Unusual Presentation of Miller Fisher Variant Syndrome

Saeed A. Alqahtani, MD* Ibrahim Alnaami, MD, FRCP** Muhammed Shubaili, MBBS***
Mohammed Saeed Alqahtani, MBBS****

Miller Fisher syndrome (MFS) is a rare, acquired nerve disorder which is a subtype of Guillain-Barré syndrome.

A thirty-five-year-old male presented with an inability to move both eyes in any direction and history of mild upper respiratory tract infection 7 days before presentation. On examination, vital signs were within the normal range. There was bilateral Intra Nuclear Ophthalmoplegia (INO) which progressed to complete ophthalmoplegia with fixed dilated pupils and facial nerve diplegia associated with normal motor strength and reflexes in all extremities. Radiological and laboratory assessments were normal except the patient tested positive for anti-GQ1b antibodies, 481% ration which indicates MFS. The patient was given three cycles of intravenous immunoglobulin for five days, after which, he improved and was discharged from the hospital.

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Miller Fisher syndrome is a rare, acquired nerve disorder which is a subtype of Guillain-Barré syndrome[1]. It is characterized by weakness of eye muscles (ophthalmoplegia), loss of deep tendon reflexes (areflexia) and lack of muscle coordination (ataxia)[1,2]. This presentation may be preceded by a viral infection similar to Guillain-Barré syndrome[3]. Other symptoms may include extremity muscle weakness and respiratory failure[4]. The cause is unknown; however, it is an autoimmune disease in which some autoantibodies attack the nerves. In most cases of MFS anti-GQ1b antibody is identified[5]. Immunotherapy (plasma exchange or immunoglobulin IVIG) are the main therapy for this disorder. Few cases are reported using repeated cycles of IVIG in refractory cases.

The aim of this report is to present a rare case of MFS which has been improved after the third cycle of IVIG.

THE CASE

A thirty-five-year-old Saudi male who is not known to have any medical illness presented with inability to move both eyes in any direction. The patient reported a mild upper respiratory tract infection 7 days before these symptoms.

On physical examination, vital signs were within normal with no signs of distress. He was fully alert and oriented with comprehensive fluent speech.

No visual field or acuity defects. Both pupils were equally and slowly reactive to the light with preserved near light reflex. The initial extraocular motility exam revealed right-side one and a half syndrome. No changes in sensory modalities and motor exam showed normal strength and reflexes in all extremities. Coordination and gait examination was normal.

Ophthalmology evaluation revealed no visual or retinal changes. Within a few days, the patient deteriorated; his symptoms worsened and had complete ophthalmoplegia and dilated fixed pupils in both eyes with no response to pupillary light reflex, bilateral facial drop, mild dysphagia and voice changes.

Laboratory investigation revealed normal complete blood count, metabolic panel, thyroid-stimulating hormone, and erythrocyte sedimentation rate was 70 mm/hour. The serum anti-cholinesterase antibody test results were negative. All other inflammatory markers and laboratory results were unremarkable.

* Associate Professor of Neurology
Department of Medicine
College of Medicine
King Khalid University, Abha
Consultant Intervention Neurology
Neurology Unit, Medicine Department
Armed Forces Hospital–Southern Region
** Associate Professor of Neurosurgery
College of Medicine
King Khalid University, Abha
*** Consultant Neurosurgery
Neurology Unit, Medicine Department
Armed Forces Hospital–Southern Region
**** Senior Registrar Internal Medicine
Neurology Unit, Medicine Department
Armed Forces Hospital–Southern Region, Saudi Arabia
Resident Neurology
Neurology Department
King Fahad Hospital-Jeddah
Kingdom of Saudi Arabia
E-mail: dr.mohd1993@gmail.com

Routine chest x-ray and Pan CT scan had no abnormality. CT and repeated MRI of the brain with and without contrast were completely normal. Electromyography and nerve conduction studies were normal.

The rapid plasma test for syphilis was negative. The serum antineutrophil cytoplasmic (ANCA) IgG titer, ANA, DsDNA, and other serology and immunology tests were within normal. Cerebrospinal fluid (CSF) analysis revealed clear appearance, no xanthochromia with normal opening pressure, CSF WBC: 24 CSF RBC:1 no organism seen on gram stain. Negative Mycobacterium and other cultures. Protein: 464, glucose: 3.4 and serum is 3.6, all paraneoplastic panel were not significant.

The test for Ganglioside GD1b and GQ1b (IgG, IgM) antibodies were highly positive, 88 and 481++ ration respectively, which confirmed our suspicion for Miller Fisher syndrome.

The patient was given intravenous immune globulin infusion 0.4g/kg/day for 5 consecutive days.

