Detection of Inflammatory Lesions by F-18 Fluorodeoxyglucose Positron Emission Tomography in Patients with Polymyositis and Dermatomyositis

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ABSTRACT. ***Objective.*** To evaluate the usefulness of F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) imaging in the management of patients with inflammatory myopathy. We examined whether FDG-PET scanning detects myositis or extramuscular lesions in patients with polymyositis (PM) and dermatomyositis (DM).

Methods. FDG-PET imaging was performed in 24 patients with active inflammatory myopathy (PM, 11; DM, 13). The images were read by radiologists in a blinded manner. FDG uptake into muscles was judged positive when the intensity of muscles was higher than or equal to that of the liver. As controls, FDG imaging findings of patients with a lung mass and without muscle diseases were used. To investigate associations between FDG-PET findings and clinical/laboratory findings, the patients' medical records were reviewed retrospectively.

Results. Increased FDG uptake in muscles was found in 8 of 24 (33%) patients. In 67 of 69 (97%) controls without muscle diseases, no muscle FDG uptake was detected. The sensitivity of FDG-PET to detect myositis was lower than that of electromyogram (EMG), magnetic resonance imaging, and muscle biopsy. There were no significant differences in clinical manifestations between patients with and without increased FDG uptake in muscles, although patients with FDG muscle uptake had a tendency to have extended myositis with endomysial cell infiltration. FDG-PET detected neoplasms in patients with associated malignancy. FDG uptake in lungs was found in 7 of 18 patients with interstitial lung disease.

Conclusion. FDG-PET imaging has limited usefulness for the evaluation of myositis in patients with PM/DM because of its low sensitivity, although it might be useful for detection of malignancy in these patients. (J Rheumatol First Release July 1 2012; doi:10.3899/jrheum.111597)

Key Indexing Terms:
F-18 FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY POLYMYOSITIS
DERMATOMYOSITIS LESIONS

F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) is a sensitive imaging technique used to detect neoplastic lesions, and it has been widely used in the screening for occult neoplasms, evaluation of diagnosed malignancy, and detection of metastases to lymph nodes and distal organs[1,2]. Because FDG behaves similarly to glucose *in vivo*, and FDG-PET visualizes glucose metabolism, FDG accumulates not only in neoplastic lesions but also in inflammatory lesions[3,4]. FDG-PET scanning has been reported to be useful for detection of inflammation in patients with osteomyelitis, metastatic infectious diseases, rheumatoid arthritis, vasculitis, inflammatory bowel diseases, sarcoidosis, and fevers of unknown origin[3,4].

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Polymyositis (PM) and dermatomyositis (DM) are chronic inflammatory diseases that affect systemic skeletal muscles and extramuscular organs including the lungs[5,6]. Patients with PM/DM, particularly those with DM, have been reported to have an increased risk of malignancy[7,8]. FDG-PET scanning is useful for cancer screening in patients with PM/DM[9,10,11,12,13,14,15]. In addition, an FDG-PET scan can also detect unsuspected infections in such patients[16]. However, it remains unknown whether FDG-PET scans detect muscle inflammation and extramuscular lesions in PM/DM.

To determine this and the clinical usefulness of FDG-PET scanning in the management of PM/DM, we examined FDG uptake in muscles and extramuscular lesions in patients with PM/DM and in patients without muscle diseases. The clinical features of patients with PM/DM were also reviewed, and comparisons made of the detection sensitivities for muscle inflammation of FDG-PET, electromyogram (EMG), muscle magnetic resonance imaging (MRI)[17], and muscle biopsy.

MATERIALS AND METHODS

Patients. Twenty-four patients were enrolled in our study. They were initially

diagnosed as having PM/DM and had undergone whole-body FDG-PET scanning to screen for malignancy at Dokkyo Medical University between 2004 and 2010. The diagnosis of PM/DM was based on the criteria by Bohan and Peter[18,19], and only patients with definite or probable disease were included. Cancer-associated myositis was defined according to the modified Bohan and Peter classification[20] as cancer within 1 year of the myositis diagnosis and observation that cure of the cancer resulted in cure of the myositis. As control subjects, 63 patients without muscle diseases who had undergone FDG-PET scanning in 2010 were also examined. We conducted our study with the approval of the local ethics committee.

