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CASE STUDY

A case of anti-OJ antibody-positive polymyositis with marked muscle involvement and interstitial lung disease

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Abstract

An 83-year-old man with muscle involvement and interstitial lung disease (ILD) was diagnosed with anti-OJ antibody (Ab)-positive polymyositis (PM). He did not have Raynaud's phenomenon, heliotrope rash, Gottron's sign, fever, arthralgia, or mechanic's hand. A literature review of 21 anti-OJ Ab-positive patients described that the diagnoses were as follows: 10 with PM, five with dermatomyositis, five with ILD, and 1 with overlap syndrome of PM and rheumatoid arthritis. Myositis was observed in 16, ILD in 19, and skin rash in 5. Physicians need to be aware of the existence of patients with anti-OJ Ab who have myositis and ILD.

KEYWORDS
anti-OJ antibody, anti-synthetase syndrome, interstitial lung disease, polymyositis

1 | INTRODUCTION

A number of autoantibodies (autoAbs) are found in patients with idiopathic inflammatory myopathy, including polymyositis (PM) and dermatomyositis (DM). Classifying PM/DM patients according to their myositis-specific Abs (MSAs) guides the clinician to focus on particular manifestations during the follow-up of individual patients.[1] Eight anti-aminoacyl-tRNA synthetase (ARS) Abs have been described: anti-Jo-1 Ab, anti-PL-7 Ab, anti-PL-12 Ab, anti-EJ Ab, anti-OJ Ab, anti-KS Ab, anti-Zo Ab, and anti-Ha Ab. Based on a unique combination of clinical features commonly observed in patients with anti-ARS Abs, Targoff proposed a disease entity termed "anti-synthetase syndrome," which is characterized by myositis, interstitial lung disease (ILD), Raynaud's phenomenon, fever, arthritis, and mechanic's hand.[2] Although anti-synthetase syndrome has common clinical manifestations, further observations have distinguished differences in clinical features associated with individual anti-ARS Abs.[3] Therefore, the accumulation of single cases with anti-ARS Abs is clinically important to understand the entire picture of anti-synthetase syndrome. Anti-OJ antibody Ab is an anti-ARS Abs that reacts with isoleucyl-tRNA.[4] Clinical features of anti-OJ Ab currently remain unclear due to the small number of reported cases because immunoprecipitation assay is required to identify it.[5] We report the case of an anti-OJ Ab-positive PM patient with marked muscle involvement and ILD who was successfully treated using oral prednisolone and high-dose intravenous immunoglobulin therapy.

2 | CASE REPORT

An 83-year-old Japanese man was referred to our hospital with a 3 month history of muscle pain and weakness in his trunk and extremities. When he visited our hospital, he had difficulties walking and raising the upper extremities. He did not exhibit coughing or

