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Case Report

Muscle weakness as a presenting symptom in ANCA-associated vasculitis

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Abstract

Muscle weakness is rarely a presenting symptom of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), although the disease frequently involves the lungs, skin, neurons, and kidneys. Here we describe a case of AAV presenting with muscle weakness in which only muscle biopsy could confirm the diagnosis. The literature review, including three similar cases, suggested that patients with ANCA-associated muscle vasculitis likely had myalgia, normal levels of creatine kinase, pulmonary fibrosis, rheumatoid factor, and muscle edema on MRI.

Keywords: anti-neutrophil cytoplasmic antibody, ANCA-associated vasculitis, muscle weakness, muscle biopsy, granulomatosis with polyangiitis

Introduction

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is characterized by small-vessel vasculitis, preferentially involving the kidneys, lungs, skin, and nerves. Musculoskeletal symptoms include arthralgia and muscle pain (1). To our knowledge, muscle weakness is a rare presenting symptom of this disorder. Therefore, the role of muscle biopsy in diagnosing this disorder has not been well-studied. Here, a case of AAV presenting with muscle weakness of the lower extremities, which was histologically diagnosed through muscle biopsy, is described.

Case Presentation

A 76-year-old woman was referred to us for the evaluation of muscle weakness. Three months before referral, she first noticed weakness in her lower extremities. A month and a half later, she also had pain in her lower extremities and was unable to squat and stand by herself. Around the same time, she had dry cough. She was diagnosed with interstitial lung disease on the basis of chest radiographic findings at a neighborhood clinic. Subsequently, she was referred for evaluation of her muscle weakness. The patient had had Raynaud phenomenon for 26 years but denied a history of fever, rash, paresthesia, arthralgia, or sicca symptoms. Her medical history included diabetes mellitus and chronic thyroiditis. Four months before referral, she had bilateral otitis media and was treated with a tympanostomy tube. Physical examination showed tenderness of all extremities, and manual muscle testing showed proximal weakness bilaterally; iliopsoas muscle of 2 (with 5 as the maximum); quadriceps of 3; and ankle dorsiflexor of 5. Laboratory data showed a white blood cell count of 8400/mL, C-reactive protein (CRP) level of 8.452 mg/dL, erythrocyte sedimentation rate of 76 mm/h, and creatine kinase (CK) level of 25 IU/L (reference range, 45-163 IU/L). The dipstick test showed no proteinuria or hematuria, with normal urinary sediment. Immunological tests showed an antinuclear antibody ratio of 1:160 with a speckled pattern, anti-SSA/Ro antibody 1:16, rheumatoid factor 123.9 IU/mL (<15), positive direct Coombs test, and myeloperoxidase (MPO)-ANCA 129 U/mL (<3.5), whereas the tests for cryoglobulin, anti-hepatitis C, anti-aminoacyl transfer RNA synthetase, anti-double-strand DNA, anti-RNP, anti-Sm, anti-SSB/La, and anti-phospholipid antibodies were all negative. The levels of complement were not decreased. Results of ophthalmologic examination and a biopsy of the minor salivary gland, performed to rule out Sjögren syndrome, were normal. CT of the chest showed bilateral ground-glass opacity and irregular reticular opacities with traction bronchiectasis, which was compatible with nonspecific interstitial pneumonia. The results of the electromyogram and the nerve conduction study were not remarkable. T2-weighted and STIR sequences on magnetic resonance imaging (MRI) of the thigh showed high-intensity lesions demonstrating muscle edema.

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Muscle biopsy revealed small-vessel vasculitis with significant invasion of CD4-positive lymphocytes and small grouped atrophy of muscle fibers, suggesting intramuscular denervation (Figure 1). Kidney biopsy was performed because of transient uric blood, which did not show abnormal findings. A clinical diagnosis of ANCA-associated vasculitis in the muscle with unclassified connective tissue disease was made, although the patient's condition could be categorized as granulomatosis with polyangiitis, according to the classification for epidemiologic studies (2). Therapy with high-dose prednisolone (1 mg/kg) was initiated when she could not walk without a caster walker. Her muscle weakness improved with therapy within a few months. Half a year later, when she was on a daily dose of 9-mg prednisolone, symptomatic relapse with discomfort of the lower extremities occurred concurrently with re-elevation of CRP and MPO-ANCA levels. Therapy with a moderate dose of prednisolone (20 mg daily) and azathioprine improved her symptom again. One year and a half after the relapse, her condition remained in remission while she was taking 5 mg prednisolone daily and 75 mg azathioprine daily.

