18F-FDG PET/CT Useful for the Early Detection of Rapidly Progressive Fatal Interstitial Lung Disease in Dermatomyositis

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Abstract

Interstitial lung disease (ILD) frequently accompanies polymyositis (PM) and dermatomyositis (DM) and is a major cause of mortality. The rapid diagnosis of ILD is paramount. However, the early changes of pre-symptomatic ILD are difficult to detect. We present a patient with DM who had positive uptake in the lung of FDG-PET/CT as well as ‘mechanic’s hands’ appearance, increased serum ferritin and serum anti-CADM-140 antibody, all before the detection of ILD by CT. Although aggressive treatment was initiated, the patient died of diffuse alveolar damage. These observations suggest that the pulmonary uptake of 18F-FDG predicts rapidly progressive ILD in DM.

Key words: dermatomyositis, interstitial lung disease, 18F-FDG PET/CT, anti-CADM-140 antibody


Introduction

Polymyositis (PM) and dermatomyositis (DM) are classified as idiopathic inflammatory myopathies (1-3). PM/DM is frequently accompanied by interstitial lung disease (ILD) that is known to portend a poorer prognosis in this disease (4). Early identification of ILD complicating the course of PM/DM is necessary to determine the start of intensive immunosuppressive therapy, including corticosteroids and other immunosuppressive agents. Several candidates such as serum ferritin, ‘mechanic’s hands’ appearance, and anti-CADM (clinically amyopathic dermatomyositis)-140 antibody have been reported to predict rapidly progressive ILD (5-8). We show here a case of fatal rapidly progressive ILD in the setting of DM. The patient showed a positive uptake of 18F-fluorodeoxyglucose (FDG) on positron emission tomography (PET)/computed tomography (CT) of the lung as well as mechanic’s hands, the elevation of serum ferritin and positive anti-CADM-140 antibody, before the clinical onset of ILD. 18F-FDG-PET/CT may be useful for the early detection of ILD, regardless of the absence of any respiratory symptoms and changes on CT scan of the lung.

Case Report

A 77-year-old Japanese housewife was admitted to our hospital because of general malaise and fever. One month prior to admission, she had mild polyarthralgia and appetite loss. She had a history of mild hypertension. On admission, her blood pressure was 120/60 mmHg, pulse rate was 80/min, respiratory rate was 16 per minutes and temperature was 38.6°C. Her oxygen saturation at room air was 95%. Her breath sounds were normal on auscultation. She had symmetric proximal muscle weakness and erythema occurring in a symmetric fashion over the metacarpophalangeal and interphalangeal joints (Gottron’s sign) (Fig. 1A). Similar lesions can be seen over the extensor aspects of the elbows, knees and the forehead. There was hyperkeratosis and scaling with dark red erythema along the ulnar aspect of both thumbs and the radial aspect of both index fingers (mechanic’s hands) (Fig. 1B). Laboratory tests showed the following values: white blood cells 5,400/μL (neutrophils 80.0%, eosinophils 0%, lymphocytes 11.0%, monocytes

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globulin A 284 mg/dL, and Immunoglobulin M 68 mg/dL. The complement level was not decreased. Antinuclear antibody and anti-Jo-1 antibody tests were negative. Anti-CADM-140 antibody was positive. KL-6 was 685 U/mL (normal, less than 500 U/mL). Arterial blood gas analysis at room air revealed pH of 7.41, PaO₂ of 77 Torr and PaCO₂ of 37 Torr. Urinalysis showed 1+ protein.