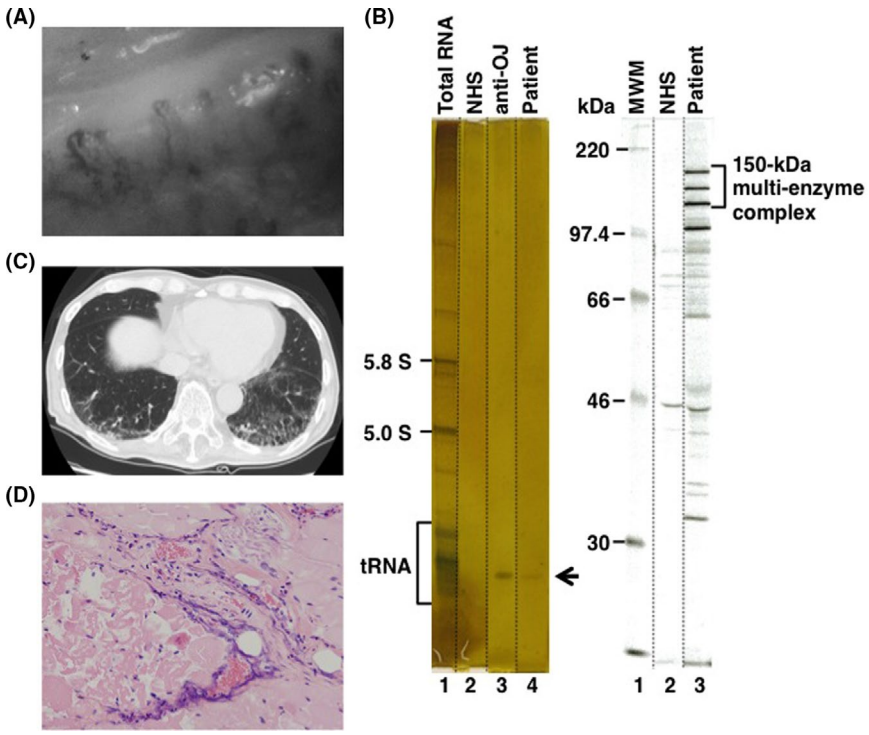

FIGURE 1 (A) Capillaroscopy revealed reduced capillaries, irregularly enlarged capillaries, hemorrhage, and capillary ramifications. (B) The patient's serum precipitated isoleucyl-tRNA (arrow) in an RNA immunoprecipitation assay. Total RNA, with the 5.8S and 5.0S small ribosomal RNAs and tRNA region, is indicated; Lane 1, total RNA; Lane 2, normal healthy serum (NHS); Lane 3, anti-OJ antibody-positive serum; and Lane 4, patient serum (left panel). The patient's serum also precipitated at least three tRNA synthetases, considered to be glutamine, isoleucine, and leucine, in a protein immunoprecipitation assay; Lane 1, molecular weight marker (MWM); Lane 2, NHS; and Lane 3, patient serum (right panel). (C) Bilateral interstitial lung disease was observed on chest computed tomography. (D) Biopsy of the right vastus lateralis muscle showing notable lymphocyte infiltration among muscle fibers and around the perivascular area, in addition to the degeneration of muscle fibers (x200)

dyspnea on exertion. He also did not have Raynaud's phenomenon, fever, heliotrope rash, Gottron's sign, arthralgia, or mechanic's hand. Capillaroscopy revealed reduced capillaries, irregularly enlarged capillaries, hemorrhage, and capillary ramifications (Figure 1A). A manual muscle test demonstrated marked muscle weakness in the trunk and extremities (3/5), and contraction of the pharynx and esophagus was observed on swallowing function evaluation. Laboratory tests revealed marked increases in serum creatinine kinase (4861 IU/L) and aldolase (44 IU/L). Liver enzymes were also high (aspartate aminotransferase: 215 IU/L, alanine aminotransferase: 168 IU/L, and lactate dehydrogenase: 830 IU/L). Serum Krebs von den Lungen-6 (KL-6) was moderately increased (491 U/ml). Indirect immunofluorescence (IIF) assay demonstrated a cytoplasmic staining pattern. Anti-ARS Abs were not detected using a commercially available enzyme-linked immunosorbent assay (ELISA) (Medical & Biological Laboratories [MBL], Nagoya, Japan).[6] However, his serum precipitated isoleucyl-tRNA in an RNA immunoprecipitation assay and 150 kDa multi-enzyme complexes in a protein immunoprecipitation assay, suggesting positivity for anti-OJ Ab (Figure 1B). On chest computed tomography (CT), bilateral ground-glass opacities and mild fibrotic changes consistent with ILD were observed (Figure 1C). Biopsy of the right vastus lateralis muscle revealed notable lymphocyte infiltration among muscle fibers and around the perivascular area, in addition to the degeneration of muscle fibers (Figure 1D). Malignancy was not detected in a detailed examination. Therefore, he was diagnosed with anti-OJ Ab-positive PM with ILD. He was hospitalized and treated using oral prednisolone (PSL) at 50 mg/day (1 mg/kg/day), followed by high-dose intravenous immunoglobulin therapy because intensive immunosuppressive therapy was not recommended due to his age. Muscle weakness rapidly recovered and muscle enzymes decreased. Ground-glass opacities on chest CT also improved. PSL was tapered, and he was discharged from the hospital while receiving PSL at 25 mg/day.

