably attributable to the higher sensitivity of $^{18}$F-FDG PET for detecting active sarcoid lesions compared to MRI, or the microangiopathy might only be identified by $^{18}$F-FDG PET. In fact, $^{67}$Ga scintigraphy and MRI do not depict such ischemic lesions with a high sensitivity. Conversely, fibrotic changes with scarce viable cardiomyocytes can be detected by $^{18}$F-FDG PET as cold spots, although no such focal reductions in $^{18}$F-FDG uptake were observed in the present case. LGE on MRI or $^{99m}$Tc-MIBI scintigraphy may be more suitable for detecting such advanced fibrotic changes (17).

No pathological verification that $^{18}$F-FDG uptake had depicted early CS lesions was able to be achieved in the present case. While myocardial biopsy might have provided pathological confirmation, the sensitivity of this highly invasive procedure is reportedly less than 20%. In this regard, we have recently reported an autopsy case in which histopathology indicative of sarcoidosis was superimposed on the area showing cardiac $^{18}$F-FDG accumulation (8).

The present findings suggest that $^{18}$F-FDG PET could promise for the early diagnosis of CS. It is recommended that a positive finding on $^{18}$F-FDG PET alone should be interpreted carefully and close follow-up is warranted. More studies are needed to clarify the clinical role of $^{18}$F-FDG PET and other modalities in detecting early CS lesions and achieving better clinical outcomes in patients with sarcoidosis.

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

References

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