Data collection. The medical records of 24 eligible subjects were reviewed from the time of diagnosis until death, loss to followup, or the end of the study period. Collected data included age of onset, sex, clinical features at presentation, laboratory test results from the first visit, and the findings of electrophysiological, imaging and muscle biopsy studies. Muscle strength was examined by manual muscle testing. When patients showed a score of 4 or lower on 2 proximal muscle groups, patients were judged as having muscle weakness. Laboratory data including serum levels of creatine kinase (CK) and C-reactive protein were measured routinely from the first visit. EMG and MRI of muscles were performed before muscle biopsy and treatment for PM/DM, and the findings of EMG and muscle MRI were read by neurologists and radiologist in a blinded manner. The muscle biopsy sample was obtained from a region with myalgia or weakness on physical examination, myopathic changes on EMG, or muscle edema on MRI. Interstitial lung disease (ILD), one of the frequent and serious extramuscular complications in PM/DM, was diagnosed using high-resolution computed tomography (HRCT), and when ground-glass opacity was found, ILD was considered active. All patients were routinely screened for associated collagen diseases.

FDG-PET imaging. Subjects underwent FDG-PET routinely conducted for detection of neoplastic lesions. To eliminate the effects of blood glucose and exercise, all patients were told to avoid exercise except for activities of daily living for at least 24 h, and they fasted for at least 6 h prior to FDG injection. Two hours (early and delayed) after the intravenous injection of 5 MBq/kg 18F-FDG in the resting state, whole-body FDG-PET images were obtained using a dedicated full-ring 3-D PET scanner (Siemens Biograph Sensation 16, Siemens Biograph LSO; Siemens, Tokyo, Japan) or Philips Allegro (Philips Electronics, Tokyo, Japan).

FDG-PET images were read in a blinded manner by radiologists experienced in reading PET images. FDG uptake in regions of interest (ROI) including proximal muscles of the 4 limbs was graded on a 3-point scale by visual interpretation: none and lower than liver uptake (grade 1); equal to liver uptake (grade 2); and higher than liver uptake (grade 3). Increased FDG uptake was interpreted as positive if FDG accumulation in the ROI was equal to or higher than that in physiological liver uptake[21].

Statistical analysis. Statistical analysis was conducted using JMP 7 (SAS Institute, Tokyo, Japan). All analyses were 2-sided, and the level of significance was set at $p < 0.05$. For comparisons of 2 groups, Fisher's exact test, the Mann-Whitney U test, and logistic regression analysis were used.

RESULTS

Demographic and background characteristics of patients. Demographics and clinical features of patients enrolled in our study are shown in Table 1. Of the 24 patients, 11 had PM and 13 had DM, and 1 patient had an associated malignancy. All patients had active myositis with elevated serum CK levels. ILD was detected in 18 patients. Six patients received glucocorticoids before the MRI.

Control patients were those with pulmonary mass lesions; most of them had lung cancers. These patients did not have myalgia, muscle weakness, or serum CK elevation.

FDG uptake into muscles seen in some patients with PM/DM but not in those without muscle disorders. Patients underwent FDG-PET examination under the routine protocol for detection of malignancy. FDG uptake into muscles, the intensity of which was equal to or higher than that of liver, was detected (Figure 1) in 8 of 24 patients (33%) with PM/DM (Table 2). In contrast, only 2 of 69 patients without muscle diseases showed significant FDG uptake into muscles. The frequency of FDG uptake into muscles was significantly higher in patients with PM/DM than in patients without muscle diseases (Figure 2).

In patients with PM/DM, FDG uptake was found mainly in symmetrically bilateral and proximal lesions, such as in the shoulder, arms, back, hip, and thigh (Table 2). In patients without muscle diseases, accumulation of FDG into muscles was asymmetrical.

