Atypical Miller Fisher Syndrome: Case Report

Atipik Miller Fisher Sendromu

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ABSTRACT Guillain-Barre syndrome (GBS) is the most frequent cause of acute generalized paralysis, with an annual incidence rate of 0.75-2/100 000. Miller Fisher syndrome (MFS), one of the frequent variants of GBS, is characterized by the triad of opthalmoplegia, ataxia, and areflexia. The anti-GQ1b immunoglobulin G (IgG) antibody is an important marker in the diagnosis of MFS since 90-95% of the patients test positive for it. Atypical MFS cases that do not feature the clinical triad have been reported in the literature. Herein, we present a patient with MFS who had ophthalmoplegia and ataxia without areflexia whose diagnosis was supported by the presence of the anti-GQ1b antibody in the serum.

Key Words: Guillain-Barre syndrome; Miller Fisher syndrome; GQ1b ganglioside; ophthalmoplegia

ÖZET Guillain Barre Sendromu akut jeneralize paralizinin en sık görülen sebebidir ve yıllık insidansı 0,75-2/100 000'dir. Miller Fisher Sendromu Guillain Barre Sendomunun sık görülen varyantlarından biridir ve oftalmopleji, ataksi ve arefleksi triyadından oluşur. Serumda Anti GQ1b antikorlarının varlığı Miller Fisher Sendromu tanısı için önemli bir belirteçtir ve hastaların %90-95'inde pozitif olarak saptanır. Klinik triyadı tam olarak karşılamayan atipik Miller Fisher Sendromu olguları literatürde bildirilmiştir. Bu yazıda arefleksinin eşlik etmediği oftalmoparezi ve ataksi bulguları ile prezente olan ve anti GQ1B antikor pozitifliği ile tanının desteklendiği bir Miller Fisher Sendromu olgusu sunulmuştur.

Anahtar Kelimeler: Guillain-Barre sendromu; Miller Fisher sendromu; GQ1b gangliosid; oftalmopleji

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Guillian-Barre syndrome (GBS) is the most frequent cause of acute generalized paralysis, and it has an annual incidence rate of 0.75-2/100 000.[1,2] Miller Fisher syndrome (MFS) was defined as a variant of GBS for the first time in 1956 by Miller Fisher and is composed of the triad of opthalmoplegia, ataxia, and areflexia.[1-10] Approximately 5% of the GBS cases develop the MFS variant, which is typically found more in Asian countries.[1,2,4] In recent years, some ganglioside complexes (GSCs), such as anti-GQ1b, have been detected as target antigens for serum antibodies in GBS cases, and 90-95% of MFS cases test positive for this particular GSC, making it an important marker in diagnosis.[5,11-15] However, it

should be noted that atypical MFS cases have been reported in the literature that have the clinical triad.[8,12-14]

We present an atypical MFS case without areflexia whose cerebrospinal fluid and laboratory findings support the diagnosis of this GBS variant.

CASE REPORT

A 55-year-old male patient was admitted to our hospital because of a headache that had started the day before along with diplopia and ataxia that began the next day. The patient had suffered from a flu-like infection with symptoms of coughing and fatigue one week before the presentation. In addition, there was Familial Mediterranean fever (FMV) in his medical history, thus he was taking two colchicine tablets every day. The patient had not been exposed to canned food or any other toxic substance. An examination of the patient revealed that his blood pressure was 110/70 mmHg, his pulse was 72/minute, and his temperature was 36°C. There were no pathological findings in the other system examinations. In the neurological examination, the patient's bilateral direct and indirect light reflexes were negative, and he had bilateral pupil dilatation. His left eye was minimally deviated medially in the primary position, and he had an ataxic gait with a wide base that veered to the right. The other neurological examination findings were normal. During the patient's follow-up, a limitation developed bilaterally in the lateral and upward views, and he experienced pain in the examination of eye movements. The patient then underwent a brain computed tomography (CT) scan, brain magnetic resonance imaging (MRI), magnetic resonance venography (MRV), and diffusion MRI, but these revealed nothing abnormal. Furthermore, no pathological abnormalities were detected in the routine hemogram and biochemical parameters except for an elevation in triglicerides (458 mg/dL). In the examination of the cerebrospinal fluid (CSF) that was obtained via lumbar puncture, protein was detected at a rate as high as 73 mg/dL, and no cell was observed in the microscopic examination. Electroneuromyography (ENMG) was also performed, and the right median and ulnar nerve motor and sensorial conductions, right peroneal and posterior tibial nerve motor conduction, and right and left sural nerve sensorial conductions along with the F latencies were normal. The patient was suspected of having the MFS variant of GBS, so he underwent blood tests to detect the ganglioside panel of anti-GM1, anti-GD1b, and GQ1b. He tested positive for anti-GQ1b, but negative for the the other two antibodies. The patient was then diagnosed with MFS according to these results, and plasmapheresis was performed five times on alternating days. After the third regimen of plasmapheresis, the patient had a substantial decrease in the number of headaches, saw improvement in his eye movements, and experienced a decrease in the ataxia. The patient became mobile, and his eye movements improved even more by the end of the plasmapheresis therapy.