Electromyography (EMG) demonstrated multiple polyphasic potentials with low amplitude, sharp edges, and short duration, as well as fibrillations typical of myogenic injury. Magnetic resonance imaging (MRI) revealed abnormal high signal changes in the inflammation on her adductor magnus muscle on axial and T2-weighted images (Fig. 2) and severe atrophy of the iliopsoas muscles. Chest X-ray and CT scan on hospital-day 5 showed no sign of interstitial pneumonia (Fig. 3). There was no evidence of malignancy on abdominal and pelvic contrast-enhanced CT scan. We then performed ¹⁸F-FDG-PET/CT on the 11th day after admission for the screening of malignant neoplasm and found the accumulation of ¹⁸F-FDG distributed peripherally in both lungs, although malignant disease was not detected (Fig. 4). There was no evidence of hemophagocytosis in smear specimens of the bone marrow. Random skin biopsy did not detect intravascular large B-cell lymphoma. Thus, we made a diagnosis of DM on the basis of the criteria of Bohan et al. (9).

We initiated oral prednisolone at 50 mg/day on hospital day 7. She began to show an improvement of fever and muscle weakness within 2 weeks after the steroid therapy. KL-6 was elevated to 935 U/mL and ground-glass opacity (GGO) and bilateral interstitial shadows were noted on chest CT scan performed on the 28th day after admission (Fig. 5A). We immediately started pulse cyclophosphamide (500 mg) every 2 weeks because of the emergent nature of DM complicated by ILD. Auscultation of the chest identified audible fine crackles on the both lower lungs on hospital-day 40. The patient’s respiratory state did not improve, and the serum KL-6 level gradually elevated to a maximum value of 3,540 U/mL (Fig. 6). Four weeks after the beginning of steroid therapy, ILD rapidly progressed with acute respiratory failure requiring intubation and mechanical ventilation (Fig. 5C). Oral cyclosporine A (100 mg/day) was administrated in combination with prednisolone and cyclophosphamide. Cyclosporine A was maintained to keep serum trough levels between 100 and 200 ng/mL. However, cytomegalovirus antigenemia was detected on day 70. Her respiratory state and CT findings became gradually worse (Fig. 5D) and she finally died on day 75 of her hospital stay.

An autopsy revealed acute and organizing diffuse alveolar damage (DAD) and organizing acute lung injury. Some lesions mainly consisted of a hyaline membrane, which is a hallmark of acute DAD. Other lesions had the typical features of organizing DAD, including membranous organization with occlusion of alveoli, dilation of alveolar ducts and sacs with collapsed alveoli (Fig. 7). There was evidence of

Figure 1. A. Gottron’s sign in a symmetric fashion over the metacarpophalangeal and interphalangeal joints. B. Hyperkeratosis and scaling with dark red erythema along the radial aspect of the index finger (‘mechanic’s hands’).

Figure 2. MRI reveals abnormal high signal changes in the inflammation on her adductor magnus muscle on axial and T2-weighted images.

3.0%), hemoglobin 13.1 g/dL, platelets 121,000/μL, serum creatinine 1.2 mg/dL, blood urea nitrogen 33 mg/dL, C-reactive protein (CRP) 0.99 mg/dL, prothrombin time 11.5 seconds, activated partial thromboplastin time 36 seconds, total protein 6.2 g/dL, serum albumin 3.2 g/dL, creatine phosphokinase 74 IU/L, alanine aminotransferase 332 IU/L, aspartate aminotransferase 147 IU/L, lactate dehydrogenase 383 IU/L, aldolase 20.5 U/L (normal, less than 6.1 U/L), serum myoglobin concentration 61 ng/mL (normal, less than 60 ng/mL), serum ferritin level 2,417 ng/mL (normal, 39.4-340 ng/mL), Immunoglobulin G 1,821 mg/dL, Immunoglobulin A 284 mg/dL, and Immunoglobulin M 68 mg/dL. The complement level was not decreased. Antinuclear antibody and anti-Jo-1 antibody tests were negative. Anti-CADM-140 antibody was positive. KL-6 was 685 U/mL (normal, less than 500 U/mL). Arterial blood gas analysis at room air revealed pH of 7.41, PaO₂ of 77 Torr and PaCO₂ of 37 Torr. Urinalysis showed 1+ protein.

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infection with cytomegalovirus and aspergillus in the lung.