Clinical features of PM/DM patients with/without FDG uptake into muscles. Clinical features of patients with PM/DM were examined to determine whether there were differences in those features between patients with and without FDG uptake into muscles. As shown in Table 3, no significant differences were found in age, sex, incidence of myalgia and muscle weakness, serum CK levels, positivity for anti-Jo-1 antibody, muscle MRI findings, and coincidence of ILD and malignancy.

However, patients with FDG uptake showed tendencies to have extended and/or endomysium inflammation, suggested by high frequencies of myopathic changes on EMG ($p = 0.051$) and inflammatory cell infiltration into the endomysium on muscle biopsy ($p = 0.109$).

Low sensitivity of FDG-PET imaging for PM/DM compared to conventional examinations. To evaluate the usefulness of FDG-PET imaging in the diagnosis of myositis, sensitivities for detecting muscle involvement were compared for FDG-PET, EMG, muscle MRI, and muscle biopsy. The sensitivity of FDG-PET was 33.3%, which was significantly lower than for EMG (16/22; 72.6%), MRI (12/21; 57.1%), and muscle biopsy (17/17; 100%; Figure 3). MRI findings were T2 high-intensity and T1 iso-intensity lesions, indicating edema that might be caused by inflammation. On muscle biopsy, all cases showed degeneration, necrosis, and regeneration of muscle fibers, or inflammatory cell infiltration to the endomysium and/or perimysium.

Extramuscular abnormalities in FDG-PET imaging in patients with PM/DM. As shown in Table 2, extramuscular abnormalities on FDG-PET were found in some patients. In 1 DM patient with malignancy, FDG uptake into lung cancer was seen. As for ILD, it was detected in 18 of 24 patients, using HRCT. Of the 18 patients with ILD, accumulation of FDG into the lung was found in only 7. Interestingly, all patients with FDG uptake into the lung had active ILD with respiratory symptoms, expansion of the area of ground-glass opacity, or a decrease in PaO_2, and they were judged to require therapy for ILD.

Table 1. Demographic and background characteristics of patients.

Case		Age, Sex	Myalgia	Muscle Weakness	CK, IU/l	Jo-1 Ab	Abnormalities EMG	MRI	Biopsy	Muscle Pathology Fiber Damage*	Cell Infiltration	Complications ILD	Malig-nancy	Treatment, mg
1	PM	30F	–	–	720	–	+	ND	+	+	Perimysium	+	–	PSL12.5
2	PM	55 M	+	+	6759	–	+	+	ND	ND	ND	+	–	PSL 3
3	PM	17 F	–	–	2260	–	+	+	+	+	Peri/Endomysium	–	–	–
4	PM	44 M	–	+	6120	–	+	+	+	+	–	+	–	–
5	PM	56 F	+	+	3042	–	+	+	+	+	Peri/Endomysium	–	–	–
6	PM	71 F	–	–	360	–	+	–	+	+	Peri/Endomysium	+	–	–
7	PM	73 F	+	+	8145	–	+	+	+	+	Peri/Endomysium	–	–	–
8	PM	57 F	–	+	8388	–	+	+	+	+	–	–	–	–
9	PM	59 F	+	+	821	–	+	–	+	+	Peri/Endomysium	+	–	–
10	PM	52 F	–	+	2958	+	+	–	+	+	Peri/Endomysium	+	–	–
11	PM	60 F	+	–	897	–	–	–	+	+	–	+	–	–
12	DM	47 F	+	+	485	+	ND	+	+	+	Perimysium	+	–	PSL 30**
13	DM	74 M	+	+	2469	–	+	ND	ND	ND	ND	+	–	–
14	DM	73 M	–	+	2243	–	–	ND	ND	ND	ND	–	–	DEX 8**
15	DM	26 F	+	+	4050	+	+	+	+	+	Perimysium	–	–	–
16	DM	67 F	–	+	3381	–	+	–	ND	ND	ND	+	–	PSL 60**
17	DM	69 F	+	+	334	–	+	+	+	+	–	+	–	–
18	DM	53 M	+	+	16,955	–	+	+	+	+	Perimysium	+	–	–
19	DM	50 M	+	–	1017	–	–	+	+	+	–	+	–	–
20	DM	56 F	+	+	968	+	–	–	+	–	Perimysium	+	–	–
21	DM	65 M	+	–	1302	–	–	–	ND	ND	ND	+	–	–
22	Dm	72 F	–	+	491	–	ND	–	+	+	Perimysium	+	–	PSL 7.5
23	DM	75 F	–	+	547	–	–	–	ND	ND	ND	+	–	–
24	DM	63 M	–	+	13,189	–	+	–	+	ND	ND	+	Lung Ca.	–

