Seronegative Myasthenia Gravis and Muscle Atrophy of the Tongue

Key words: seronegative myasthenia gravis, muscle atrophy, muscle-specific receptor tyrosine kinase (MuSK) antibody, tongue atrophy

Myasthenia gravis (MG) is an autoimmune disorder with easy fatigability of the muscles based on a neuromuscular transmission defect. Most myasthenic patients have anti-acetylcholine receptor antibodies which attach to the acetylcholine receptor of the postsynaptic membrane of the skeletal muscles and decrease the amplitude of miniature endplate potentials (mepp) and endplate potentials (epp) causing subthreshold epp, which become too low to produce muscle action potentials after exercise and subsequently muscle contraction power is reduced. Some myasthenic patients do not have Ach receptor antibodies in the serum; these cases are termed seronegative MG (1). In generalized MG 67–93% of patients have serum antibodies, but 10–15% of patients with generalized MG and 30–50% of ocular MG do not have Ach receptor antibodies even with repeated studies. Recently serum antibody against the muscle-specific receptor tyrosine kinase (MuSK) have been reported and this antibody is present in 70% of seronegative MG patients (1). How this antibody causes myasthenic symptoms to develop is still controversial. The hypothesis is that MuSK antibody may block agrin, which is a protein released from the nerve endings, to meet MuSK for cluster formation of acetylcholine (Ach) receptor (2). However, the report of Selcen et al (3) does not agree with this hypothesis and MuSK antibody does not cause deficiency of MuSK, nor Ach receptor. Clinical characteristics of seronegative MG (2) can be summarized as 1) female preponderance (M:F=4:23), 2) no thymoma, 3) bulbar palsy and respiratory muscle weakness, and some of the cases have muscle atrophy of the face and the tongue, 4) poor response to pyridostigmine, and some may respond to high-dose prednisolone, cyclosporin, or mycophenolate mofetil. The response to thymectomy among seronegative and seropositive MG patients was studied by Guillermo et al (4) and the results showed no differences between the two groups: 21% of the thymectomized patients had remission and 30–36% of the thymectomized patients had improvement, and no change in 36–44% of the patients. Most effective therapy for seronegative MG is apheresis. Ishii et al (5) reported a 24-year-old Japanese woman, a case of generalized MG with anti-MuSK antibody who had a progressive muscular atrophy and weakness mainly in the bulbar region and the upper extremities.

See also p 671.

She had thymectomy and no thymoma was found, and was treated with pyridostigmine, and oral prednisolone, but relatively poor response to conventional therapy and had progressive muscle atrophy. The muscle biopsy of the biceps muscle revealed atrophic muscle fibers without cell infiltration. She had respiratory failure and was treated with IVlg, prednisolone, and tacrolimus, but the therapeutic response was rather poor and required mechanical ventilatory support. The characteristic clinical features of this case are the muscle atrophy of the tongue and upper extremities, and poor response to conventional MG therapy. Localized muscle atrophy may occur in about 5–10% of the myasthenic patients and the tongue atrophy is the most frequent among the localized muscle atrophy in MG. Oosterhuis (6, 7) reported 12 out of 418 myasthenic patients with localized tongue muscle atrophy and De Assis et al (8) reported 10 cases of tongue atrophy with persistent dysphonia in a group of 752 generalized MG patients. They had bulbar involvement and were refractory to treatment. In addition to the tongue atrophy, the palate was atrophic and the larynx was immobile. Vincent et al (1) described that several patients with MuSK antibody-positive cases presented with myopathic electromyographic changes and a representative case of a 20-year-old woman who had MuSK antibody-positive MG since age 2.5 years had severe atrophy of the orbicularis oris muscle and the wasting of the tongue with central fatty displacement demonstrated by MRI. The latter case was similar to Ishii’s case in terms of the marked tongue atrophy. In the long standing MG cases which are relatively refractory to conventional therapy, muscle atrophy may occur as disuse atrophy due to neuromuscular transmission failure. Why certain muscles rather than other muscles are more involved in such atrophic process is rather difficult to answer.

Apart from seronegative MG, another possible pathophysiologous mechanism of muscle atrophy in myasthenia is motor neuronopathy associated with myasthenia. In 1999 Asanuma et al (9) reported a 63-year-old woman with myasthenia gravis who developed distal muscle atrophy and weakness of the upper extremities after thymectomy. She did not have nerve conduction block, nor slowing of the nerve conduction, and the biceps muscle biopsy revealed grouped
atrophy of the muscle fibers. They concluded that she developed subacute motor neuronopathy associated with myasthenia. Some antibody against the motor neuron or axon may cause this motor neuronopathy and muscle atrophy.

Teruyuki KURIHARA, MD
Division of Neurology, Department of Internal Medicine,
Toho University Ohashi Hospital,
2-17-6 Ohashi, Meguro-ku, Tokyo 153-8515

References