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Predictive factors for long-term outcome in polymyositis/dermatomyositis-associated interstitial lung diseases

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ABSTRACT

Background: Interstitial lung disease (ILD) is strongly associated with polymyositis (PM), dermatomyositis (DM), and clinically amyopathic dermatomyositis (CADM). It is also related to mortality. Previous studies have highlighted that the acute form of PM/DM/CADM-associated ILD (PM/DM/CADM-ILD) has a poor short-term prognosis. However, little is known about the long-term clinical features of patients with PM/DM/CADM-ILD. The aim of the present study is to clarify the clinical characteristics and the predictive factors for long-term outcomes in patients with PM/DM/CADM-ILD.

Methods: Thirty-four patients with PM/DM/CADM-ILD who were followed up for more than 12 months were analyzed retrospectively. The patients were classified as "stable" or "deterioration" according to respiratory symptoms, serial changes in forced vital capacity (FVC) or arterial oxygen pressure, and radiologic findings during the follow-up period.

Results: Twenty-six patients (76%) were in the stable group and eight patients (24%) were in the deterioration group. Home oxygen therapy was performed in six cases in the deterioration group because of chronic respiratory failure due to progression of ILD. The deterioration group, in comparison to the stable group, had a significantly lower %FVC and a higher positive rate for the anti-PL-7 antibody. Multivariate logistic regression analysis revealed that a positive anti-PL-7 antibody test and a lower %FVC were independently associated with deterioration during long-term follow-up.

Conclusions: Patients with PM/DM/CADM-ILD are at risk for chronic respiratory failure due to the deterioration of ILD during long-term follow-up. The presence of anti-PL-7 antibody and

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a lower %FVC at initial diagnosis may predict long-term deterioration in patients with PM/DM/CADM-ILD.

1. Introduction

Polymyositis (PM) and dermatomyositis (DM) are a group of systemic autoimmune diseases that affect the skeletal muscles and the skin. They can also affect organs, such as the lungs, and joints [1]. Clinically amyopathic dermatomyositis (CADM) is a distinct subgroup of DM that causes a skin rash typical of classic DM, but with little or no evidence of muscular manifestations [2,3]. Among the extramuscular manifestations of PM/DM/CADM, interstitial lung disease (ILD) is a typical pulmonary comorbidity that causes morbidity and mortality [3–7].

The available data on the characteristics of long-term follow-up in patients with PM/DM/CADM-associated ILD (PM/DM/CADM-ILD) are limited. It is known that considerable heterogeneity exists in the spectrum of PM/DM/CADM-ILD [5,7]. Multiple factors, including underlying collagen-vascular diseases (PM, DM, or CADM) and different forms of ILD (e.g., acute, subacute, or chronic), are associated with heterogeneity [8–10]. We have previously assessed the clinical differences between PM-associated ILD (PM-ILD) and DM-associated ILD (DM-ILD), and have shown that DM-ILD was more refractory to corticosteroid therapy and had a lower survival rate than PM-ILD [8]. Our previous report, which compared the acute/subacute form of ILD with the chronic form, demonstrated that four of nine patients (44%) with acute/subacute CADM-associated ILD (CADM-ILD) died of respiratory failure due to progression of the ILD within two months after diagnosis, whereas none of the patients with chronic CADM-ILD died; this indicated that acute/subacute ILD had a worse prognosis than chronic ILD in CADM-ILD patients [9]. Several studies, including ours, have highlighted the clinical features of the acute form of PM/DM/CADM-ILD and describe its poor prognosis in the short term [9–13]. However, the long-term characteristics of PM/DM/CADM-ILD have not been fully elucidated.

In a survival curve of PM/DM/CADM-ILD, a rapid drop, especially in the first year after diagnosis, and subsequently a slower decline were observed in cohorts from multiple studies [10,12,14], indicating that deaths from acute fatal ILD occurred in the short term, mostly within a year, and that a modest deterioration of ILD may occur in patients who successfully survive the initial treatment. These findings suggest that clinical features and prognostic factors for patients with acute fatal ILD may be different from those in patients with PM/DM/CADM-ILD who survive more than a year following successful initial treatment. Given that there is considerable heterogeneity in the clinical course of PM/DM/CADM-ILD, the predictive factors for long-term deterioration should be analyzed in order to separate them from the factors involved in short-term mortality. In the present study, we retrospectively assessed the clinical characteristics and factors contributing to deterioration during long-term follow-up in patients with PM/DM/CADM-ILD.

2. Patients and methods

2.1. Subjects

The study included 52 consecutive patients diagnosed as having PM/DM/CADM-ILD between January 1990 and December 2013 at Hamamatsu University Hospital. Six patients (four CADM-ILD and two DM-ILD) died within a year from acute respiratory failure due to the progression of ILD. Of the 46 patients with a follow-up period of over one year, 12 had limited long-term follow-up data and were excluded. Thirty-four patients (four PM-ILD, 17 DM-ILD, and 13 CADM-LD) who had clinical, physiological, and radiological data collected for more than one year were analyzed retrospectively in the current study (Fig. 1). The diagnosis of PM or DM was confirmed according to the Bohan and Peter criteria [15] as described in a previous study [14]. The patients with definite or probable PM/DM were included in the study. The diagnosis of CADM was based on the presence of a skin rash characteristic of DM, and no clinical evidence of muscular disorder along with little or no evidence of subclinical features of myositis, as described in previous studies [2,9,14,16]. This retrospective study was approved by the Institutional Review Board of the Hamamatsu University School of Medicine

Abbreviations: ILD, interstitial lung disease; PM, polymyositis; DM, dermatomyositis; CADM, clinically amyopathic dermatomyositis; FVC, forced vital capacity; HRCT, high-resolution computed tomography; PaO_2, arterial oxygen tension; ARS, anti-aminoacyl-tRNA synthetase; anti-Jo-1, anti-histidyl; anti-PL-7, anti-threonyl; anti-PL-12, anti-alanyl; anti-EJ, anti-glycyl; anti-KS, anti-asparaginyl; anti-OJ, anti-isoleucyl; anti-MDA5, anti-melanoma differentiation-associated gene 5; BAL, bronchoalveolar lavage; KL-6, Krebs von den Lungen-6; SP-D, surfactant protein D; IIM, idiopathic inflammatory myopathy; ASS, anti-synthetase syndrome

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