Identification of Cardiac Sarcoidosis with ^{13}N-NH_3/^{18}F-FDG PET

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To our knowledge, no study investigating the usefulness of cardiac PET for detection of myocardial involvement of sarcoidosis is available. We investigated whether ^{13}N-NH_3/^{18}F-FDG PET could identify cardiac involvement in patients with sarcoidosis. **Methods:** Seventeen patients with cardiac sarcoidosis underwent cardiac ^{13}N-NH_3/^{18}F-FDG PET under fasting condition. Systemic sarcoidosis was diagnosed by histologically proven noncaseating epithelioid granuloma, and cardiac sarcoidosis was diagnosed according to the Japanese Ministry of Health and Welfare guidelines for diagnosing cardiac sarcoidosis. **Results:** Only 6 patients exhibited myocardial ^{201}Tl defects and only 3 patients exhibited abnormal ^{67}Ga accumulation in the heart. Thirteen patients exhibited ^{13}N-NH_3 defects, and 14 patients exhibited increased ^{18}F-FDG uptake in the heart; 12 patients exhibited both ^{13}N-NH_3 defects and increased ^{18}F-FDG uptake, 2 patients exhibited increased ^{18}F-FDG uptake but no ^{13}N-NH_3 defect, and 1 patient exhibited ^{13}N-NH_3 defects but no increased ^{18}F-FDG uptake. ^{13}N-NH_3 defects were observed frequently in the basal anteroseptal wall of the left ventricle, and increased ^{18}F-FDG uptake was observed frequently in the basal and midanteroseptal-lateral wall of the left ventricle. Involvement of the apex was rare. Seven patients were treated with steroid hormone and underwent follow-up cardiac PET 1 mo after steroid therapy. ^{13}N-NH_3 defects exhibited no significant change after steroid therapy, whereas increased ^{18}F-FDG uptake was markedly diminished in size and intensity in 5 patients and disappeared completely in 2 patients. **Conclusion:** Our findings suggest that cardiac ^{13}N-NH_3/^{18}F-FDG PET is the most useful method both for the identification of cardiac involvement of sarcoidosis and for the assessment of cardiac sarcoidosis disease activity.

Key Words: ^{18}F-FDG; PET; sarcoidosis

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Sarcoidosis is a multisystem disorder of unknown etiology. Although the organ most frequently affected is the lung, all parts of the body can be affected. Overall prognosis is good because organ involvement is usually asymptomatic and the disease is often self-limiting (*1*). Cardiac sarcoidosis, however, sometimes causes fatal ventricular tachyarrhythmias, conduction block, and left ventricular (LV) dysfunction (*2*,*3*) and may lead to a poor prognosis. Myocardial involvement is present in at least 25% of patients with systemic sarcoidosis (*3*), and sudden death due to ventricular tachyarrhythmias or conduction block is responsible for 30%–85% of deaths from sarcoidosis (*2*). Endomyocardial biopsy may be essential for establishing the diagnosis of cardiac sarcoidosis. However, it is invasive and may be insensitive because myocardial involvement is not homogeneous (*2*,*4*). ^{201}Tl, ^{67}Ga (*1*,*2*,*5*–*7*), and ^{123}I-metaiodobenzylguanidine scintigraphy (*8*) and magnetic resonance imaging (*9*) are also used to detect cardiac involvement in patients with sarcoidosis. Areas with ^{201}Tl defects are considered areas of fibrogranulomatous replacement, although ^{201}Tl defects in the myocardium are not specific to sarcoidosis and may occur with ischemic heart disease or other cardiomyopathies (*1*,*2*,*5*). Accumulation of ^{67}Ga is considered an indicator of inflammatory change, and ^{67}Ga scintigraphy is useful in diagnosis of cardiac sarcoidosis and in prediction of effects of steroid therapy (*5*).

