# Binocular Diplopia as Ocular Manifestation in Pediatric Miller Fisher

**Dinda Zhafira[1], Reni Prastyani[1], Prastiya Indra Gunawan[2], Riza Noviandi[2], Sunny Mariana Samosir[2]**

*[1]Department of Ophthalmology, Faculty of Medicine Universitas Airlangga Dr. Soetomo Hospital, Surabaya, Indonesia*
*[2]Department of Pediatrics, Faculty of Medicine Universitas Airlangga Dr. Soetomo Hospital, Surabaya, Indonesia*
*Email: reni-p@fk.unair.ac.id*

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Diplopia, Exotropia, Ophtalmoplegia, Miller Fisher Syndrome.

**ABSTRACT**
Miller Fisher Syndrome (MFS) is a rare variant of neuropathy spectrum of Guillain-Barré syndrome that occur less frequently in children. 11 years old suffered from weakness of limbs with walking and posture bearing difficulty for 3 days before admission. Patient also had complaint of double vision with gaze restriction and difficulty while chewing or swallowing. During admission patient had respiratory failure that inquired intubation and ventilator support. Clinical improvement was achieved after patient was intravenous immunoglobulin (IVIG) for 5 days. First ophthalmology examination showed 15 degrees exotropia of left eye with 30 prism dioptres (PD) at near and far distance. The Worth four dot test revealed crossed diplopia, along with gaze restrictions in all directions. Follow-up 2 months after admission, the patient's symptoms had resolved. Miller Fisher Syndrome (MFS) is diagnosed clinically, characterized by the triad of ataxia, areflexia, and ophthalmoplegia. Treatment for MFS primarily involves supportive care, including respiratory support and immunotherapy if required. The prognosis for MFS is generally favorable. Recovery usually starts in two until four weeks after onset and generally completing within six months.

## 1. Introduction

Miller Fisher Syndrome (MFS) is a neuropathy autoimmune disorder. It is a rare variant of Guillain-Barré Syndrome (GBS)(1). In patients with GBS, MFS occurred 14% of the time and typically only impacted one to two persons per million every year(2)(3). There are very few case reports or case series about MFS, and the number of MFS cases in pediatric patients is significantly lower than in adults(4)(5).

Miller Fisher Syndrome usually involves lower cranial and facial nerves but other neurological signs and symptoms has been described(6)(7). A variety of infections can precede the onset of signs and symptoms with ophthalmoplegia and diplopia as the first manifestations, associated with ataxia and areflexia (8)(9)(10)(11). There can be serious concern due to rapid change in vision also walking and breathing problem (12)(13)(14).

## 2. Case Illustration

11-year-old-boy patient suffered from weakness of limbs with walking and posture bearing difficulty for 3 days before hospital admission. Patient had history of respiratory infection 4 weeks before admission and was treated with antibiotics for 6 days. 3 weeks after, patient could not move his eyeball and needed to turn his head to glance followed by chewing and swallowing difficulty. He also complained of double vision. According to patient's mother, she noticed an imbalance and fall tendency when patient walking. During his hospital stay, he developed shallow breathing and became bedridden, and by the following day, he experienced respiratory failure.

On initial examination, patient's visual acuity was 5/5 on both eyes with exotropia of left eye. Ocular motility was restricted in all gaze directions. Krimsky examination at near and far distance showed 30 prism dioptres base in with cross diplopia on worth four dot test. Neurological examination showed dysphagia, ataxia, bilateral facial weakness, and limb weakness. The cranial nerve examination found weakness of all extraocular muscles. There was also dysphagia due to weakness from 9$^{th}$ and 10$^{th}$ cranial nerve. The motoric strength examination showed moderate weakness in the upper and lower extremities with manual muscle testing (MMT) score were 3. The deep tendon reflexes in the upper and lower extremities of the left biceps, triceps, knees, and ankle reflex were absent and tandem gait test showed an ataxic gait.