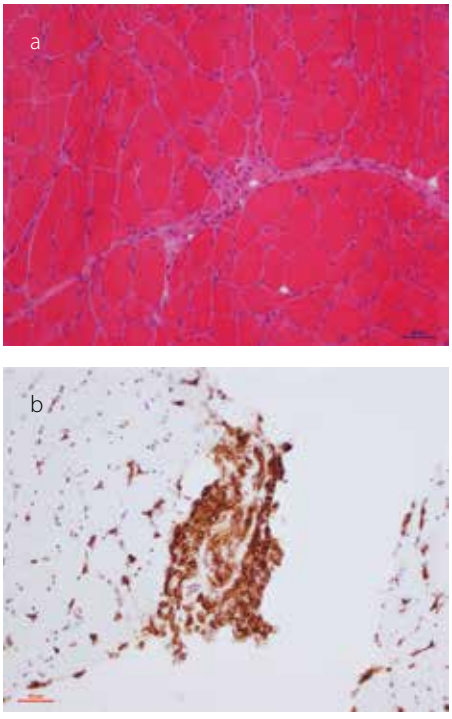

Figure 1. a-b. Muscle biopsy revealed small-vessel vasculitis with small grouped atrophy of muscle fibers (hematoxylin-eosin staining) (a); perivascular lesions consisted of significant invasion of CD4-positive lymphocytes (CD4 staining) (b)

Informed consent for publication was obtained from the patient.

Discussion

Our case presenting with muscle symptoms was diagnosed with muscle involvement of AAV on the basis of histological evidence of small-vessel vasculitis. As well as muscle pain, neural damage in the muscle due to AAV may have caused significant weakness, unproportional for negative results of muscle enzyme test and electromyogram. A relapsing course with re-elevation of MPO-ANCA suggested that muscle vasculitis was caused by this antibody.

To our knowledge, only three cases of muscle vasculitis due to AAV that presented mainly with muscle symptoms have been reported (Table 1). Birnbaum et al. reported a case of microscopic polyangiitis (MPA) presenting with myalgia and weakness at the proximal extremities, which was finally diagnosed as vasculitis of the muscle and lung (3). Kim et al. (4) reported an MPA case presenting with bilateral calf claudication that was histologically diagnosed as vasculitis of the muscle and kidney. Ours was the third case presenting with muscle symptoms in which histological evidence of vasculitis was seen on muscle biopsy. Interestingly, all the three cases had preceding pulmonary fibrosis, rheumatoid factor, and MPO-ANCA. MRI of the muscles always showed a high-intensity area on the T2-weighted image, similarly to idiopathic inflammatory myopathies (IIM). A retrospective analysis of 22 cases with histologically confirmed muscular involvement of small- and medium-vessel vasculitis showed that 10 (45%) and 3 (15%) showed myalgia and elevated CK levels, respectively (5). In contrast to IIM, ANCA-associated muscle vasculitis may also tend to have myalgia and normal CK levels, as seen in the previous cases (Table 1).

An observational study focusing on pulmonary fibrosis in MPA showed that myalgia was frequently observed in MPA cases with pulmonary fibrosis, compared with cases without pulmonary fibrosis (46% vs. 5%, p=0.008) (6). Another case series with pulmonary fibrosis in AAV also described that 4 (33%) of 12 cases had muscle involvement (7). Moreover, cases of idiopathic pulmonary fibrosis with MPO-ANCA are likely to show the presence of rheumatoid factor, compared with those without (8, 9). Accordingly, muscle symptom in AAV may likely be associated with pulmonary fibrosis and rheumatoid factor, as also seen in the previous cases (Table 1).

Hervier et al. (5) investigated the role for muscle biopsy in the diagnosis of systemic vasculitis and described that muscle biopsy provided histological evidence of vasculitis in 22 (67%) of 33 biopsies. Of their 31 cases, there were only two cases in which muscle biopsy provided the only specific evidence of systemic vasculitis (5). Our experience and these observations suggest that muscle biopsy should be considered in suspected cases of muscle vasculitis due to AAV, when biopsy of the other organs is clinically impractical.

Table 1. Cases of ANCA-associated vasculitis presenting with muscle symptoms

Ref.	Age Sex	Muscle symptoms	Lung	Kidney	Muscle MRI	Histology of the muscle	CK↑	Ald.↑	CRP*	ANCA	RF†
3	77F	myalgia & weakness	PF	none	dffuse edema	vasculitis of perimysial vessels	(-)	(-)	NA	MPO	913 (<20)
4	71M	calf claudication	PF	FNG	abnormal fat infiltration	necrotizing granulomatous vasculitis	(-)	NA	9.57	MPO	18.8 (≤14)
ours	76F	weakness & myalgia	PF	none	muscle edema	small-vessel vasculitis	(-)	(-)	8.452	MPO	123.9 (<15)

* CRP (mg/dL), †RF, expressed as IU/mL for the first two, and U/mL for ours

CK: creatine kinase; ANCA: anti-neutrophil cytoplasmic antibody; ARS: anti-aminoacyl transfer ribonucleic acid synthetase antibody; RF: rheumatoid factor; CRP: C-reactive protein; PF: pulmonary fibrosis; MPO: myeloperoxidase; NA: not available; FNG: focal necrotizing glomerulonephritis

In conclusion, muscle weakness can be a chief complaint in AAV. The patients with ANCA-associated muscle vasculitis may tend to involve myalgia, normal levels of CK, pulmonary fibrosis, rheumatoid factor, and muscle edema on MRI. The indication for muscle biopsy may be considered in such cases.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

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