Recent studies revealed that ^{18}F-FDG in PET accumulated in the lung and bilateral hilar lymph nodes in patients with sarcoidosis (*10*,*11*). Moreover, in patients with pulmonary sarcoidosis, ^{18}F-FDG uptake of the lung was concordant with histologic activity in lung and was decreased after high-dose steroid therapy (*10*). It is thus possible that areas of fibrogranulomatous replacement in the heart may show increased ^{18}F-FDG uptake and that ^{18}F-FDG PET may provide a means of assessment of disease activity of pulmonary sarcoidosis. However, to our knowledge, no study investigating the usefulness of cardiac PET for detection of myocardial involvement of sarcoidosis is available, with the exception of one case report (*12*).

In this study, we investigated whether ^{13}N-NH_3/^{18}F-FDG PET could identify cardiac involvement in patients with sarcoidosis.

MATERIALS AND METHODS

Patients

We retrospectively identified 17 patients (4 men, 13 women; mean age, 58 ± 12 (±SD) y; range, 29–72 y) in our patients'

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database with cardiac sarcoidosis who underwent cardiac ^{13}N-NH_3/^{18}F-FDG PET. Systemic sarcoidosis was diagnosed by histologically proven noncaseating epithelioid granuloma with giant cells, and cardiac sarcoidosis was diagnosed according to the Japanese Ministry of Health and Welfare guidelines for diagnosing cardiac sarcoidosis (*13*) described in Table 1. Characteristics of the 17 patients with cardiac sarcoidosis are summarized in Table 2.

PET

For PET imaging, a Shimadzu-SET 1400 W-10 PET scanner (HEADTOME IV; Shimadzu Corp.) was used. This scanner can obtain 7 slices simultaneously with a 13-mm interval, a slice thickness of 11-mm full width at half maximum (FWHM), and a spatial resolution of 4.5-mm FWHM. Axial, 6.5-mm-interval Z-motion of the scanner provides 14 contiguous transverse slices of the myocardium.

A 10-min transmission scan was obtained using a rotating ^{68}Ge rod source. The acquired data were used to correct emission images of ^{13}N-NH_3 and ^{18}F-FDG for body attenuation. After completion of the transmission scan, the patient remained in the supine position and was injected intravenously with 555–740 MBq ^{13}N-NH_3. After a 5-min delay to allow pulmonary background activity to clear, myocardial perfusion imaging was performed for 10 min.

After at least 5 h of fasting and 3–4 h after completion of the perfusion scan, the patient received an intravenous injection of 259–370 MBq ^{18}F-FDG. Fifty minutes were allowed for cardiac uptake of ^{18}F-FDG. Imaging of glucose utilization was then performed for 10 min.

Images were collected in 256 × 256 matrices and reconstructed using Butterworth and ramp filters along the short axis, horizontal axis, and vertical long axis of the heart by a computer system (Dr. View; Asahi-Kasei Joho System Co.).

The LV myocardium was divided into 9 segments (basal anterior, midanterior, basal septal, midseptal, basal inferior, midinferior, basal lateral, midlateral, and apex). Each short-axis slice of the LV was divided into 36 sectors, 10° each, and a bull's eye polar map was reconstructed from the short-axis slices extending from the base to the apex. The maximal count in the LV was selected, and the value of each pixel was normalized to a maximal count of 100 in ^{13}N-NH_3 and ^{18}F-FDG images. The mean values of ^{13}N-NH_3 (% ^{13}N-NH_3) and ^{18}F-FDG (% ^{18}F-FDG) counts in each segment were calculated.

Analysis of PET Images

The short-axis, horizontal-axis, and vertical long-axis images were normalized to the maximum count in each image set and were displayed as color scale images. Two experienced nuclear cardiologists visually interpreted ^{13}N-NH_3 and ^{18}F-FDG uptake in 9 LV segments and in the right ventricular free wall. ^{13}N-NH_3 defects were defined as definitely decreased ^{13}N-NH_3 uptake (% ^{13}N-NH_3, approximately <60%). A myocardial segment with normal ^{13}N-NH_3 uptake and minimal % ^{18}F-FDG was considered as a normal control segment. In the segments with a ^{13}N-NH_3 defect, ^{18}F-FDG uptake equal to or higher than that in the normal control segment was defined as increased. In the segments without a ^{13}N-NH_3 defect, definitely higher ^{18}F-FDG uptake than that in the normal control segment was defined as increased. Segmental ^{18}F-FDG uptake index quantitatively indicating the degree of increase in ^{18}F-FDG uptake was calculated as follows: ^{18}F-FDG uptake index = % ^{18}F-FDG of each segment/% ^{18}F-FDG of the normal control segment.