DISCUSSION

Miller Fisher syndrome usually has a benign course.[1-4] Our case had opthalmoplegia and ataxia, but areflexia was not present in the beginning or during the follow-up. Other atypical MFS cases exist in the literature.[8,12-14] Paine et al. presented a 69-year-old male case with a headache accompanied by MFS. This patient had normal deep tendon reflexes (DTRs), but the diagnosis was supported by anti-GQ1b positivity.[8] Chan et al., reported a 35-year- old patient with bilateral pupil dilatation, no light reflexes, accompanying opthalmoplegia, and normal DTRs along with routine electromyography (EMG) findings. As in our case, this patient was diagnosed with MFS by antibody positivity.[13] Additionally, Matsubara et al. presented a 6-year-old case with cranial neuropathy but no ataxia and areflexia. They emphasized that a patient that tested positive for anti-GQ1b and anti-GT1a could have a variant of MFS or Bickerstaff's encephalitis secondary to an asymptomatic *Campylobacter* infection.[14] In spite of not having areflexia, when the anti-GQ1b positivity and the evidence from the literature were considered, we determined that our patient had the MFS variant. Since 1990, serum anti-GQ1b immunoglobulin G (IgG) antibody levels had been efficiently noted in the pathophysio-

logy and diagnosis of MFS.[2,10] The presence of the anti-GQ1b IgG antibody is an important factor for determining whether a patient has MFS, and it has been found to be positive in the serum in the acute phase in 90% of MFS patients.[1,11] Peripheral nerves contain gangliosides, which are complex glycosphingolipids, and these gangliosides are potential antigenic targets in peripheral neuropathies. It has been indicated in immunohistochemical studies that the ganglioside GQ1b can be located in the paranodal regions of the extramedullary parts of oculomotor nerves (cranial nerves 3,4,6), and this can cause the opthalmoplegia that is seen in MFS.[1,2,15] Furthermore, anti-GQ1b IgG is also associated with the opthalmoplegia in GBS and Bickerstaff's brain stem encephalitis.[14]

In cases like ours with atypical presentation that does not include the complete clinical triad of MFS, the presence of anti-GQ1b IgG helps considerably in the diagnosis. In the literature, headaches have been indicated in some MFS cases, but this is not a common symptom.[1,8,12] Friedman et al. reported a case who had no previous history of headaches but developed a prolonged headache that started concurrently with the diagnosis of MFS. The headache in their case was initially not responsive to treatment with narcotics, but after three months of treatment, there was improvement.[12] In our case, the patient's headache disappeared gradually with the improvement of MFS clinic concurrently. Some inexact mechanisms have been suggested to explain the pathogenesis of headaches associated with MFS. For example, headaches can accompany MFS when there is involvement of the central nervous system or when there is obstruction in the CSF circulation because of increased amounts of protein. In addition, headaches can occur with MFS when there is activation of the trigeminal pain tract via demyelinization caused by antibodies against gangliosides.[12] Intravenous immunoglobulin (IVIG) and plasmapheresis are administered in the treatment of MFS; however, their contributions to the course of the disease is controversial because of the syndromes benign characteristics.[1,6,7,16] Mori et al. discovered in a study composed of 55 patients that, there was no significant difference between the plasmapheresis group and the group without plasmapheresis with regard to the elapsed time until the patients' symptoms improved.[6] Kambara et al. reached the same conclusion in a study involving four patients, although they had predicted that the results would be better with plasmapheresis than IVIG.[7] In our case, we saw significant improvement in the ataxia of our patient after the third regimen of the plasmapheresis, and, more improvement was seen in other areas after the completion of the fifth regimen.

In conclusion, GBS and its variants include a very wide clinical spectrum and can emerge with different neurological findings. The presence of the GQ1b antibody can provide important diagnostic information in atypical cases such as ours.

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