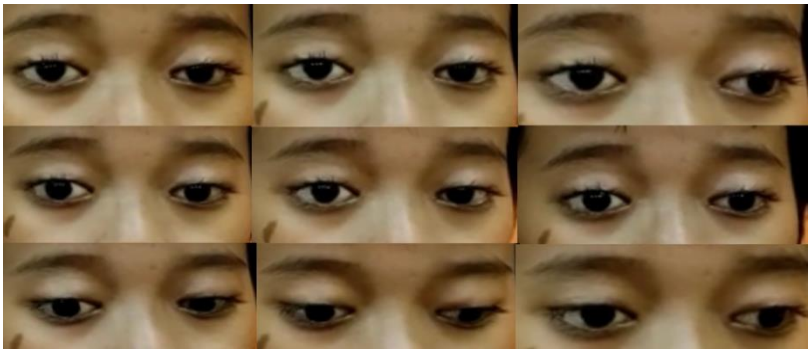
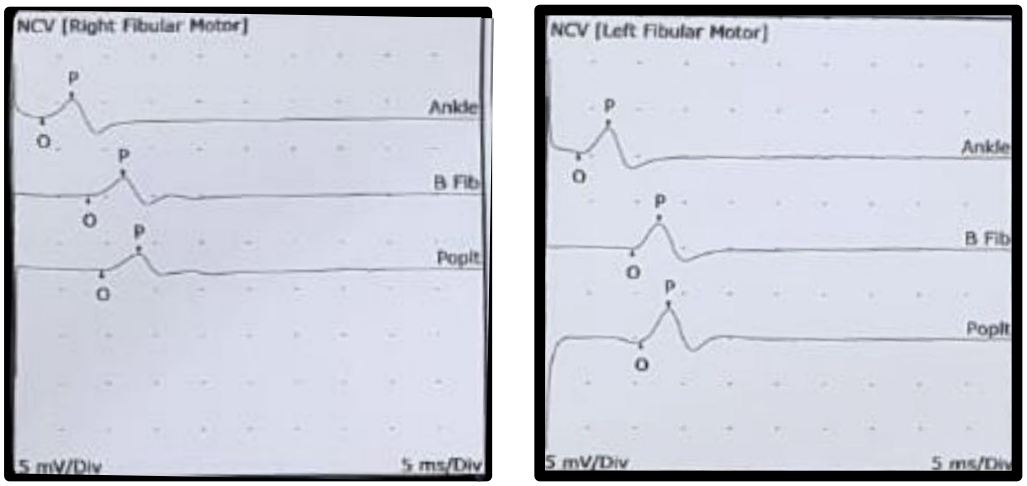


Figure 1. Ocular motility during hospital stays. There were limitations in all directions of gaze

Clinical trial of opthalmoplegia, ataxia and areflexia were found in this patient. Head CT-scan and liquor analysis of cerebrospinal fluid showed no abnormality. There was an episode of electrolyte imbalances and respiratory acidosis as complications from respiratory failure but other results of blood examination were within normal limit. Electromyography examination was performed and there was a low amplitude in right peroneal nerve conduction. Patient was diagnosed with Bilateral opthalmoplegia due to Miller Fisher Syndrome.




(A) (B)

Figure 2. Electromyograph study. (A) Right peroneal nerve conduction. (B) Left peroneal nerve conduction

During hospitalization patient had history of respiratory failure that inquired intubation and ventilator support. Patient was then given treatment of intravenous immunoglobulin (IVIG) 15 grams once a day for 5 days and had an improvement of symptoms. Outpatient management was given for his eye complaint of double vision. Patient was given correction spectacle with 6° base in prism.

On the next visit at the outpatient clinic, the ocular motility showed improvement with only -1 restriction toward medial on both eyes. The misalignment still remains with 15 degrees exotropia but the complaint of diplopia was stated slightly reduced. Patient was educated to do regular exercise of push up pencil exercise.