^{201}Tl and ^{67}Ga Scintigraphy

Eleven patients underwent myocardial ^{201}Tl SPECT, and 15 patients underwent whole-body ^{67}Ga planar imaging, 9 of whom underwent myocardial ^{67}Ga SPECT. Experienced nuclear cardiologists visually interpreted ^{201}Tl defects, and experienced nuclear radiologists visually interpreted ^{67}Ga accumulation unaware of the findings of cardiac PET.

Statistics

Values are given as mean ± SD. The % ^{13}N-NH_3 or the ^{18}F-FDG uptake index before and after steroid therapy were compared with the paired *t* test.

RESULTS

Findings of myocardial ^{201}Tl and ^{67}Ga scintigraphy and cardiac PET in 17 patients with cardiac sarcoidosis are summarized in Table 3. Six patients exhibited myocardial ^{201}Tl defects and 3 patients exhibited abnormal ^{67}Ga accumulation in the heart. The ^{67}Ga accumulation in the heart in the latter 3 patients was observed in both planar and SPECT images. Thirteen patients (76%) exhibited ^{13}N-NH_3 defects, and 14 patients (82%) exhibited increased ^{18}F-FDG uptake

TABLE 1
Guidelines for Diagnosis of Cardiac Sarcoidosis from Japanese Ministry of Health and Welfare

Histologic diagnosis group
- Cardiac sarcoidosis is diagnosed when histologic analysis of operative or endomyocardial biopsy specimens demonstrates epithelioid granuloma without caseating granuloma

Clinical diagnosis group
- In patients with histologic diagnosis of extracardiac sarcoidosis, cardiac sarcoidosis is diagnosed when item (a) and 1 or more of items (b–e) are present
  - (a) Complete right bundle branch block, left-axis deviation, atrioventricular block, ventricular tachycardia, premature ventricular contraction (>grade 2 in Lown's classification), or abnormal Q or ST–T change on electrocardiogram or Holter electrocardiogram
  - (b) Abnormal wall motion, regional wall thinning or thickening, or dilatation of LV on echocardiogram
  - (c) Perfusion defect in ^{201}Tl myocardial scintigram or abnormal accumulation in ^{67}Ga-citrate or ^{99m}Tc-pyrophosphate myocardial scintigram
  - (d) Abnormal intracardiac pressure, low cardiac output, or abnormal wall motion or depressed ejection fraction of LV
  - (e) Interstitial fibrosis or cellular infiltration over moderate grade in endomyocardial biopsy even if findings are nonspecific