* Presence of necrotic or regenerating fibers. ** Duration of high-dose glucocorticoid therapy before magnetic resonance imaging (MRI) was < 3 weeks. CK: creatine kinase; DEX: dexamethasone; DM: dermatomyositis; EMG: electromyography; ILD: interstitial lung disease; Lung Ca: lung cancer; ND: not done; Peri: perimysium; PM: polymyositis; PSL: prednisolone.

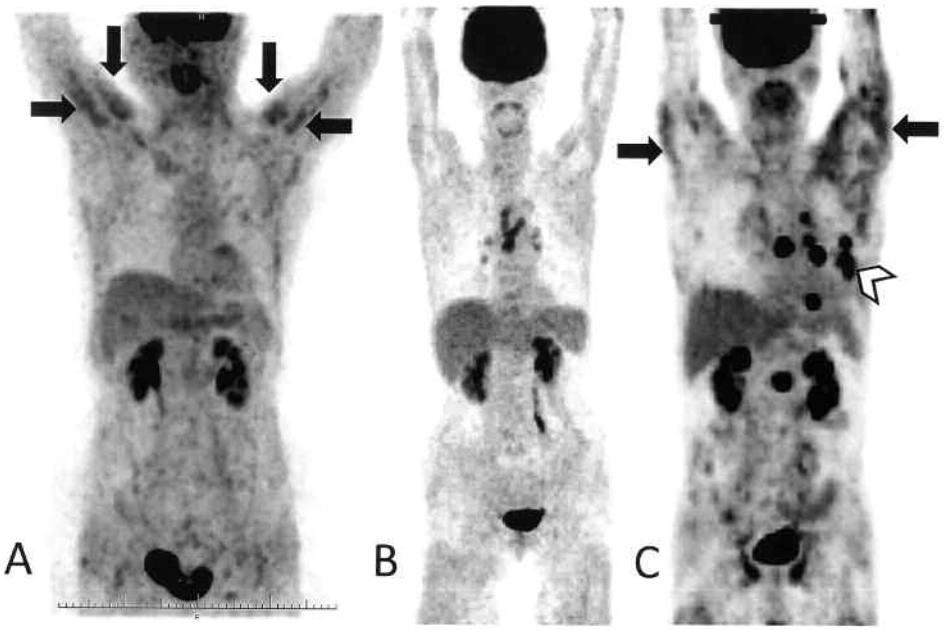

Figure 1. F-18 fluorodeoxyglucose (FDG) positron emission tomography in patients with polymyositis/dermatomyositis (PM/DM). (A) Patient with FDG uptake in muscles (Case 17). (B) Patient without FDG uptake in muscles (Case 7). (C) Patient with DM associated with malignancy (Case 24). Arrows indicate FDG accumulation, arrowhead indicates lung cancer.

Table 2. Findings of FDG-PET imaging in patients with polymyositis and dermatomyositis.