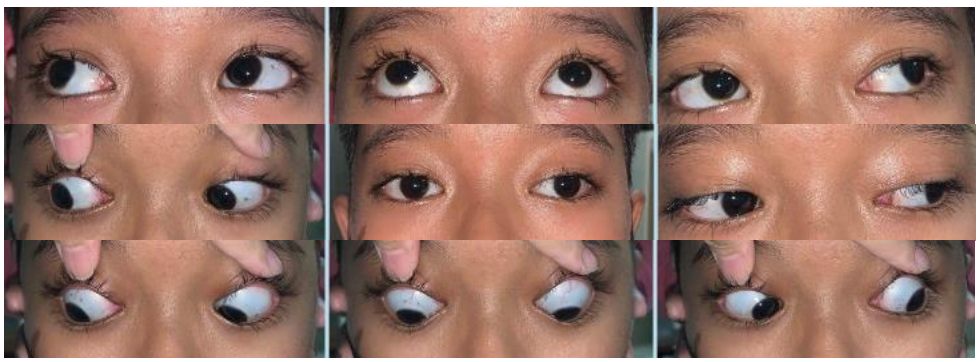


Figure 3. Nine gaze position at final follow up in outpatient clinic show clinical improvement in all directions of gaze.

## 3. Discussion

Miller Fisher syndrome (MFS) is a rare variant of Guillain-Barré syndrome (GBS) that typically progresses over a few days, presenting with clinical trial of eye muscle weakness (ophthalmoplegia), loss of coordination (ataxia), and absence of reflexes (areflexia) (15)(16)(17)(18). Patients often seek medical help due to sudden vision problems and difficulty walking (19)(20). In this case, the patient had previously been hospitalized in the pediatric ward for generalized limb weakness, difficulty walking, and double vision (binocular diplopia) caused by ophthalmoplegia.

Ophthalmoplegia itself is a cardinal sign in several neurological disorders, but its presentation varies depending on the underlying cause and the location of the lesions (21) (22). When a patient has deficits in one or more eye muscles, myasthenia gravis should always be considered as a potential diagnosis. MFS and ocular myasthenia gravis can cause similar neurological signs, which can complicate the initial diagnosis. Both can result in external ophthalmoplegia and uneven or fluctuating ptosis. However, in MFS, the ophthalmoplegia is generally bilateral and complete as can be seen in this patient (23)(24).

The primary pathological mechanism of MFS is demyelination of peripheral nerves. Gangliosides, molecules composed of glycosphingolipids (ceramide and oligosaccharide), are concentrated in the nervous system(25)(26). MFS is linked to high levels of antiganglioside IgG anti-GQ1b antibodies, specifically GQ1b, which is abundant in the cranial nerves controlling the extraocular muscles. This antibody is present in 85-90% of MFS cases but is not exclusive to the condition(27)(28)(29).

Cerebrospinal fluid (CSF) analysis generally shows increased protein levels with a normal white blood cell count, a condition known as albuminocytologic dissociation(30)(31). Though rare, a white blood cell counts exceeding 10 per high-power field may appear, more commonly in related conditions like Lyme disease, sarcoidosis, and AIDS. Since CSF may show normal cell and protein levels early in the disease, its diagnostic value is limited(32)(33).

Electrophysiological studies are more reliable for diagnosis. Indicators of demyelination include conduction block or reduced conduction velocity(34). F-wave recordings and abnormalities such as signal dispersion or dropout can help identify early involvement of proximal nerves. In this case, electromyography revealed reduced amplitude in right peroneal nerve conduction, though the test was conducted after the disease had progressed. Prolonged F-wave findings can confirm the diagnosis if tested early(35)(32)(36).

Treatment of MFS typically involves supportive care, pain management, respiratory support when necessary, and immunotherapy(37)(38). Most MFS patients recover spontaneously and do not require immunotherapy. However, intravenous immunoglobulin (IVIG) may be considered for severe cases involving difficulty swallowing or breathing(39)(40).

## 4. Conclusion

Miller Fisher syndrome (MFS) is a rare form of Guillain-Barré Syndrome, and it occurs less commonly in children. There are no definitive tests to confirm MFS, making diagnosis primarily clinical, relying on the presence of the classic triad: ataxia, ophthalmoplegia, and generalized areflexia, with minimal limb weakness. Treatment is generally supportive, though intravenous immunoglobulins (IVIG) or plasmapheresis may be used in severe cases. The prognosis is typically favorable, though respiratory failure can occur. Most patients start to improve within two to four weeks of symptom onset, with full recovery usually occurring within six months.