TABLE 2
Characteristics of 17 Patients with Cardiac Sarcoidosis

Patient no.	Age (y)	Sex	Symptom	Involved organs	ACE (IU/L)	Lysozyme (μg/mL)	ECG	Echocardiography		Steroid therapy	
								LV wall	LVEF (%)	Initial dose	Outcome after steroid therapy
1	29	F	Dyspnea	Heart, eye, LN, lung, skin*	53.0	NA	Frequent PVC	Normal	57	ND	
2	35	M	Dyspnea	Heart, LN, lung*	44.1	37.4	Frequent PVC	Normal	66	ND	
3	48	M	Dyspnea	Heart, LN,* lung	<1.0	NA	Trifascicular block, VT	Diffuse hypokinesis, thinning and akinesis of basal septum	41	ND	
4	58	M	Syncope	Heart, LN*	10.9	NA	3rd degree AVB, PM	Normal	57	ND	
5	61	F	Dyspnea	Heart, LN,* lung, skin	25.8	NA	3rd degree AVB, PM	Normal	60	ND	
6	62	F	Dyspnea	Heart, eye, LN,* lung	10.1	6.5	3rd degree AVB, PM	Diffuse hypokinesis, thinning and akinesis of basal septum	37	ND	
7	66	F	Dyspnea	Heart, LN*	NA	NA	3rd degree AVB, PM	Diffuse hypokinesis, thinning and akinesis of basal septum	34	ND	
8	70	F	Palpitation	Heart, LN*	NA	NA	3rd degree AVB, PM	Thinning and akinesis of basal anteroseptal wall	50	ND	
9	71	F	Syncope	Heart, LN*	13.1	NA	3rd degree AVB, VT	Severe hypokinesis of anterolateral wall	61	ND	
10	72	F	Dyspnea	Heart, skin*	NA	NA	Frequent and short-run PVC	Diffuse hypokinesis, thinning and akinesis of basal septum	36	ND	
11	53	F	Dyspnea	Heart, LN, lung,* skin*	31.9	22.2	Poor R in V1,2; Q in V3	Normal	64	40 mg/d	No change
12	53	F	Dyspnea	Heart, muscle*	31.0	15.0	2nd degree AVB	Thinning and akinesis of basal anteroseptal wall	51	30 mg/d	Improvement to 1st degree AVB
13	53	F	Syncope	Heart, eye, LN, lung, skin*	29.2	10.6	3rd degree AVB, VT	Diffuse severe hypokinesis, thinning of basal septum	37	30 mg/d	No change
14	54	F	Palpitation	Heart, muscle*	24.5	13.5	Trifascicular block, VT	Diffuse hypokinesis, thinning and akinesis of basal septum	50	30 mg/d	Disappearance of VT
15	59	M	Dyspnea	Heart, muscle,* skin*	29.7	9.7	3rd degree AVB	Diffuse hypokonesis	44	30 mg/d	Improvement to 2nd degree AVB, improvement of LVEF
16	65	F	Palpitation	Heart, LN,* lung	35.8	NA	Negative T in I and aVL, VT	Diffuse hypokinesis, thinning and akinesis of basal septum	26	30 mg/d	No change
17	72	F	Dyspnea	Heart, LN,* lung	14.0	9.4	3rd degree AVB, PM	Diffuse severe hypokinesis	25	30 mg/d	No change

*Organ for diagnostic histology.

ACE = angiotensin-converting enzyme; ECG = electrocardiography; LVEF = LV ejection fraction; LN = lymph node; NA = not available; PVC = premature ventricular contraction; ND = not done; VT = ventricular tachycardia; AVB = atrioventricular block; PM = permanent pacemaker implanted; aVL = left augmented limb lead.

TABLE 3
Results of Visual Analysis in Myocardial ^{201}Tl and ^{67}Ga Scintigraphy and Cardiac PET

Patient no.	Base				Middle						
	Sept.	Ant.	Lat.	Inf.	Sept.	Ant.	Lat.	Inf.	Apex	RV	LN
1*	–	–	–	–	–	–	–	–	–	–	○
2	–	–	–	–	–	–	–	–	–	–	△○
3†	●	●	–	–	–	–	–	–	–	–	–
4†	●○	●○	–	–	–	–	–	–	–	–	△○
5†	–	○	–	–	–	○	○	–	○	●	–
6	▲●○	●○	–	–	–	–	○	–	–	–	△
7†	●○	–	–	–	○	–	–	–	–	–	–
8*†	●○	●○	–	–	●○	○	●○	○	–	–	–
9	●	○	○	–	○	○	○	–	–	–	△
10*	▲●	▲●	–	○	△○	▲△●○	▲△●○	▲△●○	●	–	–
11	○	–	–	–	–	–	–	–	–	–	△○
12*	▲△●○	▲△●○	○	–	○	○	–	–	–	○	–
13*†	△●○	△●○	–	–	○	○	○	○	–	–	△○
14	▲●	▲●	○	–	○	○	–	–	–	–	–
15	▲●○	○	–	–	○	○	–	–	–	○	–
16	●○	▲●	▲●○	–	○	●○	●○	–	–	–	△○
17	●	○	○	–	○	○	○	○	–	–	△