Case	Increased FDG Uptake in Muscles Uptake	Site of Increased FDG Uptake	Abnormal Uptake	Increased FDG Uptake in Extramuscular Lesions
1	–		+	Lung
2	–		–	–
3	+	Bil. shoulders, upper arms, back	–	Parotid gland and cervical LN*
4	+	Bil. shoulders, forearms, bil. hip, lower legs	–	Mediastinal LN*
5	+	Neck, bil. upper arms, forearms, hip	–	–
6	+	Bil. upper arms, bil. thigh	+	Lung, mediastinal LN*
7	–		–	–
8	–		–	Hilar LN
9	+	Bil. upper arms, back	+	Lung
10	–		–	Cervical and mediastinal LN*
11	–		–	Hilar LN*
12	–		–	Ascending and sigmoid colon*
13	+	Bil. shoulders, upper arms	–	–
14	–		–	Thyroid gland*
15	–		–	Palatine tonsil*
16	–		+	Lung
17	+	Bil. shoulders, upper arms, back	–	Hilar and mediastinal LN*
18	–		–	Cervical LN*
19	–		+	Lung
20	–		+	Lung
21	–		–	Mediastinal LN*
22	–		–	Rectum*
23	–		+	Lung
24	+	Bil. shoulders, upper arms, bil. hip, thigh, back	+	Lung and lung cancer

* Physiological FDG uptake. FDG-PET: F-18 fluorodeoxyglucose positron emission tomography; Bil. bilateral; LN: lymph nodes.

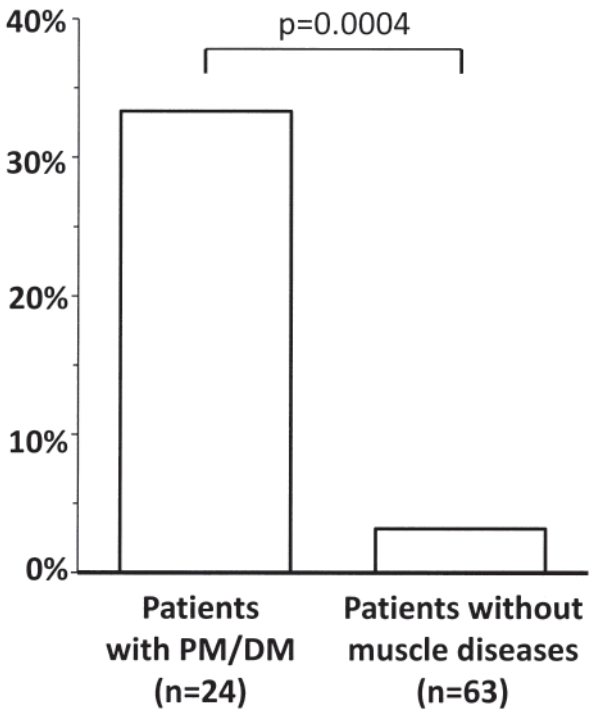

Figure 2. Incidence of F-18 fluorodeoxyglucose (FDG) uptake into muscles in patients with polymyositis/dermatomyositis (PM/DM) and subjects without muscle diseases. Significant difference in incidence of FDG uptake into muscles was found between patients with PM/DM and controls.

DISCUSSION

In our study, it was demonstrated that routine FDG-PET examinations in the screening for malignancy could detect myositis in patients with PM/DM. However, the sensitivity of FDG-PET for myositis was inferior to that of EMG, MRI, and muscle biopsy. No significant differences were found in clinical features between patients with and those without muscle FDG uptake, although patients with FDG uptake had a tendency to have extended or endomysium inflammation. However, FDP-PET detected malignancy and active ILD. These findings suggest an FDG-PET scan can detect myositis, but the usefulness of the routine PET examination in the evaluation of myositis in patients with PM/DM is limited because of its low sensitivity. It could, however, be a good modality for screening for malignancy associated with myositis. Our report is the first, to our knowledge, to summarize FDG-PET examinations in patients with PM/DM and the usefulness and limitations of this imaging modality. There are a few case reports about the detection of myositis with FDG-PET in patients with DM[11,22].

FDG behaves similarly to glucose *in vivo*. FDG-PET allows visualization of glucose metabolism because FDG accumulates in lesions with active glucose metabolism, such as neoplasms and inflammation[1,2,3,4]. FDG accumulates not only in neoplastic and inflammatory lesions, but also physiologically in some organs. Under physiological conditions, the

Table 3. Clinical features of PM/DM patients with increased FDG uptake in muscles. Data are number (%) unless otherwise indicated.

