Inflammatory Myopathy with Anti-Golgi Antibody and Anti-SS-A/Ro Antibody

Hidenori Hattori1, Eiichiro Nagata1, Tadayuki Ishihara3, Kiyo Jinnouchi2, Yoko Ogawa1, Toshihiro Nagai4, Shigeaki Suzuki1, Toshihiko Shimizu1, Junichi Hamada1 and Norihiro Suzuki1

Abstract

We report a 74-year-old woman with anti-Golgi antibody and anti-SS-A/Ro antibody who contracted inflammatory myopathy presenting 'ALS-like' symptoms. We identified anti-Golgi antibody directly using confocal microscopy and successfully treated her with steroid. This report suggests that there is a new categorized subgroup of inflammatory myopathy with these specific antibodies and the pattern of autoantibody in these patients indicates the specific clinical course and treatment strategy.

Key words: anti-Golgi antibody, anti-SS-A/Ro antibody, inflammatory myopathy, myositis

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Introduction

The idiopathic inflammatory myopathies are composed of a heterogeneous group of chronic muscle disorders of unknown origin and varying prognosis. This group consists of three major clinical and histopathological categories; polymyositis, dermatomyositis, and inclusion body myositis (1). However, recent studies have indicated that some autoantibodies with inflammatory myopathy are correlated with clinical phenotype and prognosis. Here we report a case of idiopathic inflammatory myopathy with anti-Golgi antibody and anti-SS-A/Ro antibody presenting 'ALS-like' symptoms which passed through a benign course with steroid treatments.

Materials and Methods

All muscle biopsy specimens were taken from the left biceps. Immunohistochemical analysis was performed according to a standard protocol using mouse monoclonal antibodies (Nichirei, Tokyo, Japan) to CD4 and CD8. Briefly, consecutive 5-mm-thick frozen sections were air dried, fixed in acetone for 20 minutes at room temperature, and rehydrated in phosphate-buffered saline (PBS). Non-specific binding was inhibited by incubating the specimens with 5% rabbit serum in PBS for 30 minutes at room temperature. The sections were incubated with the optimally diluted primary antibody at 4°C for overnight followed by incubation with a peroxidase-conjugated rabbit anti-mouse IgG antibody (Dako, Glostrup, Denmark) for 45 minutes. The bound antibodies were visualized by the addition of diaminobenzidine tetrahydroxychloride (DAB). A negative control section without the primary antibody was prepared for each tissue specimen. Another piece was fixed in 2.5% glutaraldehyde in 0.1M cacodylate buffer at 4°C for overnight for electron microscopy, and post-fixed with 1% osmic acid in 0.1 M cacodylate buffer. It was dehydrated with ethanol and embedded in epoxy resin. 80nm ultra-thin sections were double-stained with uranyl acetate and lead citrate, and examined under transmission electron microscope (TEM, JEOL 1230, JEOL, Tokyo, Japan).

The day before transfection, Hela cells were seeded in 35 mm dishes with Dulbecco’s modified eagle medium (DMEM) without antibiotics for immunocytochemistry. 1.6 μg pEGFP-Golgi vector DNA (Clontech laboratories Inc., CA, 

1Department of Neurology, Keio University School of Medicine, Tokyo, 2Laboratory Medicine, Keio University School of Medicine, Tokyo, 3Ophthalmology, Keio University School of Medicine, Tokyo, 4Electron Microscope Laboratory, Keio University School of Medicine, Tokyo and 5Department of Neurology, National Hakone Hospital, Odawara

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Correspondence to Dr. Hidenori Hattori, hidehatt@1999.jukuin.keio.ac.jp
USA) and 16 μl Plus™ Reagent were diluted into 100 μl D-MEM without serum, and incubated at room temperature for 15 min. 4 μl Lipofectamine™ Reagent (Invitrogen, CA, USA) was also diluted into 100 μl D-MEM without serum in a second tube. We mixed both tubes and incubated for 15 min at room temperature. Finally the mixture was added to each dish of HeLa cells, and we incubated them at 37°C at 5% CO₂ for 3 hours. After the incubation, we replaced the medium by normal D-MEM with serum. After 24 hours cell growth, the cells were stained by PE-labeled anti-human serum antibody, and analyzed by confocal microscopy.

Case Report

A 74-year-old housewife visited our office reporting a swallowing disturbance and lower leg weakness. Neurological examination uncovered proximal muscle weakness in her extremities (manual muscle test; grade 5- in the right, grade 4+ in the left) and neck (manual muscle test; anteflexion: grade 2+, retroflexion: grade 3+) and atrophy in her upper limb girdle muscles, quadriceps muscles, and left thenar and hypothenar muscles. Fasciculation was absent in the tongue and other muscles, and muscle tone was normal. Deep tendon reflexes were slightly hyperactive, but no pathologic reflexes and sensory impairment were detected. There were no cranial nerve signs except for weakness of soft palatal movement. It was difficult for her to swallow solid foods and to walk without putting her hand on her knee. Biochemical analysis showed elevated creatine kinase (466 IU/L; normal range, 51-155 in women), lactate dehydrogenase (342 IU/L; normal range, 120-200), aldolase (7 IU/L; normal range, 2-5), and myoglobin (103 ng/ml; normal range, <60) levels, indicating muscle breakdown. One and a half years before visiting the neurology department, she was aware of the gradual progression of weakness in her legs and she had to use a cane for assistance walking. She had a history of paroxysmal atrial fibrillation and chronic thyroditis with thyroglobulin antibody and thyroid peroxidase antibody, but her electrocardiogram and thyroid hormones have been within normal limits during her entire disease course. Her family members had shown no myopathy or other neurological disorders. She was admitted to the neurology department in our hospital for suspected myopathy or motor neuron disease.