*^{67}Ga scan was not done.
†Myocardial ^{201}Tl scan was not done.
RV = right ventricle; LN = lymph node; Sept. = septum; Ant. = anterior wall; Lat. = lateral wall; Inf. = inferior wall; – = no abnormality; ○ = increased ^{18}F-FDG uptake; △ = ^{67}Ga accumulation; ● = ^{13}N-NH_3 defect; ▲ = ^{201}Tl defect.

in the heart; 12 patients exhibited both ^{13}N-NH_3 defects and increased ^{18}F-FDG uptake, 2 exhibited increased ^{18}F-FDG uptake but no ^{13}N-NH_3 defect, and 1 exhibited ^{13}N-NH_3 defects but no increased ^{18}F-FDG uptake. Only 2 patients (12%) (patients 1 and 2) exhibited neither ^{13}N-NH_3 defect nor increased ^{18}F-FDG uptake. Five patients showed significant uptake of ^{18}F-FDG in hilar or mediastinal lymph nodes. ^{13}N-NH_3 defects were observed frequently in the basal anteroseptal wall of the LV, and increased ^{18}F-FDG uptake was observed frequently in the basal and midanteroseptal-lateral wall of the LV. Both ^{13}N-NH_3 defects and increased ^{18}F-FDG uptake were rare in the apex. Of 14 patients with increased ^{18}F-FDG uptake in the heart, 13 underwent ^{67}Ga scanning, of whom only 3 (23%) exhibited abnormal ^{67}Ga accumulation in the heart.

Seven patients were treated with steroid hormone and underwent follow-up cardiac PET 1 mo after steroid therapy. On visual analysis, ^{13}N-NH_3 defects exhibited no significant change after steroid therapy, whereas increased ^{18}F-FDG uptake was markedly diminished in size and intensity in 5 patients and disappeared completely in 2 patients (patients 10 and 15). The % ^{13}N-NH_3 in 13 LV segments with ^{13}N-NH_3 defects before steroid therapy did not differ significantly after steroid therapy (42.0% ± 6.7% before steroid therapy vs. 45.0% ± 7.0% after steroid therapy; $P = 0.08$). However, the ^{18}F-FDG uptake index in 30 LV segments with increased ^{18}F-FDG uptake before steroid therapy was significantly decreased after steroid therapy (1.8 ± 0.6 before steroid therapy vs. 1.2 ± 0.2 after steroid therapy; $P < 0.0001$).

Two representative cases are shown in Figures 1 and 2.