## Reference

[1] Teener J. Miller Fisher's Syndrome. Semin Neurol [Internet]. 2013 May 15;32(05):512–6. Available from: http://www.thieme-connect.de/DOI/DOI?10.1055/s-0033-1334470

[2] Yang MC, Liu A. Surge of Miller Fisher variant and Guillain-Barré syndrome in two downtown Los Angeles community teaching hospitals. Clin Case Reports [Internet]. 2020 Nov 16;8(11):2245–50. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ccr3.3132

[3] Waqar K, Nasir S, Sher K, Fatima M, Malik A. Frequency of miller fisher variant of guillain barré syndrome at a tertiary care hospital , Karachi. Pakistan J Neurol Sci. 2017;12(1):16–9.

[4] Mane SS, Nagesh U, Sathe VT, Janadhanan J. Miller Fisher Variant of Guillain-Barré Syndrome in a Child. J Pediatr Neurosci [Internet]. 2020;15(1):60–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32435311

[5] Mane S, Nagesh U, Sathe V, Janadhanan J. Miller Fisher variant of Guillain–Barré syndrome in a child. J Pediatr Neurosci [Internet]. 2020;15(1):60. Available from: https://journals.lww.com/10.4103/jpn.JPN_146_18

[6] Leonhard SE, Mandarakas MR, Gondim FAA, Bateman K, Ferreira MLB, Cornblath DR, et al. Diagnosis and management of Guillain–Barré syndrome in ten steps. Nat Rev Neurol [Internet]. 2019 Nov 20;15(11):671–83. Available from: https://www.nature.com/articles/s41582-019-0250-9

[7] Bandeira LP, Palaoro LG, Degenszajn J. Miller Fisher syndrome: a rare variant of Guillain-Barré syndrome. Autops Case Reports [Internet]. 2012;2(3):57–61. Available from: http://doi.editoracubo.com.br/10.4322/acr.2012.027

[8] Koga M, Gilbert M, Li J, Koike S, Takahashi M, Furukawa K, et al. Antecedent infections in Fisher syndrome. Neurology [Internet]. 2005 May 10;64(9):1605–11. Available from: https://www.neurology.org/doi/10.1212/01.WNL.0000160399.08456.7C

[9] Martins-Filho PR, Pereira de Andrade AL, Pereira de Andrade AJ, Moura da Silva MD, de Souza Araújo AA, Nunes PS, et al. Miller Fisher Syndrome in Patients With Severe Acute Respiratory Syndrome Coronavirus 2 Infection: A Systematic Review. J Clin Neurol [Internet]. 2021;17(4):541. Available from: https://thejcn.com/DOIx.php?id=10.3988/jcn.2021.17.4.541

[10] Unit OA, Hospital C. Persistent Diplopia in Miller Fisher Syndrome: A Case Report. 2017;49:9–12.

[11] Ravlic M, Knezevic L, Krolo I, Herman J. Ocular Manifestations of Miller Fisher Syndrome: a Case Report. Med Arch [Internet]. 2021;75(3):234. Available from: https://www.ejmanager.com/fulltextpdf.php?mno=96835

[12] Bukhari S, Taboada J. A Case of Miller Fisher Syndrome and Literature Review. Cureus [Internet]. 2017 Feb 22; Available from: http://www.cureus.com/articles/6150-a-case-of-miller-fisher-syndrome-and-literature-review

[13] Manganotti P, Pesavento V, Buoite Stella A, Bonzi L, Campagnolo E, Bellavita G, et al. Miller Fisher syndrome diagnosis and treatment in a patient with SARS-CoV-2. J Neurovirol [Internet]. 2020 Aug 11;26(4):605–6. Available from: https://link.springer.com/10.1007/s13365-020-00858-9

[14] Mayer JE, McNamara CA, Mayer J. Miller Fisher syndrome and Guillain-Barré syndrome: dual intervention rehabilitation of a complex patient case. Physiother Theory Pract [Internet]. 2022 Jan 2;38(1):245–54. Available from: https://www.tandfonline.com/doi/full/10.1080/09593985.2020.1736221

[15] Fisher M. An Unusual Variant of Acute Idiopathic Polyneuritis (Syndrome of Ophthalmoplegia, Ataxia and Areflexia). N Engl J Med. 1956;255(2):57–65.

