Characterization of Dermatomyositis with Coexistence of Anti-Jo-1 and Anti-SRP Antibodies

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Abstract

We describe a patient with dermatomyositis who presented with rapidly developing severe muscle weakness complicated by massive pleural effusion with interstitial lung disease. Myopathological analysis was suggestive of dermatomyositis. This patient showed both anti-Jo-1 and anti-SRP antibodies in serum. To our knowledge, the coexistence of these two myositis-specific autoantibodies (MSA) is considered extremely rare and is clearly an exception to the rule of having only one MSA. Our findings provide compelling evidence that the coexistence of these two MSAs may lead to more severe clinical symptoms, interacting in a complex fashion, thus expanding the clinical spectrum of idiopathic inflammatory myopathy.

Key words: idiopathic inflammatory myopathy, dermatomyositis, pleural effusion, myositis-specific autoantibody, anti-Jo-1 antibody, anti-SRP antibody

(DOI: 10.2169/internalmedicine.51.6566)

Introduction

Idiopathic inflammatory myopathies such as polymyositis (PM) and dermatomyositis (DM) are systemic autoimmune connective tissue diseases characterized by chronic muscle inflammation with involvement of various organs (1). The pathogenesis of PM/DM is unknown, but autoantibodies directed against various cellular constituents have been identified in patients with PM/DM. Some autoantibodies found almost exclusively in PM/DM are known as myositis-specific autoantibodies (MSA), including anti-Jo-1 (histidyl tRNA synthetase) antibody, anti-PL-7 antibody, anti-signal recognition particle (SRP) antibody, anti-Mi-2 antibody, and anti-CADM-140 antibody. Each MSA is associated with a set of unique clinical features (2, 3).

We describe a 61-year-old man with DM who presented with severe muscle involvement characterized by rapidly developing proximal weakness, culminating in severe disability. He also showed massive pleural effusion with interstitial lung disease (ILD). Interestingly, both anti-Jo-1 and anti-SRP antibodies were positive in his serum. To our knowledge, the coexistence of these two types of MSA is considered extremely rare. Only one other case of idiopathic inflammatory myopathy with these two MSAs has been described in a recent report (4). Our findings suggest that coexistence of these two MSAs is associated with specific clinicopathological features.

Case Report

A 61-year-old man was admitted in June because of a 1-month history of rapidly progressive severe weakness of all four extremities. His skin was discolored, and he had dyspnea. The past history was noncontributory to the present illness. On admission, he presented with difficulty in getting up from bed and lifting his arms above his head. Physiological examination showed severe symmetric proximal weakness (less than grade 3 according to the Medical Research Council scale) of all four extremities. There were no other motor deficits. Sensory and stretch reflexes were normal. Erythematous rashes were present on the arms, trunk, legs, and face, including a typical heliotrope rash and Gottron’s papules.

Laboratory examinations showed very high levels of creatine kinase (CK) (5,685 IU/L; normal: <160) in serum. The erythrocyte sedimentation rate and C-reactive protein were slightly elevated (80 mm/hr, <10; 2.6 IU/L, <0.1). Serum
antinuclear antibody was detected, accompanied by positivity for both anti-Jo-1 and anti-SRP antibodies, but negativity for other MSA, such as anti-PL-7 antibody. Among myositis-associated autoantibodies, anti-SS-A, anti-SS-B, anti-U1-RNP, and anti-Scl-70 antibodies were not detected. Electromyography showed short duration, small amplitude, and pleural effusion were mildly decreased. The erythematous rashes decreased, but persisted slightly. Four months after the start of treatment, a progressive gastric cancer (papillary adenocarcinoma, stage IIIA) was diagnosed. A gastrectomy was thus performed. Subsequently, the muscle weakness and respiratory difficulties worsened despite an increase in the dose of steroids. One year after gastrectomy, the patient died of progressive ILD with massive pleural effusion and multiple liver metastases from gastric cancer.

**Discussion**

We described a patient with idiopathic inflammatory myopathy accompanied by ILD with massive pleural effusion, who presented with rapidly developing severe proximal weakness and respiratory difficulty. His skin lesions were suggestive of DM. Histopathological examination of a muscle specimen revealed many necrotic and regenerative fibers with marked perimysial cell infiltration (Fig. 2). The infiltrating CD4+/CD8+ T cell ratio at perimysial sites (mean ± SD) was 1.58±0.28. Characteristic perifascicular muscle fiber atrophy was seen. Strong major histocompatibility complex class I (MHC-I) expression, especially in perifascicular atrophic fibers, was positive in cytoplasm. There was no expression of CD8/MHC-I complex, which suggested DM rather than PM. Interestingly, the present patient showed both anti-Jo-1 and anti-SRP antibody in his serum. The presence of these two MSAs is considered extremely rare and is clearly an exception to the rule of having only one MSA in association with PM/DM (7). To our knowledge, the coexistence of these MSAs has only been documented one time previously (4). That patient had severe muscle weakness and ILD, characterized by the presence of both anti-Jo-1 and anti-SRP antibody. Although the reason for this association and the pathogenic roles of these two MSAs are unclear, MSA may play a key, yet indirect part in the etiology of PM/DM.

Each MSA is associated with a set of unique clinical features (2, 3). Anti-Jo-1 antibody, one of the aminoacyl tRNA synthetases antibodies, is closely related to PM/DM, which...
is frequently associated with ILD (2). Anti-Jo-1 antibody was reported in 20-30% of patients with PM/DM. ILD was more common than myositis in the early phase of disease and seemed to be one predictor of outcomes. The onset of weakness in patients with anti-Jo-1 antibody frequently occurs between the months of February and July (8). In contrast, anti-SRP antibody is clinically associated with pure PM and is found in 4-6% of patients with PM/DM (1, 3), although three patients with DM were reported among 23 Japanese patients with myositis associated with anti-SRP antibody (9). Patients with anti-SRP antibody most often present with severe muscle involvement characterized by rapidly developing proximal weakness, culminating in severe disability; the response to steroid therapy is often poor. Peculiar histopathological features include prominent muscle fiber necrosis without clinically significant inflammatory cell infiltration.

The present patient’s condition was characterized by the coexistence of anti-Jo-1 antibody and anti-SRP antibody. Because the coexistence of these MSAs is associated with the clinical features of both antibodies, interacting in a complex fashion, affected patients may show more severe signs and symptoms. Another characteristic of our patient was the presence of massive pleural effusion associated with ILD. Although lung involvement is often found in patients with PM/DM, massive pleural effusion is very rare (10). The pathomechanism of the massive pleural effusion is unknown, but in this case it may have involved the exacerbation of pleural inflammation in association with pleural microvascularopathy in DM.

In conclusion, our findings strongly suggest that the coexistence of anti-Jo-1 and anti-SRP antibodies may lead to more severe clinical symptoms, including massive pleural effusion, thus expanding the clinical spectrum of idiopathic inflammatory myopathy. However, further clinical and pathological studies of similar cases are needed to establish firm conclusions.

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

Contributions: K. Sugie was responsible for the overall study design, participated in the organization, planning, and coordination of the study, and wrote the manuscript. Y Tonomura and S Ueno contributed to running the study and analyzed and interpreted the data.

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