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Case Report

양측 외전신경마비만을 보인 비전형적 Miller-Fisher 증후군

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Bilateral Sixth Nerve Palsies as the Sole Manifestation of Atypical Miller-Fisher Syndrome

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Recently, we encountered a man with isolated bilateral sixth nerve palsies and areflexia whose titer of anti-GQ1b IgG antibody was elevated. We propose that bilateral sixth nerve palsies can be the sole manifestation of "anti-GQ1b antibody syndromes" and that patients with isolated bilateral sixth nerve palsies should be administered an anti-GQ1b antibody test for the diagnosis of acute immune-related neuropathy.

Key Words: Miller-Fisher syndrome, GQ1b ganglioside, Abducens nerve

The occurrence of bilateral sixth nerve palsies is usually described in patients with tumors, demyelination, subarachnoid hemorrhage, meningitis, metabolic encephalopathy, or increased intracranial pressure.[1,2] However, until recently, there were few reports concerning Miller Fisher syndrome (MFS) with bilateral sixth nerve palsies as the initial sole manifestation of the disease. Furthermore, there has been no definite report that MFS or its variant could manifest with only bilateral sixth nerve palsies during whole period of the disease. Here, we described the clinical course of a male patient with MFS whose symptoms were confined to simultaneous bilateral sixth nerve palsies without any other neurological features.

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Case Report

A 32-year-old man was admitted to our department because of double vision. Ten days prior to admission, he experienced mild headache and blurred vision. The following morning, he noticed the presence of binocular horizontal diplopia. Initially, he visited the local hospital and was diagnosed with bilateral sixth nerve palsies. Routine blood tests and brain computed tomography were normal. He was admitted to that hospital and was treated with intravenous steroids; however, he showed no improvement of diplopia. Hence, he was referred to our hospital for further

evaluations. Prior to the development of symptoms, he was healthy and had no specific familial history of genetic disorders. At first examination, his visual acuity was normal and his light reflexes were prompt bilaterally. There was a marked limitation in his extraocular movement to lateral gaze, bilaterally. Medial and vertical movements were completely normal in both eyes. Other components of the neurological examination revealed no abnormalities, with the exception of decreased deep tendon reflexes in both upper limbs. We also diagnosed him with idiopathic bilateral sixth nerve palsies.

Routine blood tests were all normal. Both the hemoglobin A1C test and the oral glucose tolerance test (with 75 g of glucose loading) revealed no evidence of diabetes mellitus or impaired glucose-tolerance state. Acetylcholine receptor antibody levels were not elevated. Magnetic resonance imaging of the patient's brain showed no abnormal features. Cerebrospinal fluid analysis showed normal opening pressure and normal protein level (29.3 mg/dl), without cells. We performed a nerve conduction study and a repetitive nerve stimulation test on the second day after admission; both tests showed no abnormalities. We performed an enzyme-linked immunosorbent assay (ELISA) for antiganglioside antibodies in serum obtained on the third day after admission and found that it was positive for an IgG against the ganglioside GQ1b (1:160), but was negative for the gangliosides GM1, GM2, GD1a, GD1b, GD3, GT1a, and GT1b (normal range for each antibody, < 1:40).

Finally, we diagnosed him as an atypical MFS case that manifested with isolated bilateral sixth nerve palsies without ataxia. We observed him closely for the presence of ataxia or other sensory symptoms during the course of admission; however, he did not show any neurological symptoms or signs that would be suggestive of peripheral neuropathy of the limbs or ataxia. Two months after discharge, we examined him at our outpatient department. Although he still complained of mild intermittent horizontal diplopia, his bilateral lateral gaze palsies were nearly unrecognizable to the examiner. However, there were still decreased deep tendon reflexes in his upper limbs for next 3 months.

Discussion

The literature on bilateral sixth nerve palsies has been dominated by reports on structural central nervous system (CNS) lesions, such as tumors, trauma, inflammation, or hemorrhage.[1] Additionally, unilateral or bilateral sixth nerve palsies are considered as a false localizing sign that is related with increased intracranial pressure. In contrast, the present case demonstrated an acute immune neuropathy in the cranial nerve as a cause of simultaneous bilateral sixth nerve palsies. Although there was areflexia in his upper limbs and his serum was positive for an anti-GQ1b IgG antibody, we could not find a typical gait ataxia during the course of the disease. Hence, the neurological features of this case were somewhat different from the classic triad of MFS manifestations, which include ophthalmoplegia, ataxia, and areflexia. Recently, bilateral sixth nerve palsies secondary to diabetes mellitus were described as an example of peripheral nervous system (PNS) lesions.[3] However, to our knowledge, there are no definite reports on bilateral sixth nerve palsies as the sole manifestation of Guillain–Barre syndrome (GBS) or MFS during whole period of the disease.

It is well known that the anti-GQ1b IgG antibody is present in the serum of over 90% of MFS patients.[4] However, elevated levels of this antibody have also been found in GBS with ophthalmoplegia, Bickerstaff's brainstem encephalitis (BBE), acute ophthalmoplegia (AO) without ataxia, and ataxic GBS without ophthalmoplegia.[5,6] Recently, Odaka et al.[7] proposed the concept of "anti-GQ1b IgG antibody syndrome" for the conditions of MFS, GBS with ophthalmoplegia, AO, and BBE, because these disorders share some clinical features and a common auto-antibody. Hence, we can classify the present case as "anti-GQ1b IgG antibody syndrome confined to bilateral sixth nerve palsies" and consider it as a regional variant of MFS or partial MFS.

Previously, a case of "sixth nerve palsy with paresthesias" was described as a regional variant of Guillain-Barre syndrome, as were cases of other regional variants, such as pharyngeal-cervical-brachial weakness, paraparesis, bifacial weakness with paresthesias, or lumbar polyradiculopathy. Recently, Tatsumoto et al.[8] performed a retrospective review of clinical and laboratory findings (including neuroimmunological laboratory findings for serum antiganglioside antibody testing) of 100 cases of isolated abducens palsy without any neurological deficits. They found that the anti-GQ1b IgG antibody test was positive in 25 cases (25%). Hence, these authors suggested that some cases of isolated sixth nerve palsies can be categorized as a regional variant of MFS or as an anti-GQ1b antibody syndrome. In addition, several

patients had a history of antecedent infection, distal paresthesia, albuminocytological dissociations, or MRI abnormalities. They also reported that 29 cases exhibited bilateral symptoms (29%); however, this report did not allow us to assess the proportion of bilateral patients that were positive for the anti-GQ1b antibody test. Finally, positive anti-GQ1b serology correlated with antecedent infection or other clinical symptoms, such as distal paresthesia or hyporeflexia. Our patient was different from the cases in their series in that he presented with simultaneous bilateral sixth nerve palsies exclusively, without distal paresthesia, antecedent infection history, or nerve conduction abnormalities, and showed a relatively mild elevation of anti-GQ1b IgG titers. Another report by Yuki et al.[9] indicated that bilateral sixth nerve palsies followed by oculomotor nerve involvement is characteristic of AO. As such, initial sole manifestation of bilateral sixth nerve palsies are not rare finding. However, most of his cases had another extraocular manifestation or other neurological features as well. Finally we can not know there were certain cases whose clinical manifestation was confined to only bilateral sixth nerve palsies during whole period of the disease.

According to strict clinical categorization, our case could be classified as a variant of AO. We propose that bilateral sixth nerve palsies can be the sole manifestation of "anti-GQ1b antibody syndromes" and that patients with isolated bilateral sixth nerve palsies should be administered an anti-GQ1b test for the diagnosis of acute immune-related neuropathy.

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