[16] San-Juan OD, Martínez-Herrera JF, Moreno García J, Fernández Gonzalez-Aragon M, Del Castillo-Calcáneo J de D, Pérez-Neri I. Miller Fisher Syndrome: 10 Years' Experience in a Third-Level Center. Eur Neurol [Internet]. 2009;62(3):149–54. Available from: https://karger.com/ENE/article/doi/10.1159/000226599

[17] Noioso CM, Bevilacqua L, Acerra GM, Della Valle P, Serio M, Vinciguerra C, et al. Miller Fisher syndrome: an updated narrative review. Front Neurol [Internet]. 2023 Aug 24;14. Available from: https://www.frontiersin.org/articles/10.3389/fneur.2023.1250774/full

[18] Yepishin I V, Allison RZ, Kaminskas DA, Zagorski NM, Liow KK. Miller Fisher Syndrome: A Case Report Highlighting Heterogeneity of Clinical Features and Focused Differential Diagnosis. Hawaii J Med Public Health [Internet]. 2016 Jul;75(7):196–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27437164

[19] Lee JH, Jang Y, Kim S-J, Jung JH. Characteristics of pupil palsy in miller-fisher syndrome: case reports and review of the literature. Neurol Sci [Internet]. 2021 Dec 6;42(12):5213–8. Available from: https://link.springer.com/10.1007/s10072-021-05157-7

[20] Gupta SK, Jha KK, Chalati MD, Alashi LT. Miller Fisher syndrome. BMJ Case Rep [Internet]. 2016 Oct 13;bcr2016217085. Available from: https://casereports.bmj.com/lookup/doi/10.1136/bcr-2016-217085

[21] Keane JR. Bilateral Ocular Paralysis. Arch Neurol [Internet]. 2007 Feb 1;64(2):178. Available from: http://archneur.jamanetwork.com/article.aspx?doi=10.1001/archneur.64.2.178

[22] Ryu WY, Kim YH, Yoon B-A, Park HT, Bae JS, Kim JK. Pattern of Extraocular Muscle Involvements in Miller Fisher Syndrome. J Clin Neurol [Internet]. 2019;15(3):308. Available from: https://www.thejcn.com/DOIx.php?id=10.3988/jcn.2019.15.3.308

[23] Glover K, Mishra D, Singh TRR. Epidemiology of Ocular Manifestations in Autoimmune Disease. Front Immunol [Internet]. 2021 Nov 2;12. Available from: https://www.frontiersin.org/articles/10.3389/fimmu.2021.744396/full

[24] Anthony SA, Thurtell MJ, Leigh RJ. Miller Fisher Syndrome Mimicking Ocular Myasthenia Gravis. Optom Vis Sci [Internet]. 2012 Dec;89(12):e118–23. Available from: https://journals.lww.com/00006324-201212000-00022

[25] Schengrund C-L. Gangliosides: glycosphingolipids essential for normal neural development and function. Trends Biochem Sci [Internet]. 2015 Jul;40(7):397–406. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0968000415000481

[26] Muñiz AE. Multiple cranial nerve neuropathies, ataxia and, areflexia: Miller Fisher syndrome in a child and review. Am J Emerg Med [Internet]. 2017 Apr;35(4):661.e1-661.e4. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0735675716304429

[27] Palakkuzhiyil N, Taggu A, Saleem S, Uvais N. Anti-GQ1b IgG and anti GD1b IgG positive recurrent miller fisher syndrome. Ann Indian Acad Neurol [Internet]. 2020;23(5):729. Available from: https://journals.lww.com/10.4103/aian.AIAN_253_19

