Overlap of Myasthenia Gravis and Miller Fisher Syndrome

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Abstract

In this case report, we describe a patient with myasthenia gravis (MG) and Miller Fisher syndrome (MFS) overlap. A 69-year-old woman presented with acute bilateral ptosis, ophthalmoplegia, ataxic gait, and areflexia. The MFS diagnosis was confirmed with a positive anti-GQ1b IgG antibody test result. MG was diagnosed from electrophysiological, edrophonium, and serological test results. Although intravenous immunoglobulin therapy is effective for both diseases, two courses of the therapy did not improve the patient’s symptoms. However, steroid therapy was effective. Although the overlap of MG and MFS is very rare, it should be considered in the differential diagnosis of neuro-ophthalmic diseases.

Key words: myasthenia gravis, Miller Fisher syndrome, anti-acetylcholine receptor antibody, anti-GQ1b IgG antibody, overlap syndrome

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Introduction

Myasthenia gravis (MG) is an autoimmune disease that disrupts extraocular muscle function through the antigenic blockade of the acetylcholine receptor (AChR) at neuromuscular junctions (1). Miller Fisher syndrome (MFS) is an immune-mediated neuropathy that involves the symptom triad of acute ophthalmoplegia, ataxia, and areflexia (2). MG and MFS produce a variety of neuro-ophthalmic diseases (1, 2). However, the co-occurrence of MG and MFS is rare (3-5). Previous reports have described patients with a prior diagnosis of MG for several years who newly presented with MFS. We herein describe a patient with MG and MFS overlap who presented with acute bilateral ptosis, external ophthalmoplegia, ataxic gait, and areflexia and was serologically positive for anti-AChR and anti-GQ1b IgG antibodies.

Case Report

The patient was a 69-year-old woman who was diagnosed with chronic kidney disease at 67 years of age. She first developed bilateral ptosis and then exhibited dysarthria a week later, resulting in hospital admission. No antecedent upper respiratory or gastrointestinal infective symptoms were observed. A neurological examination revealed bilateral ptosis and external ophthalmoplegia, dysarthria, slight weakness of the neck extensor muscle, limb ataxia, ataxic gait, absent deep tendon reflexes in the extremities, and a negative Babinski response. The symptoms did not exhibit diurnal variation. The patient fit the class IIa criteria of the Myasthenia Gravis Foundation of America classification. Magnetic resonance imaging of the patient’s brain and spinal cord and a cerebrospinal fluid examination revealed normal findings. Chest computed tomography did not reveal a thymoma. Nerve conduction studies of the median, ulnar, tibial, and sural nerves yielded normal results. Repetitive nerve stimulation of the right facial and trapezius muscles and intrinsic muscles of the hand resulted in decremental responses (decremental rate, 40%). An intravenous examination with edrophonium improved the bilateral ptosis and external ophthalmoplegia and alleviated the decremental responses. A blood examination revealed positivity for anti-AChR antibodies (5.2 nmol/L; reference range, <0.2 nmol/L) and anti-GQ1b IgG antibody (antibody titer 2.002; cut-off index, <0.400). The MFS diagnosis according to the external ophthalmoplegia, ataxic gait, and areflexia symptoms was confirmed by positivity for anti-GQ1b IgG antibody. MG was diagnosed according to the electrophysiological, edrophonium, and serological test results. Therefore, the overlap of MG and MFS was established. Immediately after hospital admission,
the patient underwent her first intravenous immunoglobulin treatment (25,000 mg/day for 5 days). The second intravenous immunoglobulin treatment was administered 4 weeks later. Eight weeks after admission, it was concluded that the two intravenous immunoglobulin treatments had not improved the patient’s symptoms. Ten weeks after admission, oral prednisolone (maximum, 100 mg/2 days) was started. Steroid therapy alleviated the patient’s symptoms four months after admission.

Discussion

In this case, the MFS diagnosis, which was suggested by external ophthalmoplegia, ataxic gait, and areflexia, was confirmed by the positivity for anti-GQ1b IgG antibody, and MG was diagnosed from the electrophysiological, edrophonium, and serological test results. Thus the overlap of MG and MFS was established. Although intravenous immunoglobulin therapy is effective in both diseases, two courses of intravenous immunoglobulin therapy did not improve the patient’s symptoms. However, steroid therapy was effective.

Approximately 8-15% of all MG cases are complicated by autoimmune diseases, such as immune thyroid disease and collagen disease (1). MFS is a variant of Guillain-Barré syndrome (GBS) (2). The co-occurrence of MG and GBS is rare. The incidence of GBS has been reported as 10 to 20 cases per million persons per year (1) and that of GBS has been reported as 0.4 to 1.7 cases per million persons per year (2). Therefore, the co-occurrence of MG and GBS has been statistically estimated to be less than 1 in 10 billion (6). To date, only 15 cases of comorbid MG and GBS have been described in the literature (6, 7). Four cases had post-infectious GBS and developed MG concurrently or concomitantly within one month (7). The co-occurrence of MG and MFS is even rarer, and only three cases have been described in the literature (3-5). In the first case, a 40-year-old woman who had MG for six years presented with MFS and was treated with intravenous immunoglobulin therapy (5). These patients who had MG for several years newly presented with MFS, which was confirmed by the serological presence of anti-AChR and anti-GQ1b IgG antibodies. In the present report, we described a patient with the overlap of MG and MFS that was serologically positive for anti-AChR and anti-GQ1b IgG antibodies. To the best of our knowledge, no previous reports have described similar cases.

In both MG and MFS, the autoimmune response plays an important role. MFS is a variant of GBS. To date, some case reports have described the comorbidity of MG and GBS, however, no large-scale studies have been published. Pathogenic activation of the immune system has been speculated to be responsible for the production of cross-reacting antibodies against peripheral motor axons or motor nerve roots and ACh-R according to the experimental findings that IgG from GBS patients fulfill the criteria of a channel-blocking IgG antibody, which is similar to IgG from patients with autoimmune myasthenia (8, 9). In the overlap of MG and MFS, a similar hypothesis is suggested, however, the mechanism remains to be elucidated.

We herein described a case involving the overlap of MG and MFS. Although the overlap of MG and MFS is very rare, it should be considered in the differential diagnosis of neuro-ophtalmic diseases.

The authors state that they have no Conflict of Interest (COI).

References