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A Case of Fisher-Bickerstaff Syndrome Overlapped by Guillain-Barré Syndrome

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Key Words

Miller Fisher syndrome · Guillain-Barré syndrome · Bickerstaff's brainstem encephalitis

Abstract

We report a 72-year-old woman with overlapping Miller Fisher syndrome (MFS), Guillain-Barré syndrome (GBS) and Bickerstaff's brainstem encephalitis (BBE). She developed diplopia and unsteady gait a week after an upper respiratory infection on day 1. She had weakness of both upper limbs on day 3 and became drowsy, and her respiratory status worsened on day 5. Neurologic examination revealed ophthalmoplegia, ataxia, symmetrical weakness, areflexia, and consciousness disturbance. We diagnosed her with MFS on day 1, GBS on day 3 and overlapping BBE on day 5. She underwent immunoadsorption therapy and two courses of intravenous immunoglobulin therapy. Ten months after onset, her symptoms had fully recovered. Anti-GM1 IgG, GD1a IgG, GQ1b IgG, and GT1a IgG antibodies were positive. Our case supports the notion that MFS, GBS, and BBE are all part of a continuous clinical spectrum, which is an antibody-mediated process.

Introduction

Miller Fisher syndrome (MFS) is characterized by the acute onset of external ophthalmoplegia, ataxia of cerebellar type, and the loss of tendon reflexes. It is considered a variant of Guillain-Barré syndrome (GBS), because some patients who present with MFS progress to GBS [1]. In contrast, patients who show drowsiness, brisk reflexes, extensor plantar responses and hemisensory disturbance are usually considered to have Bickerstaff's brainstem encephalitis (BBE) rather than MFS. The fact

that BBE and MFS share a common autoantibody suggests that they are closely related. Bickerstaff and Cloake [2] speculated that the etiology of BBE is similar to that of GBS because they found areflexia and cerebrospinal fluid albuminocytologic dissociation; however, a case of overlapping MFS, GBS and BBE has not been fully reported. We here report a case with overlapping MFS, GBS and BBE.

Case Report

A 72-year-old woman developed diplopia and unsteady gait in the morning (day 1) a week after an upper respiratory infection. The next day, she had bilateral blepharoptosis. She was admitted to our hospital due to weakness of both upper limbs on day 3. On admission, the general physical examination was normal. On neurological examination, she had bilateral blepharoptosis. Pupils showed mydriasis and light reflexes were absent. Her eyeballs were fixed in the central position. She had weakness of both upper limbs. Her gait was markedly ataxic. Mann's test was positive and standing on one foot was impossible. All deep tendon reflexes were absent. Sensory and autoimmune systems were intact. Hematological investigation showed an elevated white blood cell count of 9,500/ μ l (segmented leukocytes, 86.5%; lymphocytes, 10.5%), and her cerebrospinal fluid (CSF) showed 2/ μ l (100% mononuclear cells) and 30 mg/dl protein. Magnetic resonance imaging (MRI) showed a normal brain. We diagnosed MFS on day 1, and she developed GBS on day 3. On day 5, she became drowsy, with a worsened respiratory status and weakness in all four limbs. She had no spontaneous respiration and required mechanical ventilation. This condition was considered to be overlapping BBE. On day 12, electroencephalography (EEG) showed background activity at 7–8 Hz with no epileptiform discharges. On day 21, a nerve conduction study of the right median nerve showed abnormal amplitude reductions in both the forearm and upper arm. Motor nerve conduction velocity in the left median nerve was decreased (44.3 m/s). No F wave was elicited in either median nerve. The sensory nerve action potential amplitude in both median nerves was reduced, and sensory nerve conduction velocity was normal. On day 51, brainstem auditory evoked potentials showed obscured IV and V waves on both sides. Antiganglioside antibody assays were performed on serum obtained on day 6. Anti-GM1 IgG, GD1a IgG, GQ1b IgG, and GT1a IgG antibodies were positive, and anti-GQ1b IgG antibody titer was the highest.

