Miller-Fisher Syndrome

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Guillain-Barré syndrome (GBS) represents a group of acute immune-mediated polyneuropathies preceding an infection usually of the gastrointestinal tract or respiratory tract. GBS is thought to result from faulty production of antibodies against self-antigen, also commonly understood by a process known as molecular mimicry. Among the many variants of GBS, Miller-Fisher syndrome (MFS) is a rare subtype. Most cases occur in Japan and are characterized by areflexia, ophthalmoplegia, and ataxia.[1]

Although MFS presents with an array of symptoms, extremity weakness is the chief. Varying forms of MFS exist, including the incomplete forms of MFS—ie, acute ataxic neuropathy without ophthalmoplegia, and acute ophthalmoplegia without ataxia.[2,3] Anti-GQ1b is an antiganglioside antibody that is self-reactive to the GQ1b ganglioside component of a nerve and is present in 85% to 90% of all patients with MFS.[4,5]

We describe the case of a patient with MFS presenting with a triad of ophthalmoplegia, areflexia, and ataxia concomitant with altered mental status and lower extremity paresis.

CASE PRESENTATION

A 39-year-old woman presented to the emergency department (ED) with altered mental status, ophthalmoplegia, paroxysms of extremity weakness associated with progressive ataxia, and diminished lower extremity reflexes over the past 8 days. When further prompted, the patient reported that she had had a "chest infection" 1 month prior. She denied any recent travel and stated that she had gone out for a walk the previous month and had gotten a cold, for which she was hospitalized for 4 days. The patient also stated that for the past few weeks, she had started "walking funny" and bumping into furniture, a symptom that had been progressively worsening despite no association with pain, change in urine color, activity, or use of new medication. Upon further questioning, the patient denied weakness in the face, pain with eye movement, pain with neck movement, halos, photophobia, hand weakness, numbness or tingling sensations in the extremities, and breathing difficulty.

On initial examination, the patient's temperature was 36.4°C, heart rate was 71 beats/min, respiration rate was 19 breath/min, blood pressure was 141/94 mm Hg, and partial pressure of oxygen was 98%. Examination of the head, eyes, ears, nose, and throat showed normocephalic and atraumatic findings. Cardiac examination revealed an S_3 heart sound, but no thrills, heaves, or murmurs were noted. Pulmonary examination findings were significant for bilateral wheezes, and gastrointestinal examination findings were normal.

On further examination, the patient appeared confused and oriented only to person, with no aphasia or difficulty comprehending commands. Motor strength was markedly reduced at 2/5 bilaterally in the lower extremities, soft touch sensation was not elicited, and reflexes were diminished bilaterally—specifically 1/5 at the ankles and 3/5 at the knees. Shin-to-heel coordination was noted to be abnormal. A preliminary diagnosis of acute stroke was made based on the initial clinical presentation.

Routine and specific tests were conducted. Notable findings included a positive anti-GQ1b antibody, suggestive of MFS. Computed tomography scans of the head without contrast and magnetic resonance imaging of the brain and cervical spine were done to rule out stroke and other etiologies. Serum thiamine and cyanocobalamin levels were within normal range, and oligoclonal immunoglobulin G (IgG) band test results came back negative for abnormal findings. After ruling out thyroid disorders, encephalitis, and stroke, a diagnosis of MFS was made.

As her condition further deteriorated with a decreasing respiratory rate and impending respiratory arrest, the patient was intubated. Immunoglobulin A levels were assessed and cerebrospinal fluid was drawn to confirm albuminocytologic dissociation. Confirmation of these results preceded the administration of intravenous immunoglobulin (IVIG), 95 g (0.5 g/kg/d) for 6 days with intravenous normal saline (0.9%), which led to

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improvement in the patient's confusion. Respiratory rate, vital capacity, and negative inspiratory force were checked hourly in the intensive care unit.

On the fourth day of admission, the patient's condition was improving, with increased muscular effort and strength, but her respiratory status had not improved. The patient underwent plasmapheresis on the fifth hospital day, which led to improvement in respiratory efforts.

The patient was discharged from the hospital after 21 days. She was prescribed physical and occupational therapy to assist in recovery of muscular strength, and a 6-month follow-up visit showed that her muscular weakness, fatigue, ophthalmoplegia, and ataxia had resolved. Normal reflexes were also elicited at the ankle and knees.

DISCUSSION

GBS is an acute autoimmune phenomenon that exhibits different variants of immune-mediated polyneuropathies. MFS is a rare variant of GBS that has a worldwide incidence of 1 per 1 million per year.[6] Children and adults of all ages can be affected by MFS. In a recent study including 466 patients with MFS, the median age of onset was 44 years, and age distribution was shown to have two peaks, one at 30 to 39 years and another from 50 to 59 years.[6] Patients in even younger age groups are believed to experience recurrent symptoms.[7] MFS has been understood to be preceded by respiratory tract infection, as opposed to gastrointestinal tract infection, which is the common trigger in GBS.

Although it is understood to be a postviral or postbacterial infection, MFS may have a genetic predisposition.[8]

Patients with MFS usually present with progressive and almost always bilateral symmetric lower extremity weakness associated with diminished or absent deep-tendon reflexes. In rare circumstances, patients can present with weakness starting in the face or upper extremity, in which case other causes of facial and upper extremity weakness such as stroke and botulism toxin ingestion should be ruled out. Paresthesia and lower extremity pain may be associated with the lower extremity weakness in the acute phase of the illness.[9-12]

The antiganglioside antibody GQ1b has been reported to be distributed in large amounts throughout the extramedullary peripheral to nodal areas of cranial nerves, specifically the oculomotor, trochlear, and abducens nerves.[13] These research findings further confirm the specificity of autoimmunity to GQ1b ganglioside, therefore, since ophthalmoplegia is the chief finding in MFS. Although widely believed to be a postbacterial infection secondary to *Campylobacter jejunum*, a large prospective case-controlled serological study revealed that the associated infective agents for most cases remain unknown.[14]

Conditions that may present in a similar manner to MFS include stroke, Bickerstaff encephalitis, Wernicke encephalitis, myasthenia gravis, multiple sclerosis, botulism, and myotonic dystrophy, making it difficult to diagnose MFS in the acute setting. Clinicians can spot the disease based on the acute onset of the MFS triad: ataxia, ophthalmoplegia, and lower extremity weakness in a patient with a history of recent respiratory infection. Additionally, absence of tremor and autonomic excitation can rule out chronic alcoholism or toxin ingestion.

In conclusion, MFS presents with a wide array of signs and symptoms that can completely subside with prompt identification and treatment, although research shows that some populations with a genetic predisposition may experience recurrent attacks of ataxia, ophthalmoplegia, and/or lower extremity weakness. Plasmapheresis and IVIG is a widely used treatment regimen administered to patients presenting with GBS and its variants such as MFS.

In this patient, ophthalmoplegia completely resolved within 2 months, and ataxia and lower extremity weakness completely resolved within 3 months. Recovery is based on the time to treatment initiation, the presenting symptoms, the patient's age, genetic predisposition, and triggering infection. ■

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