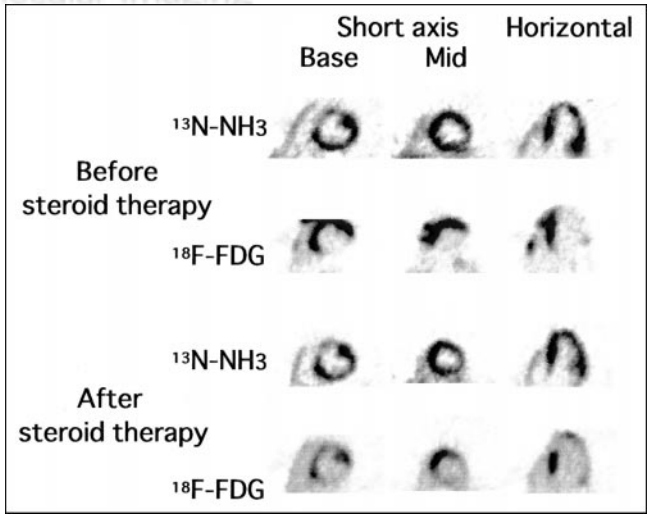

FIGURE 1. ^{13}N-NH_3 and ^{18}F-FDG PET images before and after steroid therapy in patient 12. Cardiac ^{13}N-NH_3 PET revealed moderate defects in basal anteroseptal wall of LV, and ^{18}F-FDG PET revealed increased ^{18}F-FDG uptake in basal anteroseptal-lateral wall and midanteroseptal wall of LV and free wall of right ventricle. After 1 mo of steroid therapy (prednisolone, 30 mg/d), increased ^{18}F-FDG uptake in basal anteroseptal-lateral wall and midanteroseptal wall of LV was markedly diminished both in size and in intensity and that in free wall of right ventricle disappeared completely, whereas ^{13}N-NH_3 defects exhibited no significant change. ^{18}F-FDG uptake indices of midanterior wall before and after steroid therapy were 2.8 and 1.8, respectively. Base = basal level of LV; Mid = middle level of LV.

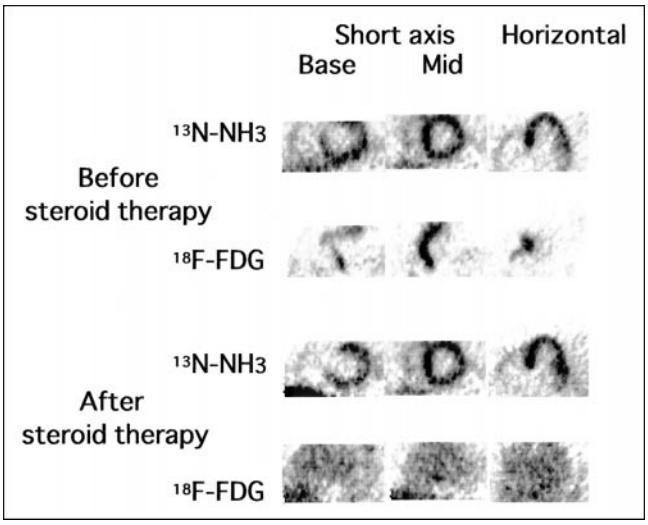

FIGURE 2. ^{13}N-NH_3 and ^{18}F-FDG PET images before and after steroid therapy in patient 15. Cardiac ^{13}N-NH_3 PET revealed moderate defects in basal ventricular septum, and ^{18}F-FDG PET revealed increased ^{18}F-FDG uptake in basal and midanteroseptal wall of LV and free wall of right ventricle. After 1 mo of steroid therapy (prednisolone, 30 mg/d), increased ^{18}F-FDG uptake in basal and midanteroseptal wall of LV and free wall of right ventricle disappeared completely, whereas ^{13}N-NH_3 defects exhibited no significant change. ^{18}F-FDG uptake indices of midseptum before and after steroid therapy were 3.0 and 1.2, respectively. Base = basal level of LV; Mid = middle level of LV.

DISCUSSION

^{13}N-NH_3 defects and increased ^{18}F-FDG uptake on cardiac ^{13}N-NH_3/^{18}F-FDG PET were observed frequently in patients with cardiac sarcoidosis diagnosed with orthodox diagnostic criteria for cardiac sarcoidosis. ^{13}N-NH_3 defects were observed frequently in the basal anteroseptal wall of the LV, and increased ^{18}F-FDG uptake was observed frequently in the basal and midanteroseptal-lateral wall of the LV. Increased myocardial ^{18}F-FDG uptake was observed even in patients with no abnormal myocardial accumulation of ^{67}Ga. Moreover, the increased myocardial ^{18}F-FDG uptake was significantly diminished both in size and in intensity after steroid therapy. Thus, our study suggests the possibility of increased ^{18}F-FDG uptake in the heart as a sensitive marker of cardiac sarcoidosis disease activity.

Scintigraphy with ^{67}Ga has been used to diagnose and assess disease activity of sarcoidosis (*6,14–19*). The mechanism of ^{67}Ga uptake is unclear in many disorders in which this tracer is used for diagnostic purpose. However, it is believed that ^{67}Ga is actively taken up by macrophages in the lesions in patients with active sarcoidosis. Measurable uptake of ^{67}Ga is interpreted as evidence of active inflammatory disease. Pulmonary uptake of ^{67}Ga was observed in >90% of active cases of pulmonary sarcoidosis (*20*) and was markedly decreased after steroid therapy (*21*). However, little information concerning diagnosis of cardiac sarcoidosis with ^{67}Ga scintigraphy has been available. Okayama et al. investigated 2 patients with myocardial accumulation of ^{67}Ga and concluded that patients with myocardial uptake of ^{67}Ga might be more responsive to steroid therapy (*5*).