[28] Liu J-X, Willison HJ, Pedrosa-Domello¨f F. Immunolocalization of GQ1b and Related Gangliosides in Human Extraocular Neuromuscular Junctions and Muscle Spindles. Investig Opthalmology Vis Sci [Internet]. 2009 Jul 1;50(7):3226. Available from: http://iovs.arvojournals.org/article.aspx?doi=10.1167/iovs.08-3333

[29] Chiba A, Kusunoki S, Obata H, Machinami R, Kanazawa I. Serum anti-GQ 1b IgG antibody is associated with ophthalmoplegia in Miller Fisher syndrome and Guillain-Barré syndrome. Neurology [Internet]. 1993 Oct;43(10):1911–1911. Available from: https://www.neurology.org/doi/10.1212/WNL.43.10.1911

[30] Nomani AZ, Iqbal M, Majeed H, Badshah M, Nabi S, Jan Z, et al. Albuminocytological dissociation in different electrophysiological gbs variants. Pakistan J Neurol Sci. 2015;10(4):32–6.

[31] Rath J, Zulehner G, Schober B, Grisold A, Krenn M, Cetin H, et al. Cerebrospinal fluid analysis in Guillain–Barré syndrome: value of albumin quotients. J Neurol [Internet]. 2021 Sep 2;268(9):3294–300. Available from: https://link.springer.com/10.1007/s00415-021-10479-9

[32] Wijdicks EFM, Klein CJ. Guillain-Barré Syndrome. Mayo Clin Proc. 2017;92(3):467–79.

[33] Donofrio PD. Guillain-Barre´ Syndrome. Continuum (N Y). 2017;5(23):1295–309.

[34] Coggan J, Bittner S, Stiefel K, Meuth S, Prescott S. Physiological Dynamics in Demyelinating Diseases: Unraveling Complex Relationships through Computer Modeling. Int J Mol Sci [Internet]. 2015 Sep 7;16(9):21215–36. Available from: https://www.mdpi.com/1422-0067/16/9/21215

[35] Lyu R-K, Chu C-C, Kuo H-C, Chang K-H, Ro L-S. Motor Conduction Findings in Fisher Syndrome. Eur Neurol [Internet]. 2013;70(5–6):276–80. Available from: https://karger.com/ENE/article/doi/10.1159/000353286

[36] Gordon PH, Wilbourn AJ. Early Electrodiagnostic Findings in Guillain-Barré Syndrome. Arch Neurol [Internet]. 2001 Jun 1;58(6):913. Available from: http://archneur.jamanetwork.com/article.aspx?doi=10.1001/archneur.58.6.913

[37] Ghani MR, Yousaf MIK, Van Bussum K, Shi P, Cordoves Feria RM, Brown M. Miller Fisher Syndrome Presenting Without Areflexia, Ophthalmoplegia, and Albuminocytological Dissociation: A Case Report. Cureus [Internet]. 2022 Mar;14(3):e23371. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35475055

[38] Kara S, Wilson MA, Youssef P, Nedd K. Course and Treatment of a Rare Neurological Sequelae After COVID-19: Miller Fisher Syndrome. Cureus [Internet]. 2022 Oct 6; Available from: https://www.cureus.com/articles/100250-course-and-treatment-of-a-rare-neurological-sequelae-after-covid-19-miller-fisher-syndrome

[39] Sonoo M. [Keypoints of the guideline for management of Guillain -Barré syndrome and Fisher syndrome, 2013]. Nihon Rinsho [Internet]. 2015 Sep;73 Suppl 7:394–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26480731

[40] van Doorn PA, Kuitwaard K, Walgaard C, van Koningsveld R, Ruts L, Jacobs BC. IVIG Treatment and Prognosis in Guillain–Barré Syndrome. J Clin Immunol [Internet]. 2010 May 16;30(S1):74–8. Available from: http://link.springer.com/10.1007/s10875-010-9407-4