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Myopathy with anti-signal recognition particle antibodies: Clinical and histopathological features in Chinese patients ☆

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Abstract

Myopathy with anti-signal recognition particle antibodies (SRP) is generally thought to be immune-mediated necrotic myopathy in previous studies. We report the clinical and histopathological features of myopathy with anti-SRP antibodies in Chinese patients. Muscle biopsy and immunoblots for myositis antibodies were carried out in 123 patients with idiopathic inflammatory myopathy. Among them, 16 (13.0%) patients had anti-SRP antibodies. Age of onset ranged from 24 to 77 years, and the disease began insidiously. Fourteen of 16 patients presented with chronic progression of proximal limb weakness, with 6 having myalgia. Serum creatine kinase levels ranged from 400 to 9082 IU/L. Muscle biopsies showed necrotic and/or regenerative muscle fibers in all 16, infiltrates of lymphocytes in 11 and morphological features of muscular dystrophy in 7. Eleven patients showed focal or diffuse major histocompatibility complex class 1 expression in sarcolemma or cytoplasm of muscle fibers, with 9 showing deposition of membrane attack complex in necrotic muscle fibers and 2 around capillaries. These findings indicate that anti-SRP antibodies are most likely to be related to IMNM. Myopathy with anti-SRP antibodies is not infrequent in Chinese patients with idiopathic inflammatory myopathy.

Keywords: Signal recognition particle; Myositis; Pathology; Immunoblot

1. Introduction

Myopathy with anti-SRP antibodies is generally regarded as an immune-mediated necrotic myopathy, a new subtype of inflammatory myopathy [1–8]. Typical clinical features are adult-onset, proximal and symmetrical muscle weakness, incomplete or non-response to corticosteroids, and marked elevation of serum creatine kinase (CK). Myopathy with anti-SRP antibodies is usually an acute or subacute disease [9,10], histopathologically characterized by necrotic and regenerative muscle fibers without inflammatory infiltrates [3–5]. Since some patients present with muscle fiber hypertrophy and proliferation of connective tissue, the disease can be misdiagnosed as limb-girdle muscular dystrophy [10].

Myopathy with anti-SRP antibodies has been described in many countries [11,12], especially in Japan [2,10]. It is not clear if the clinical and pathological features of this disease in Chinese patients are similar to those in other populations. We describe here the clinical and histopathological features of 16 Chinese patients diagnosed with myopathy with anti-SRP antibodies.

2. Materials and methods

Serum samples were collected from 123 patients with idiopathic inflammatory myopathy (IIM; according to the criteria of the European Neuromuscular Centre [1]) in the Department of Neurology at Peking University First Hospital from January 2009 to January 2013. The 123

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patients were divided into 16 polymyositis (PM), 42 dermatomyositis (DM), 3 inclusion body myositis (IBM), 18 non-specific myositis and 44 immune-mediated necrotizing myopathy (IMNM) patients. All patients had been diagnosed by muscle biopsy and myositis antibodies test.

2.1. Muscle biopsy

Muscle biopsies were taken from the left biceps brachii of all patients for initial diagnostic investigation. Serial frozen sections were stained with hematoxylin and eosin (HE), modified Gomori trichrome, periodic acidic Schiff, oil red O, adenosine triphosphatase, nicotinamide adenine dinucleotidetetrazolium reductase, succinate dehydrogenase, cytochrome c oxidase, and nonspecific esterase (NSE). The sections were also immunohistochemically stained with primary antibodies against human CD8, CD20, CD68, major histocompatibility complex class 1 (MHC-1) and membrane attack complex (MAC). By indirect-counting method, we estimated the numbers of necrotic/regenerative fibers and total fibers, and then calculated the ratio between them [13].