3 | DISCUSSION

Although anti-synthetase syndrome has common clinical manifestations, identification of each anti-ARS Ab is clinically important to predict clinical features, severity, and prognosis.[6] For example, patients with anti-Jo-1 Ab, anti-EJ Ab, and anti-PL-7 Ab have a higher frequency of muscle weakness than those with anti-PL-12 Ab, anti-KS Ab, and anti-OJ Ab.[3] Skin manifestations were predominantly found in patients with anti-EJ Ab, anti-PL-7 Ab, and anti-PL-12 Ab.

Regarding the clinical diagnosis, more than half of the patients with anti-Jo-1 Ab, anti-EJ Ab, or anti-PL-7 Ab had myositis, including DM, PM, and PM/DM overlap. The ratio with ILD alone was different. In particular, 77% of patients with anti-KS Ab and 63% of patients with anti-OJ Ab were diagnosed with ILD alone.[3] Although the frequency was relatively low, some patients with anti-ARS Abs were diagnosed with systemic sclerosis or systemic lupus erythematosus.[3] Therefore, the clinical features of patients with anti-ARS Abs are not uniform.

We analyzed the clinical features of 21 anti-OJ Ab-positive patients.[7-12] The median age of these patients was 52 years (13–75 years). They comprised 13 females and 8 males. The clinical diagnoses of these patients were as follows: 10 with PM, 5 with DM, 5 with ILD, and 1 with overlap syndrome of PM and rheumatoid arthritis. Myositis was observed in 16 of 21 patients (76%), ILD was observed in 19 (90%), and skin rash was observed in 5 (24%). Arthralgia/arthritis was noted in 12 of 19 patients (63%), Raynaud's phenomenon was noted in 3 (16%), and fever was noted in 7 of 12 patients (58%). Treatment content was recorded for 12 out of 21 patients. Most of these patients (11 of 12 patients, 92%) were treated using moderate- or high-dose oral corticosteroids, whereas three received steroid pulse therapy. Four patients needed additional immunosuppressive agents, including azathioprine, cyclosporine A, and cyclophosphamide. Treatment responses were generally good because 10 out of 11 patients had good responses. Our patient had myositis and ILD, but he did not have Raynaud's phenomenon, fever, arthralgia, or mechanic's hand. Therefore, identification of anti-OJ Ab was beneficial because he only had 2 of the 6 common manifestations observed in patients with anti-synthetase syndrome.

Microcirculation abnormalities detected by nail-fold video capillaroscopy (NVC) are a characteristic finding of microangiopathy in not only systemic sclerosis, but also DM. An association between NVC findings and disease activity in patients with DM was reported.[13] Although clinical importance of NVC findings in patients with anti-ARS Abs has not been elucidated, our case showed similar NVC findings that are commonly observed in patients with DM. Accumulation of cases with anti-ARS Abs is needed to evaluate whether NVC findings are a useful marker for diagnosis and disease activity in patients with anti-ARS Abs.

An ELISA system has been developed to detect any one of five anti-ARS Abs (anti-Jo-1 Ab, anti-PL-7 Ab, anti-PL-12 Ab, anti-EJ Ab, and anti-KS Ab); however, anti-ARS Ab specificity cannot be identified because recombinant antigens are coated on the plate as a mixture. In addition, this ELISA Kit does not identify anti-OJ Ab.[6] A line blot assay also cannot detect anti-OJ Ab.[5] Therefore, immunoprecipitation assay is essential to identify anti-OJ Ab.

When patients have severe myopathy and their IIF staining demonstrates a cytoplasmic pattern with negative ELISA results for anti-ARS Abs, physicians may consider the presence of anti-SRP Ab. Clinical characteristics of anti-SRP Ab include rapidly progressive proximal muscle weakness, dysphagia, and persistent increases in CK levels. Muscle biopsy can distinguish anti-SRP Ab from anti-OJ Ab because anti-SRP Ab typically suggests necrotizing myopathy exhibiting active muscle fiber degeneration and regeneration, and a marked increase in endomysial connective tissue, but negligible or no inflammatory cell inflammation.[14] Thus, although muscle biopsy is useful to distinguish, additional information of MSAs aids in making an accurate diagnosis.

In conclusion, it is important to steadily accumulate single cases of anti-OJ Ab because its clinical features have yet to be fully clarified.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DECLARATIONS

Approval of the research protocol: N/A.

Informed Consent: Verbal informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

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