She underwent intravenous immunoglobulin therapy from day 3 to 7 and seven sessions of immunoadsorption therapy from day 14 to 28. On day 30, she became able to move her four limbs. We added intravenous immunoglobulin therapy from day 34 to 38. On day 40, she began to open her eyelids and move both eyeballs. On day 54, her consciousness became alert. On day 56, she was taken off the respirator. On day 63, she could stand up, but the ataxic gait remained. On day 90, she changed hospital for rehabilitation ([fig. 1](#)). On discharge, dilation of both pupils and loss of the light reflex remained. Ten months after onset, her symptoms had fully recovered.

Discussion

We report a case of overlapping MFS, GBS and BBE during the course of illness. Neurologically, the responsible lesions were suggested as the pyramidal tract, nuclear or infranuclear of the ocular motor nerves, brainstem reticular formation, cerebellum and peripheral nerves of the limbs. We diagnosed her with MFS on day 1, GBS on day 3 and overlapping BBE on day 5. Overlapping MFS/GBS and BBE/GBS syndromes have been reported [3–9]; however, only two case reports have described overlapping MFS/GBS/BBE syndrome ([table 1](#)). Arai et al. [10] described a patient with BBE on day 1, MFS on day 2 and GBS on day 5 in the presence of anti-GQ1b antibody. Stevenson et al. [11] described a patient with BBE on day 1, GBS on day 9, and MFS on day 10 in the presence of anti-GM1 antibody. Although these two patients underwent plasma exchange and intravenous immunoglobulin therapy, respectively, our patient required

mechanical ventilation and underwent immunoadsorption therapy and two courses of intravenous immunoglobulin therapy.

Anti-GM1 IgG, GD1a IgG, GQ1b IgG, and GT1a IgG antibodies were positive in our case. Anti-GM1 antibodies are classically associated with a severe axonal form of GBS. The abundant and synaptic-specific binding of anti-GQ1b, -GT1a, and -GD1b ganglioside antibodies and the rich capillary supply in the human extraocular muscles may partly explain the selective paralysis of these muscles in MFS [12]. Some large neurons of the dorsal root ganglia were immunostained with anti-GQ1b monoclonal antibody [13]. GQ1b also exists in nerve endings near the skeletal muscle spindle and anti-GQ1b IgG antibody may thus be associated with ataxia as well as ophthalmoplegia [14]. Our case supports a previous proposal by Odaka et al. [14] that BBE, MFS, GBS and acute ophthalmoparesis are all part of a continuous clinical spectrum, which is an antibody-mediated process. Anti-GQ1b antibody is detected in GBS, FS and BBE, so it is called ‘anti-GQ1b IgG antibody syndrome’ [14], and is useful for understanding the etiological relationships among those illnesses. Because of the similarities in the clinical presentation and autoimmune etiology of MFS and BBE, a terminology ‘Fisher-Bickerstaff syndrome’ may be helpful for nosology [4]. Although the clinical picture, neurophysiology, and CSF findings are usually sufficient to indicate therapies, the presence of antiganglioside antibodies is a useful guide to diagnose this group of conditions.

Disclosure Statement

All authors report no disclosures.

Table 1. Clinical features of patients with overlapping MFS, GBS, and BBE

Case	Age/ sex	Initial symptoms	Clinical course	Antiganglioside IgG antibodies	Treatment	Outcome	Author, report year, ref.
1	34/F	diplopia, unsteady gait	BBE on day 1, MFS on day 2, GBS on day 5	GQ1b	plasma exchange	favorable	Arai et al. 2002 [10]
2	43/F	numbness of the lips and tongue, diplopia, vertigo, tingling in the hands and feet, leg weakness	BBE on day 1, GBS on day 9, MFS on day 10	GM1	IVIg	favorable	Stevenson et al. 2003 [11]
3	72/F	diplopia, unsteady gait	MFS on day 1, GBS on day 3, BBE on day 5	GM1, GD1a, GQ1b, GT1a	IVIg, immuno- adsorption	favorable	Our case 2012

BBE = Bickerstaff's brainstem encephalitis; GBS = Guillain-Barré syndrome; IVIg = intravenous immunoglobulin; MFS = Miller Fisher syndrome.

Fig. 1. Clinical course of the patient. IVIg = intravenous immunoglobulin therapy.

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