After admission, fasciculation on her left thenar and triceps was noted. Otherwise, motor or sensory conduction velocity was within normal limits, but needle electromyograms showed denervation potential at rest in her interosseous muscles and tibialis anterior muscles and myopathic change at effort in her proximal muscles. Muscle biopsy of her left biceps, in which non-specific inflammatory myopathy was diagnosed, uncovered inflammatory cell infiltration into the perivascular area and endomysium (Fig. 1A) and muscle fiber necrosis with regeneration, but did not show vacuolated muscle fibers (1). We screened autoantibody tests because of positive results and a speckled pattern of antinuclear antibody, and then detected a ‘‘Golgi pattern’’ on an indirect immunofluorescence technique using HEp-2 cells (Fig. 1B) and anti-SS-A/Ro antibody (2). However, we could not detect anti-SS-B/La antibody or any other autoantibodies including anti-Jo-1 antibody. We directly confirmed directly that there was anti-Golgi antibody in her serum using confocal microscopy (Fig. 1C). Systemic screening of malignancies was negative, and muscle magnetic resonance imaging (MRI) showed no pathological intensity. There was no cervical radiculopathy on a MRI survey. Finally, we could describe this patient as inflammatory myopathy presenting anti-Golgi antibody and anti-SS-A/Ro antibody, and we proceeded to administer 3 days of pulse therapy of high-dose methylprednisolone (1,000 mg/day), which was continued to low-dose prednisolone aftercare (40→20→10 mg/day). Two days after the therapy was started, the soft palatal movement and swallowing disturbance were clearly improved, and the patient could walk without a cane after 3 weeks of therapy. At the time of hospital discharge, the creatine kinase level was dramatically improved to normal (22 IU/L). The patient has been followed for 3 years as our outpatient, and her symptoms have been controlled under low-dose prednisolone therapy (10-20 mg/day), depending on her creatine kinase level.

Discussion

Anti-Golgi apparatus autoantibody has been occasionally detected in patients with Sjögren’s syndrome (3), rheumatoid arthritis (2), and other connective tissue diseases, but its clinical significance has not yet been established (4). The cases of three women with inflammatory myopathy with anti-Golgi antibody and anti-SS-A/Ro antibody have been reported previously (Table 1) (4-6). Two cases could be controlled well by steroid therapy, but in the other case with limb-girdle muscular dystrophy, steroids failed to halt the disease progression. One of the two successful controlled cases with systemic lupus erythematosus at the onset developed overlapping syndrome. These cases, including the present case, indicated that inflammatory myopathy was correlated with this autoantibody pattern.

On the other hand, it is still necessary to exclude the other subtype of inflammatory myopathy showing a steroid-responsive clinical course. Localized nodular myositis was reported as a rare subtype of polymyositis in 1977 and its clinical course consisted of steroid-responsive and localized myalgia without any auto-antibody (7). Focal interstitial accumulation of lymphocytes and other inflammatory cell is commonly found in the muscle biopsy of this subtype, but it is also commonly seen in myasthenia gravis and drug-induced systemic lupus erythematosus (8). The patients with anti-Golgi antibody and anti-SS-A/Ro antibody showed generalized myopathy without any subcutaneous nodules and myalgia. Recently multinodular myositis was also reported as a generalized onset subtype of nodular myositis, but the nodules had a B cell-rich center surrounded by a helper T
Figure 1. A) Muscle biopsy showed mononuclear cell infiltration into perivascular area and endomysium (Hematoxylin and Eosin staining, ×500). B) HEp-2 cells reacting with patient’s serum showed “Golgi pattern” using anti nuclear antibody detection kit (Mitsubishi Kagaku Iatrony Inc., Tokyo, Japan). C) Merged picture of confocal microscopy showed PE (red)-labeled anti-human serum antibody detected with Golgi apparatus of pEGFP (green)-Golgi vector transfected Hela cells. D) Infiltrated mononuclear cells were not stained by anti-human CD4 antibody (DAB staining, ×500). E) DAB staining with anti-human CD8 antibody showed CD8 predominance of the infiltrated mononuclear cells (×500). F) There were no “granuloma-like” cellularity or calcification (Gomori Trichrome, ×500). G) Mononuclear cells extravasated through the wall of blood vessel and infiltrated the surrounding tissues (TEM, black bar=10μm).

Thus we performed immuno-histochemical assay of our patient with anti-CD4 and anti-CD8 antibodies, and it revealed CD8-positive cytotoxic T cell predominance in the infiltrated cells (Fig. 1D & E). Gomori trichrome staining of the biceps showed no “granuloma-like” cellularity and calcification, and electron microscopy investigation revealed perivascular infiltration of cells instead of cells within the vessel wall unlike nodular myositis (Fig. 1F, G) (10). A patient with human immunodeficiency virus and hepatitis C virus coinfection has been reported (11), but the present patient had no evidence of any viral infections. Our proposed subtype may be one form of...
polymyositis, but our clinical and pathological findings were clearly far from the reported nodular myositis.

Additionally, this report highlights the importance of checking for anti-Golgi antibody and anti-SS-A/Ro antibody when physicians see slowly progressive muscle weakness with bulbar palsy or suspect amyotrophic lateral sclerosis (ALS)/ALS-related syndrome in elderly patients. Otherwise, they would miss treatable benign myositis or the first stage of severe connective tissue diseases. To our knowledge, this is the fourth patient with inflammatory myopathy with these antibodies, but the first case with bulbar palsy and asymmetrical thenar/hypothenar atrophy like ‘ALS’ in which we confirmed anti-Golgi antibody directly. In conclusion, we report that there is another subtype of inflammatory myopathy with these specific antibodies which could be treated well with steroid.

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Table 1. Clinical and Laboratory Findings of Reported and Present Cases

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References


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