Letter to the Editor

Three cases of interstitial pneumonia with anti-signal recognition particle antibody

Dear Editor,

Anti-signal recognition particle antibody (SRP-Ab) is a myositis-specific antibody (MSA) that is found in serum of patients with myositis characterized by a necrotizing myopathy. Because patients with SRP-Ab have few extra-muscular manifestations,¹ the clinical characteristics of interstitial pneumonia (IP) with SRP-Ab have not been clarified. Here, we present three cases of IP with SRP-Ab. Case 1: A 51-year-old man with a one-year history of cough and sputum was referred to our hospital for gradual progression of his symptoms. On admission, he did not have muscle pain or proximal muscle weakness. CK was markedly elevated (1160 U/L), and aldolase (16.2 U/L), KL-6 (1529 U/mL) and SP-D (312.4 ng/mL) were also elevated. Auto-immune antibodies analyzed were negative. Pulmonary function tests revealed restrictive respiratory dysfunction. His CT showed consolidation in the bilateral lower lungs (Fig. 1a, b). Broncoalveolar lavage revealed an increase in lymphocytes. He was diagnosed as having IP associated with polymyositis (PM). Although the patient was suspected to have myositis, there was no evidence of myopathy after careful examination by MRI and electromyography. Monthly cyclophosphamide pulse therapy was started. Although CK, aldolase, and fibrotic markers were temporarily normalized, they gradually increased. After six times of cyclophosphamide therapy, oral prednisolone was started. As a result, muscle enzymes and fibrotic parameters were decreased to normal levels. His chest radiograph findings were gradually improved with significant increase in forced vital capacity (FVC) at 46 months after prednisolone. Positive SRP-Ab was confirmed by RNA immunoprecipitation (RIP) assay. Case 2: A 63-year-old man with an 8-year history of myositis was referred to our hospital for cough and dyspnea.

Fig. 1. Chest radiograph on admission. Case 1 (a, b): Consolidation was observed in the bilateral dorsal lower lung fields. Case 2 (c): Reticular shadows were observed in the bilateral dorsal lung bases. Case 3 (d): Ground-glass opacities were observed in the bilateral lung bases.

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on exertion. He had complained of progressive lower extremity weakness and had been treated with oral prednisolone and cyclophosphamide for five years. Although muscle strength had been improved, he developed respiratory symptoms. On admission, he did not have muscle weakness and cutaneous rash. His CT revealed reticulation in the bilateral lungs (Fig. 1c). CK (328 U/L), KL-6 (1128 U/mL) and SP-D (361.2 ng/mL) were elevated. Autoimmune antibodies analyzed were negative. Pulmonary function tests were within normal range except a low diffusion capacity. Bronchoalveolar lavage revealed a slight increase in eosinophils. He was diagnosed as having IP associated with PM, and oral prednisolone and cyclophosphamide were continued. However, due to the worsening of the patient’s dyspnea as well as development of numbness of the hands and fingers with tapering prednisolone, intravenous immunoglobulin therapy was conducted. After improvement of his symptoms, his chest radiological findings had not been worsened with oral prednisolone and immunosuppressants. Afterward, although he experienced acute exacerbation of IP twice, his radiological findings and symptoms were significantly improved after steroid pulse therapies. Positive SRP-Ab was confirmed by RIP assay. Case 3: A 54-year-old man with a 6-month history of progressive upper and lower extremity weakness was referred to our hospital. He presented with a dropped head and his muscle strength grade was 2/5 in the extremities on admission. CK (554 U/L) and aldolase (60.2 U/L) were markedly elevated. His MRI showed profound muscle edema (Fig. 2a–c), and myopathic changes were found on electromyography. A left deltoid muscle biopsy demonstrated degeneration and regeneration muscle fibers (Fig. 2d, e). His CT revealed ground-glass opacities in the bilateral lungs (Fig. 1d) and SP-D (182.6 ng/mL) was elevated. Autoimmune antibodies analyzed were negative. The patient was diagnosed as having inflammatory myopathy with IP, and oral prednisolone was started. His muscle strength was gradually improved, and CK decreased to the normal level. However, CK was elevated with tapering prednisolone and his muscle strength became impaired again. On the other hand, no significant worsening in his CT findings was observed during follow-up. Positive SRP-Ab was confirmed by RIP assay. Anti-ARS antibody (ARS-Ab) was not detected in all cases.