Increased FDG Uptake in Muscles	+	–	p
Patients, n	8	16	
PM:DM	5:3	6:10	0.39
Age, mean ± SD yrs	56.6 ± 18.7	56.9 ± 14.4	0.21
Sex, M:F	3:5	5:11	1.00
Myalgia	4/8 (50.0)	9/16 (56.3)	1.00
Muscle weakness	6/8 (75.0)	12/16 (75.0)	1.00
CK, IU/ml	3574 ± 4318	3707 ± 4453	0.31
Anti-Jo-1 AB-positive	0/8 (0.0)	4/16 (25.0)	0.26
Myopathic change on EMG	8/8 (100)	8/14 (57.1)	0.051
Abnormal findings on muscle MRI	5/7 (71.4)	7/14 (50)	0.83
Abnormal findings in biopsy samples	6/6 (100)	11/11 (100)	1.00
Necrotic/regenerating fiber	6/6 (100)	10/11 (90.9)	1.00
Inflammatory cell infiltration	4/6 (66.7)	9/11 (81.8)	0.72
Perimysium	4/6 (66.7)	9/11 (81.8)	0.72
Endomysium	4/6 (66.7)	2/11 (18.2)	0.109
Interstitial lung disease	6/8 (75.0)	12/16 (75.0)	1.00
Malignancy	1/8 (12.5)	0/16 (0.0)	0.33

CK: creatine kinase; DM: dermatomyositis; PM: polymyositis; EMG: electromyography; MRI: magnetic resonance imaging; Ab: antibody; FDG: fluorodeoxyglucose.

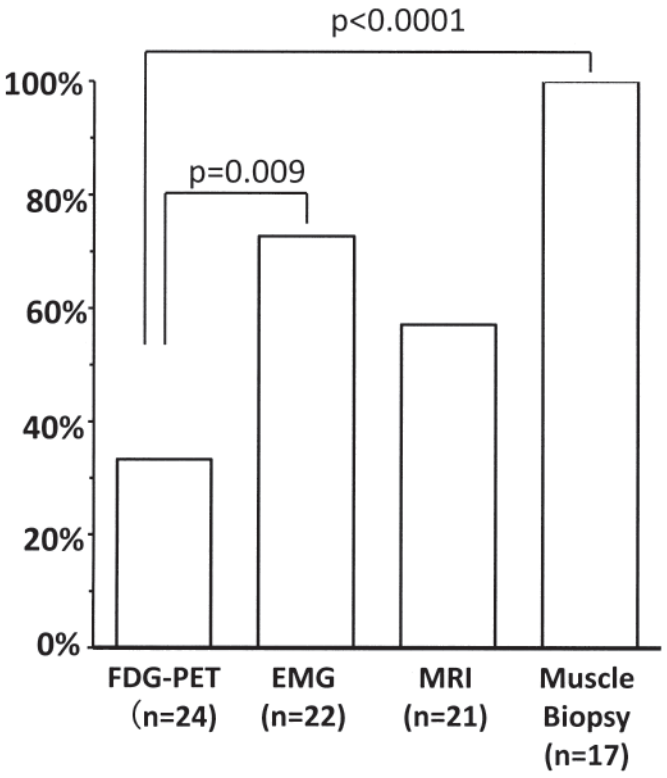

Figure 3. Comparison of sensitivity of F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) with conventional examinations for detection of myositis. Significant difference was found in the sensitivity for detection of myositis between FDG-PET and EMG (electromyography) or muscle biopsy. MRI: magnetic resonance imaging.