The patient showed no response during and after completion of the usual five-day course of intravenous immune globulin infusion. A decision was made to repeat another five-day course of intravenous immune globulin infusion 0.4g/kg/day based on the patient's condition.

On the third day of the second course, the patient started to show mild improvement of both eyes movements. Pupils were still dilated, but responsive to pupillary light reflex. There was a mild improvement on the examination of the right 7th cranial nerve. The patient was observed a few days after the 2nd cycle of IVIG. No further improvement occurred.

A decision to start the 3rd cycle was taken. During the 3rd cycle, the patient showed significant improvement in the movements of both eyes. The patient was observed for a few more days in the hospital before discharge. The patient showed full recovery in the follow-up visit 2 months after discharge.

DISCUSSION

MFS is a sudden neurological affection of the peripheral nervous system; it is manifested as incoordination and imbalance, facial droopiness, loss of reflexes, and inability to control the eyelids[6]. MFS is usually preceded by a viral illness; therefore, many people experience symptoms of respiratory, gastrointestinal, or other diseases before MFS appears[7,8]. MFS is a milder subtype of Guillain-Barré syndrome (GBS). Both are autoimmune disorders in which the immune system attacks the nervous system[9].

GBS is characterized by progressive symmetrical limb paralysis, abnormal sensation and loss or decreased deep tendon reflexes. In severe forms, the patient can present with the difficulty of breathing. Approximately 5-10% of patients with GBS deteriorate and require mechanical ventilation[10].

Nearly 90% of the patients with MFS had a positive test for the IgG anti-GQ1b antibody in their sera[11,12]. This is not unique for MFS as many other diseases, such Bickerstaff brainstem encephalitis (BBE), acute ophthalmoparesis without ataxia, isolated internal ophthalmoplegia, acute oropharyngeal palsy, acute or chronic sensory neuropathy, and other disorders can test positive for anti-GQ1b antibody[13-16]. Its high occurrence in patients with Fisher syndrome is very useful for the diagnosis.

MFS has a better prognosis. Several studies proved the efficacy of immunotherapies with either plasmapheresis or intravenous immunoglobulins (IVIg) in the treatment of MFS. Other retrospective studies revealed that these immunotherapies do not alter the clinical outcome of patients with MFS. Instead, spontaneous recovery has been seen in some of these patients[19].

Giroud et al reported a patient with Miller-Fisher syndrome with abnormal MRI as brain stem showed increased signal density on T2 sequence anterior to the fourth ventricle on the right and the left[20]. Smith et al reported a 32-year old male with unilateral external ophthalmoplegia[21]. The use of intravenous immunoglobulin in MFS was tested by Arakawa et al in a 3-year-old boy with progressive MFS[22]. The patient had 2 episodes of apnea lasting about 50 seconds each, he was given intravenous immunoglobulin (400 mg/kg/day) for 5 consecutive days. The patient showed a significant improvement in the respiratory state, general muscle strength, truncal ataxia and emotional state.

A retrospective study concluded that the second cycle of IVIG may be beneficial in selected groups of unresponsive patients[23]. A total of seven cases in different studies showed good improvement after repeated cycles of IVIG[24,25]. Our case showed improvement after the third cycle of IVIG; a similar condition was reported by Algahtani et al in a severe axonal form of GBS [26].

CONCLUSION

Miller Fisher syndrome is a neurological disorder which could present with its classical triad of symptoms or other unusual presentation. It is usually preceded with a history of viral infections. Intravenous immunoglobulin for five days showed a significant benefit in minimizing the clinical symptoms. A randomized controlled trial is needed to evaluate the management and outcome of such cases.