The inflammatory myopathies are a heterogeneous group characterized by muscle weakness, elevated serum muscle enzymes, electromyographic abnormalities, and inflammation in skeletal muscle. MSAs, including ARS-Ab and SRP-Ab, are frequently detected in serum of patients with idiopathic inflammatory myopathies (IIM) such as PM and dermatomyositis (DM). Although the etiology of IIM has not been fully clarified, the clinical characteristics of patients with IIM are closely related to the type of MSA. SRP, which consists of 7S RNA and six proteins, plays an important role on proper localization of proteins by regulating protein translocation across the endoplasmic reticulum membrane. Inside the endoplasmic reticulum, SRP recognizes secretary proteins which are synthesized by ribosomes. The proteins are delivered to the endoplasmic reticulum membrane and transported across the membrane. SRP-Ab was first reported as the antibody found in a typical PM patient, and is found in the serum of ~10% of PM/DM patients. On the other hand, myopathy with SRP-Ab has recently been considered to be distinct from other types of inflammatory myopathies, because muscle weakness was prominent with marked CK elevation and histological analysis revealed necrotizing myopathy without inflammatory cell infiltration. In our two cases, muscle weakness was not found at the diagnosis of IP. Although SRP-Ab was originally described to be associated with inflammatory myopathy, Hanaoka et al. showed that 32.1% of SRP-Ab positive cases (9/28) did not have inflammatory myopathy, suggesting SRP-Ab can be positive in patients without muscular symptoms. In addition, non immune-mediated triggers for IP and IP associated with PM. The mechanisms of this association remain unknown.
necrotizing myopathy and anti-ARS syndrome-like clinical characteristics were reported. These results suggest that clinical characteristics of patients with SRP-Ab might be variable. Although the antibody is reported to bind to the 54-kDa of the SRP (4), the biological significance of SRP-Ab is not known so far. Further studies are necessary to clarify the biological significance of SRP-Ab in patients with the antibody.

In patients with SRP-Ab, the frequency of IP has been considered to be low. However, a relatively high frequency (~20%) of IP has reported, and a recent analysis of 100 patients with SRP-Ab has shown that IP was present in 13%. In these patients, the major CT findings are ground glass attenuation which is commonly bilateral and symmetrical with subpleural predominance, irregular linear, reticular opacities and traction bronchiectasis. There findings are consistent with non-specific interstitial pneumonia (NSIP) pattern. In terms of the pathological findings of the lungs, most reports have not been described in detail, Kono et al., reported a fibrotic NSIP pattern (temporally homogenous alveolitis and interstitial fibrosis) in the specimen obtained by video-assisted thoracoscopic lung biopsy. Although a precise frequency has not been determined, the frequency of IP is significantly lower in patients with SRP-Ab than those with ARS-Ab. Because most previous reports have focused on muscle features, the clinical characteristics of IP were not known in patients with SRP-Ab. Muscle lesions have been demonstrated to be generally resistant to treatment with corticosteroid and/or immunosuppressants. However, in all of our cases, immunosuppressive therapy was effective for IP. Although there are few reports on the treatment for IP in such patients, the improvement of chest radiological findings after corticosteroid therapy was reported. In their case, high resolution CT findings showed NSIP pattern as well as our three cases, suggesting that NSIP is the major IP pattern and immunosuppressive therapy is effective in IP patients with SRP-Ab as reported in ARS-Ab positive IP.

The present cases suggest that SRP-Ab could be positive in IP patients even without significant muscle symptoms, and immunosuppressive therapy might be effective for IP in patients with SRP-Ab.

Conflict of interest
The authors have no conflict of interest to declare.

References

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