brain shows intense FDG uptake, and a relatively high uptake of FDG is also found in the palatine tonsil, gastrointestinal tract including the stomach, large intestines, and liver, in addition to physiological accumulation in the myocardium, hilar lymph nodes, and bone marrow[23]. In skeletal muscles, FDG uptake is increased by voluntary movements such as speech, chewing, and daily movement, and involuntary movements including labored breathing and stress-induced muscle spasms[23]. Further, physiological FDG uptake into muscles in healthy subjects was seen by Reinking and Osman as asymmetrical, with mild-to-moderate accumulation in the vocal cords, neck, and distal muscles such as those in the wrist, forearm and ankle[24]. In that study, FDG uptake into muscles of patients without muscle diseases was examined. FDG uptake in muscles was lower than in the liver in all but 2 patients, who showed uptake in the neck or right shoulder only. Similar to these results, increased FDG uptake in muscles was reported in 146 of 1164 patients (12.5%) with malignancies, and it was mainly in the masseter muscle, muscles of the neck, vocal cord, chest wall, forearms, fingers, and lower legs[24,25]. Based on these reports and our results in patients without muscle diseases, physiological FDG uptake in muscles was considered to be lower than in the liver. Therefore, we determined the following criterion for increased FDG uptake into muscles: increased uptake was indicated when the intensity of FDG in muscles was higher than or equal to that in the liver.

The sensitivity of FDG-PET for the detection of myositis in patients with PM/DM was examined according to this criterion. The sensitivity of FDG-PET was 33%, which was low

compared to EMG, MRI, or muscle biopsy. The low sensitivity of FDG-PET might be due to the strict criterion for muscle FDG uptake. We evaluated the FDG uptake qualitatively through comparison of the intensity of muscle to that of liver by radiologists. In most cases of patients without muscle diseases, FDG uptake in muscles was not observed and was equal to background intensity; thus, the criterion used in our study might have been too strict and caused the low sensitivity. If we had evaluated quantitatively by measuring standardized uptake values (SUV) of proximal muscles and compared SUV averaged over the proximal muscles in myositis to those in controls, the criterion might have been less strict and the sensitivity might have been greater. In addition, glucocorticoid treatment before PET might decrease the sensitivity, because FDG accumulation was not detected in all patients receiving glucocorticoid. This suggests that FDG-PET might reflect activity of myositis, as reported by Renard, *et al*[26].

Despite the low sensitivity of FDG-PET, PET might have high specificity for detection of myositis. Of patients without muscle diseases, 97.1% were negative for FDG uptake in muscles, indicating a specificity of 97.1%. The specificity of FDG-PET was calculated based on data of patients with lung masses as controls; most of the masses were cancer. Patients with lung masses in our study could represent control subjects without muscle diseases including healthy individuals and patients, because muscle involvements were rare in patients with cancer without muscle symptoms, and few patients showed muscle FDG uptake in our study, similarly to previous reports[24,25].

As controls, patients with noninflammatory myopathy might be better than those with cancer. If using patients with noninflammatory myopathy as controls, specificity discriminating inflammatory myopathy such as PM/DM from other muscle diseases might have been determined.

Additionally, PM/DM patients with FDG uptake into muscles had a tendency toward extended myositis and endomysial inflammation, suggested by the high frequency of abnormal EMG findings and endomysial infiltration on biopsy. Considering these findings together, FDG-PET might be able to detect extended and active myositis with high specificity.

In our study, the usefulness (detection of myositis with probably high specificity) and limitations (low sensitivity) of FDG-PET in the evaluation of patients with PM/DM were determined. Our study had limitations, and some questions remain. First, the number of subjects was too small, and the patients were not randomly selected. Second, it is unknown whether FDG uptake into muscles is specific for myositis rather than for muscle diseases other than myositis. Third, it remains to be determined whether muscle FDG uptake reflects disease activity and whether treatment for myositis decreases uptake.

Routine FDG-PET for malignancy could detect myositis with probably a high specificity but with low sensitivity compared to EMG, MRI, or muscle biopsy. FDG-PET detected neoplasm clearly. These results indicate that routine FDG-PET had limited usefulness for detection of myositis because of its low sensitivity, but it was effective for screening for malignancy associated with myositis. Improved FDG-PET, including measurment of standardized uptake values in muscles, might improve the sensitivity and demonstrate a relationship between PET imaging and phenotypes of myositis.

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