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REFERENCES

1. Puma A, Benoit J, Sacconi S, et al. Miller Fisher Syndrome, Bickerstaff Brainstem Encephalitis and Guillain-Barré Syndrome Overlap with Persistent Non-Demyelinating Conduction Blocks: A Case Report. BMC Neurology 2018 1; 18(1):101.
2. Muñiz AE. Multiple Cranial Nerve Neuropathies, Ataxia and, Areflexia: Miller Fisher Syndrome In A Child And Review. The American Journal of Emergency Medicine 2017; 35(4):661-E1.
3. De Silva NL, Weeratunga P, Umapathi T, et al. Miller Fisher Syndrome Developing as a Parainfectious Manifestation Of Dengue Fever: A Case Report and Review of The Literature. Journal of Medical Case Reports 2019; 13(1):120.
4. Ryu WY, Kim YH, Yoon BA, et al. Pattern of Extraocular Muscle Involvements in Miller Fisher Syndrome. Journal of Clinical Neurology 2019; 15(3):308-12.
5. Roberts M, Vincent A, Newsom-Davis J, et al. Serum Factor in Miller-Fisher Variant of Guillain-Barré Syndrome and Neurotransmitter Release. The Lancet 1994; 343(8895):454-5.
6. Fisher M. An Unusual Variant of Acute Idiopathic Polyneuritis (Syndrome of Ophthalmoplegia, Ataxia and Areflexia). New England Journal of Medicine 1956; 255(2):57-65.
7. Koga Á, Gilbert Á, Li J, et al. Antecedent Infections in Fisher Syndrome: A Common Pathogenesis of Molecular Mimicry. Neurology 2005; 64(9):1605-11.
8. Yuki N, Koga M. Bacterial Infections in Guillain-Barre and Fisher Syndromes. Current Opinion in Neurology 2006; 19(5):451-7.
9. Lo YL. Clinical and Immunological Spectrum of the Miller Fisher Syndrome. Muscle & Nerve 2007; 36(5):615-27.
10. Yeh JH, Chen WH, Chen JR, et al. Miller Fisher Syndrome with Central Involvement: Successful Treatment with Plasmapheresis. Therapeutic Apheresis 1999; 3(1):69-71.
11. Chiba A, Kusunoki S, Shimizu T, et al. Serumigg Antibody to Ganglioside GQ1b is a Possible Marker of Miller Fisher Syndrome. Ann Neurol 1992; 31:677–679.
12. Yuki N, Sato S, Tsuji S, et al. Frequent Presence Ofanti-GQ1b Antibody in Fisher's Syndrome. Neurology 1993; 43:414–417.
13. Odaka M, Yuki N, Yamada M, et al. Bickerstaff's Brainstem Encephalitis: Clinical Features of 62 Cases and a Subgroup Associated with Guillain-Barrésyndrome. Brain 2003; 126:2279–2290.
14. Funakoshi K, Kuwabara S, Odaka M, et al. Clinical Predictors of Mechanical Ventilation in Fisher/Guillain-Barré Overlap Syndrome. J Neurol Neurosurg Psychiatry 2009; 80:60–64.
15. Radzwill AJ, Steck AJ, Borruat FX, et al. Isolated Internal Ophthalmoplegia Associated with IGg Anti-GQ1b Antibody. Neurology 1998; 50:307.
16. O'Leary CP, Veitch J, Durward WF, et al. Acute Oropharyngeal Palsy is Associated with Anti-Bodiesto GQ1b And GT1a Gangliosides. J Neurol Neurosurg Psychiatry 1996; 61:649–651.
17. Mori M, Kuwabara S, Fukutake T, et al. Intravenous Immunoglobulin Therapy for Miller Fisher Syndrome. Neurology 2007; 68(14):1144-6.
18. Yeh JH, Chen WH, Chen JR, et al. Miller Fisher Syndrome with Central Involvement: Successful Treatment with Plasmapheresis. Therapeutic Apheresis 1999; 3(1):69-71.
19. Mori M, Kuwabara S. Fisher Syndrome. Current Treatment Options in Neurology 2011; 13(1):71-8.
20. Giroud M, Mousson C, Chalopin JM, et al. Miller-Fisher Syndrome and Pontine Abnormalities on MRI: A Case Report. Journal of Neurology 1990; 237(8):489-90.
21. Smith J, Clarke L, Severn P, et al. Unilateral External Ophthalmoplegia in Miller Fisher Syndrome: Case Report. BMC Ophthalmology 2007; 7(1):7.
22. Arakawa Y, Yoshimura M, Kobayashi S, et al. The Use of Intravenous Immunoglobulin in Miller Fisher Syndrome. Brain and Development 1993; 15(3):231-3.
23. Alboudi A, Sarathchandran P, Geblawi SS, et al. Rescue Treatment in Patients with Poorly Responsive Guillain–Barre Syndrome. SAGE Open Medicine Volume 2019; 7:1–5 .
24. Farcas P, Avnun L, Frisher S, et al. Efficacy of Repeated Intravenous Immunoglobulin in Severe Unresponsive Guillain Barre Syndrome. Lancet 1997; 350(9093): 1747.
25. Godoy DA, Rabinstein A. Is a Second Cycle of Immunoglobulin Justified in Axonal Forms of Guillain-Barre Syndrome. Arq Neuropsiquiatr 2015; 73(10): 848–851.
26. Algahtani H, Shirah B, Alrefaei K, et al. Are Repeated Cycles of Intravenous Immunoglobulin Justified in Patients with Poorly Responsive Guillain-Barré Syndrome. The Neurohospitalist Journal 2019. https://journals.sagepub.com/doi/abs/10.1177/1941874419893570 Accessed in June 2020.