2.2. Myositis-specific and myositis-associated antibodies

Serum myositis-specific and myositis-associated antibodies were determined by Euroimmun immunoblots according to the standard methods (Euroline Myositis Profile 3 immuno line-blot; Euroimmun), including SRP (the 54-kDa subunit), EJ, JO-1, Ku, Mi-2, OJ, PL-12, PL-7, PM-Scl75, PM-Scl100, and Ro-52. Test strips were coated with thin parallel lines of several purified, biochemically characterized antigens and incubated with serum samples. If a serum sample was positive, specific antibodies in that sample attached to antigens on the strip. Correct performance of all test steps was confirmed by staining of control bands. The EUROLineScan programme from EUROIMMUN (Lübeck, Germany) provides automated evaluation and detailed documentation of results. The incubated membrane strips are either scanned onto a protocol sheet using a flatbed scanner or photographed directly in the incubation tray using a camera system. EUROLineScan recognizes the position of the strips. It then identifies the bands and measures their intensity, correlated with antibody titer. Negative (0), weakly positive, positive and strongly positive (+∼+++) results could be easily and reliable differentiated from each other.

3. Results

3.1. Identification of antibodies

Anti-SRP antibodies were detected by myositis antibody tests in 16 (13.0%) patients with IMNM out of 123 IIM patients. Among them, anti-SRP antibodies were accompanied by anti-Ro52 antibodies in 6 patients and anti-PM-Scl 75 antibodies in 1 patient (Fig. 1).

3.2. Clinical data

The clinical features of the 16 patients with IMNM and serum anti-SRP antibodies were summarized in Table 1. There were 4 males and 12 females, ranging in age from 24 to 77 years (mean ± SD, 46.6 ± 13.2 years), with duration of disease ranging 6–48 months. The initial symptoms were limb weakness in 13 patients, myalgia in 2 and dyspnea in 1. The main symptoms were proximal limb muscle weakness in 14 patients, myalgia in 6, dysphagia in 3 and dyspnea in 2, which was associated with shortness of breath in 3, palpitation in 1, erythra in 1, arthralgia in 1, and overlapped with Sjögren syndrome (SS) in 1 patient. Physical examination at the time of diagnosis showed that muscle strength ranged 1/5–4/5 in the proximal limb muscles and 4/5–5/5 in the distal limb muscles (Medical Research Council Scale, grades 0–5). None of these patients had marked muscle wasting or sensory loss in the limbs. Deep tendon reflexes in both arms (biceps jerk, triceps jerk) and legs (knee jerk, Achilles jerk) were normal in 12 patients, decreased in 3 and absent in 1. All patients were negative for Babinski's sign.

Creatine kinase in serum from the 16 patients ranged from 400 to 9082 IU/L (Normal range: 24–195 IU/L). Needle electromyography (EMG) revealed myogenic changes in 12 patients, with normal results in the other 2. Chest radiography or high-resolution computed tomography was performed in 9 patients and reveals reduced lung volumes with bilateral reticular or reticulonodular opacities in 3. MRI of thighs was carried out on 6 patients with anti-SRP antibodies. There were 2 patients with nearly normal MRI images (Fig. 2A and B). Focally increased signal was seen on fat-saturated T1-weighted images and short-tau inversion recovery (STIR) of 2 patients, predominantly in the anterior thigh compartment (Fig. 2C and D). Leg muscle MRI of 2 patients revealed severe fatty atrophy of posterior compartment muscle bilaterally with bilateral oedematous changes within quadriceps femoris muscles (Fig. 2E and F).

3.3. Muscle pathology

The pathological findings of muscle biopsies in the 16 patients were shown in Table 2. Muscle fiber necrosis and regeneration represented 0.91–7.26% of all fibers in 16 biopsy specimens, with less than 2% in 5 cases, between 2% and 4% in 5 cases and more than 4% in 6 cases (Fig. 3A). Large variation in fiber diameter and connective tissue proliferation was obvious in 7 cases (Fig. 3C). NSE staining showed infiltrating inflammatory cells were dark in the endomysium and necrotic fibers, and CD68 positive macrophage cells were observed in/around necrotic fibers (Fig. 3B and