**Discussion**

PM/DM is frequently accompanied by ILD which is an ominous prognostic factor in this disease. The prevalence of ILD varies widely from 5 to 46% among the case series of patients with DM and PM. Since the early diagnosis of ILD is important to be able to immediately commence intensive treatment, several physiological and laboratory findings have been reported to be associated with rapidly progressive ILD (4).

Hyperkeratotic rhagadiform hand symptoms called ‘mechanic’s hands’ seems to be one of the clinical signs of DM (6). It has been indicated that mechanic’s hands are associated with ILD (6). Mechanic’s hands and ILD occur together at a frequency of 60-70% (10). Gono et al. recently reported that the serum ferritin was a useful predictor of acute/subacute ILD as well as a prognostic factor of acute/subacute ILD in DM (5). They showed that the serum ferritin was significantly higher in patients with DM with acute/subacute ILD (median, 790 ng/mL; range, 121-8,300 ng/mL) than in those with DM without acute/subacute ILD (median, 186 ng/mL; range, 4.3-1,100 ng/mL). The cumulative six-month survival rates for patients with DM complicated by acute/subacute ILD were 82.5% in the group with ferritin levels <1,500 ng/mL and only 28.6% in the group with ferritin levels ≥1,500 ng/mL. Thus, it is recommended for DM/ILD patients with hyperferritinemia, especially levels ≥1,500 ng/mL, that intensive treatment with various combinations of immunosuppressants be started early. The present patient already showed an extremely high serum ferritin of 2,417 ng/mL at the first visit, without evidence of other diseases that might manifest hyperferritinemia such as adult Still’s disease (11) and hemophagocytosis (12).

Autoantibodies to a 140-kDa polypeptide, anti-CADM-140 antibodies, were specifically associated with clinically amyopathic DM (CADM) that shows typical cutaneous features of DM without clinical evidence of myositis for at least 2 years after the onset of skin manifestations (7). She was diagnosed as having CADM because she had the typical cutaneous manifestations of DM without the marked ele-
Figure 5. Chest CT performed at hospital-day 28(A), day 41(B), day 56(C) and day 70 (D) shows worsening lung injury.

Figure 6. Clinical course
The presence of anti-CADM-140 antibodies in DM has also been reported to be one of the predictors of developing rapidly progressive ILD (7, 8). In accordance with these findings, the present patient had mechanic’s hands, hyperferritinemia and anti-CADM-140 antibody, and she terminally developed rapidly progressive ILD that was resistant to aggressive treatment, even when started in the early phase of the disease.

It is interesting to note in the present patient that the FDG-PET/CT scan showed a positive accumulation at the periphery of the lungs bilaterally, before the detection of ILD by CT. Some investigators demonstrated that FDG-PET/CT scan may be helpful in the evaluation of ILD (14, 15). Furthermore, FDG-PET/CT scan may possibly be able to evaluate disease activity in patients with ILD (16, 17). It has been reported that the monocytes/macrophages and lymphocytes are activated and the release of cytokines such as TNF-α and IL-2 are increased in ILD (18). These alterations result in an increased glucose metabolism, and FDG-PET/CT scan may correlate these physiologic alterations to the anatomic findings on CT scan, regardless of the predominant component of the disorder, whether inflammation or fibrogenesis. However, the usefulness of FDG-PET/CT for the early detection of ILD has not been proposed. A few studies suggest the possibility of predicting certain lung diseases such as radiation pneumonitis and chemotherapy-induced lung diseases (19, 20). Thus, our observation is the first to describe the usefulness of FDG-PET/CT for the detection of early inflammation in interstitial lung disease that complicates DM.

We describe here a patient with DM who showed rapidly fatal progressive ILD. Although the patient died despite aggressive immunosuppressive therapy with corticosteroids, cyclophosphamide, and cyclosporine A, this case suggests that the combination of a positive pulmonary uptake on FDG-PET, ‘mechanic’s hands’ appearance, elevation of serum ferritin and positive anti-CADM-140 antibody might be indicative of the presence of rapidly progressive ILD in DM.