Because only 3 of 15 patients with cardiac sarcoidosis, who underwent ^{67}Ga scanning, exhibited myocardial ^{67}Ga accumulation in our study, myocardial ^{67}Ga scintigraphy was considered an insensitive method for detection of cardiac involvement of sarcoidosis. However, because we did not perform myocardial ^{67}Ga SPECT on all patients in this study, which would be expected to increase the sensitivity of detection of myocardial accumulation of ^{67}Ga, myocardial ^{67}Ga SPECT must be performed in all patients with cardiac sarcoidosis to evaluate the diagnostic accuracy of myocardial ^{67}Ga scintigraphy.

Decreased ^{201}Tl uptake of the myocardium in patients with cardiac sarcoidosis is considered fibrogranulomatous replacement of the myocardium (*1,2,5*). In the remission stage of cardiac sarcoidosis, myocardium is replaced predominantly by fibrous tissue rather than by granulomatous tissue with inflammatory cell infiltration. Because myocardial ^{201}Tl scintigraphy detects cardiac sarcoidosis with and without active inflammation, it may be a sensitive but nonspecific method for detection of active cardiac sarcoidosis (*5*). Likewise, ^{13}N-NH_3 defects might represent fibrogranulomatous replacement of myocardium with and without active inflammation and might be sensitive, but nonspecific, for detection of active cardiac sarcoidosis because ^{13}N-NH_3 is a perfusion tracer like ^{201}Tl. In 2 patients (patients 9 and 17) in our study, ^{201}Tl SPECT could not identify any perfusion defect, whereas ^{13}N-NH_3 PET identified a perfusion defect in the basal septum. Because PET has a higher spatial resolution than SPECT, ^{13}N-NH_3 PET has the potential to detect a perfusion abnormality more sensitively than ^{201}Tl SPECT.

Recent studies found that ^{18}F-FDG accumulated in the lung and bilateral hilar lymph nodes in patients with sarcoidosis (*10,11*). The cellular uptake of ^{18}F-FDG in sarcoidosis is related to inflammatory cell infiltrates, which are composed of lymphocytes, macrophages, and epithelioid cells from monocytes, because ^{18}F-FDG has been observed in vitro to be accumulated by leukocytes (*22*), lymphocytes, and macrophages (*23*). In patients with pulmonary sarcoidosis, ^{18}F-FDG uptake of lung was concordant with histologic activity of pulmonary sarcoidosis, and the ^{18}F-FDG uptake of lung was decreased after high-dose steroid therapy (*10*). Thus, ^{18}F-FDG PET might provide a means of assessment of disease activity of pulmonary sarcoidosis.

Although no study investigating the usefulness of myocardial ^{18}F-FDG PET for diagnosis of myocardial involvement of sarcoidosis has been available, ^{18}F-FDG might accumulate in the myocardium of patients with cardiac sarcoidosis, as it does in pulmonary sarcoidosis. In patients with cardiac sarcoidosis, ^{18}F-FDG uptake by the heart might be concordant with inflammation activity of cardiac sarcoidosis. This consideration is consistent with the findings of diminished ^{18}F-FDG uptake in the myocardium after steroid

therapy in our patients with cardiac sarcoidosis. Increased myocardial ^{18}F-FDG uptake was observed in 10 patients without abnormal myocardial accumulation of ^{67}Ga. Therefore, ^{18}F-FDG PET has the potential to detect myocardial involvement of sarcoidosis with active inflammation more sensitively than ^{67}Ga scanning. Takeda et al. (*12*) recently reported a case of cardiac sarcoidosis with third-degree atrioventricular block. In this case, PET revealed decrease ^{13}N-NH_3 uptake and strongly increased ^{18}F-FDG uptake in the basal septal segment. Moreover, both findings disappeared and complete atrioventricular block improved to first-degree atrioventricular block after steroid therapy. These findings were concordant with our results.

