Inclusion Body Myositis in a Patient with RNA Polymerase III Antibody-positive Systemic Sclerosis

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To the Editor:

Inclusion body myositis (IBM) is the most commonly acquired myopathy in patients over 50 years of age and is classified along with polymyositis (PM) and dermatomyositis (DM) under idiopathic inflammatory myopathies. These myopathies are characterized by chronic muscle weakness and muscle wasting with mononuclear cell infiltration into skeletal muscle. IBM is distinguished from PM and DM on the basis of both histopathologic and clinical features. The majority of patients with IBM are resistant to therapy. Herein, we present a case of a patient with systemic sclerosis (SSc) who developed IBM 5 years after his initial diagnosis.

A 60-year-old man was diagnosed with SSc with diffuse cutaneous scleroderma when he developed Raynaud phenomenon, joint pains, digital ulcers, and a modified Rodnan skin score (mRSS) of 22. He started treatment with parenteral methotrexate (MTX; 25 mg/week) for significant itching and redness. He developed esophageal reflux, but no known pulmonary or renal complications. His serum creatine phosphokinase (CPK) level was initially near normal (250 U/l, normal 32–204 U/l) without muscle weakness. His skin disease improved to mRSS 8, and MTX was stopped after 16 months. He returned 2 and half years after initial presentation because of flare of his skin disease, new joint pains, and proximal muscle weakness. His physical examination confirmed more skin thickening (mRSS 24), new palpable tendon friction rubs in the hands, and significant proximal (quadriceps and shoulders) muscle weakness with prominent atrophy of these muscle groups. The distal muscle groups (hands/fingers) were less severely affected and without notable atrophy on examination. No joint swelling or hand contractures were present. The CPK was elevated at 511 U/l and he restarted treatment with weekly oral MTX (20 mg) and prednisone 5 mg daily.

One year later, the patient’s skin disease had improved (mRSS 16), but the proximal muscle weakness had progressed. Although the prednisone was increased to 40 mg daily, his CPK continued to rise, peaking at 1124 U/l (serum aldolase was 16.9 U/l, normal 1.2–7.6 U/l). Within a month, he was wheelchair-bound because of frequent falling at home, and complained of dysphagia to liquids. Positive antibodies included an antinuclear antibody titer at 1:160 (speckled pattern) and anti-RNA polymerase III. Histologic examination of the skeletal muscle biopsy from the right thigh showed atrophic, angulated, and nonangulated fibers with a tendency to group together, necrotic and regenerating fibers, also with phagocytosis, including partial invasion of intact muscle fibers by macrophages (Figure 1A). Rimmed vacuoles were present in several fibers (Figure 1B) with CD3-positive T lymphocytes scattered in the muscle. With immunohistochemistry using an antibody to MHC Class I (HLAabc), there was some staining of the sarcoclemma of non-necrotic muscle fibers. An antibody to transactive response DNA binding protein 43 kDa (TDP-43) on frozen section stained spiky and nodular deposits in the sarcoplasm of muscle fibers (Figure 2). Congo red staining on frozen sections when viewed with fluorescence microscopy using a rhodamine (Texas red) filter exhibited nodular fluorescence in some fibers. The physical and laboratory findings along with the muscle biopsy established the diagnosis of IBM according to the revised 2010 Griggs criteria. The MTX was changed to parenteral 25 mg weekly and steroid rapidly weaned to 5 mg/day because of possible steroid myopathy. Intravenous immunoglobulin (IVIG) infusions, 6% solution (96 g), once a month were begun. He also received inpatient rehabilitation. After 8 cycles (monthly) of IVIG and rehabilitation, there was gradual improvement of quadriceps and shoulder muscle strength, such that he was able to walk slowly with a cane, climb 1 flight of stairs, and perform most self-care activities himself. The dysphagia resolved. Despite this improvement, his weakness has remained a major disability preventing him from returning to work. Unlike other cases, no atrophy of the distal muscle groups has yet occurred, perhaps because of its recent onset. Most recently, his CPK returned to normal, but the aldolase has remained slightly elevated at 9.0 U/l. He continues to receive a monthly regimen of IVIG, parenteral MTX, prednisone 5 mg/day, and outpatient rehabilitation.

IBM has been reported to coexist with other autoimmune diseases such as thyroiditis, systemic lupus erythematosus, and Sjögren syndrome in 33% of cases. Its association with SSc is rare, with only a few cases reported. Herein, we report the first case of IBM and SSc with RNA polymerase III antibody. It is of interest that the presentation of this patient’s muscle weakness coincided with a flare of his SSc skin disease. His improvement may be brief but unexpected, and attributed to aggressive inpatient rehabilitation and IVIG therapy, although reversible steroid-induced myopathy could not be ruled out in this case.

REFERENCES

Figure 1. A. Muscle fiber with rimmed vacuoles undergoing partial invasion by phagocytes with other atrophic fibers (arrow), also basophilia indicating regeneration. Frozen section, H&E stain, original magnification 10×. B. Muscle fiber with rimmed vacuoles (arrow), including red-staining granules. Frozen section, Engel modified trichrome stain, original magnification 25×.

Figure 2. Muscle fiber with granular brown staining in the sarcoplasm (arrow). Immunohistochemistry using an antibody to TDP-43, labeled polymer method with DAB stain, lightly counterstained with hematoxylin, original magnification 25×. TDP-43: transactive response DNA binding protein 43 kDa; DAB: diaminobenzidine.