In our study, ^{13}N-NH_3 defects were observed frequently in the basal anteroseptal wall of the LV, and increased ^{18}F-FDG uptake was observed frequently in the basal and midanteroseptal-lateral wall of the LV. Both ^{13}N-NH_3 defects and increased ^{18}F-FDG uptake were rare in the apex. These findings were concordant with previous pathologic and morphologic studies (*24–26*) indicating that cardiac involvement of sarcoidosis was common in the basal portion of the ventricular septum and free wall with sparing of the apex. Because ^{13}N-NH_3 defects or increased ^{18}F-FDG uptake localized to such portions is uncommon in coronary artery disease, ^{13}N-NH_3 defects in the basal anteroseptal wall of the LV or increased ^{18}F-FDG uptake in the basal and midanteroseptal-lateral wall of the LV might be specific for cardiac sarcoidosis. Moreover, in our study, 5 patients showed significant ^{18}F-FDG uptake in hilar or mediastinal lymph nodes. Increased ^{18}F-FDG uptake in the heart accompanied with significant ^{18}F-FDG uptake in hilar or mediastinal lymph nodes might be specific for cardiac sarcoidosis.

In our study, 2 patients (patients 1 and 2) diagnosed as having cardiac sarcoidosis with orthodox diagnostic criteria exhibited no abnormal findings on PET. These patients exhibited only frequent premature ventricular contractions as a clinical manifestation of cardiac involvement of sarcoidosis. Because sarcoidosis lesions were not revealed in their hearts histologically, their premature ventricular contractions might have resulted from causes other than cardiac sarcoidosis.

The major limitation of this study was the small patient population. To confirm our results, studies should be performed in a larger population prospectively.

Our results demonstrated that increased ^{18}F-FDG uptake was a sensitive indicator of cardiac involvement of sarcoidosis. However, we did not investigate the specificity or positive predictive value of ^{13}N-NH_3/^{18}F-FDG PET for diagnosis of cardiac sarcoidosis. A previous study (*27*) found that some patients with idiopathic dilated cardiomyopathy exhibited heterogeneous myocardial glucose uptake, which was related to poor prognosis and lack of improvement of LV function after medical treatment. A more recent report (*28*) revealed that 6%–40% of myocardial segments in idiopathic dilated cardiomyopathy exhibited increased ^{18}F-FDG uptake. To confirm the diagnostic accuracy of increased ^{18}F-FDG uptake for diagnosis of cardiac sarcoidosis, the prevalence of increased ^{18}F-FDG uptake in patients with sarcoidosis but no cardiac involvement or in patients with heart disease other than cardiac sarcoidosis must be investigated.

In this study, we defined a myocardial segment with normal ^{13}N-NH_3 uptake and minimal % ^{18}F-FDG as a normal control segment. However, we did not confirm whether such myocardial segments were truly normal. In an advanced stage of cardiac sarcoidosis, there might be no normal myocardium remaining. Although the measurement of absolute regional myocardial glucose utilization might be preferable for detection of involved myocardium, this is complicated and inapplicable to ^{18}F-FDG SPECT.

CONCLUSION

In this study, we investigated whether ^{13}N-NH_3/^{18}F-FDG PET could identify cardiac involvement in patients with sarcoidosis diagnosed with orthodox diagnostic criteria for cardiac sarcoidosis. ^{13}N-NH_3 defects and increased ^{18}F-FDG uptake on cardiac ^{13}N-NH_3/^{18}F-FDG PET was observed frequently, and the increased myocardial ^{18}F-FDG uptake was diminished in size and in intensity after steroid therapy. Our findings suggest that cardiac ^{13}N-NH_3/^{18}F-FDG PET is the most useful both for identification of cardiac involvement of sarcoidosis and for assessment of cardiac sarcoidosis disease activity.

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