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Miller-Fisher syndrome subtype with isolated bilateral mydriasis: a pediatric case report

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Abstract

Background Miller-Fisher Syndrome (MFS), a distinct subtype of Guillain-Barré Syndrome (GBS), accounts for 5% of GBS cases and classically manifests with the triad of ophthalmoplegia, ataxia, and areflexia. Isolated bilateral mydriasis as the sole presenting feature is exceptionally rare, particularly in pediatric populations. While pupillary abnormalities have been documented in adult MFS cases, their diagnostic significance and management in children remain poorly characterized.

Case Summary We report a novel pediatric case of a 7-year-old girl presenting with 7 days of unexplained bilateral painless mydriasis unresponsive to light accommodation. Initial symptomatic management targeting potential toxic or neuropathic etiologies proved ineffective. Recognition of this atypical presentation prompted serological evaluation for autoimmune neuropathy markers, which demonstrated positivity for GQ1b IgM, GQ1b IgG, and GT1a IgG antibodies, confirming MFS diagnosis. Rapid clinical improvement followed intravenous immunoglobulin (IVIG) therapy. This case highlights the diagnostic challenges posed by incomplete or atypical MFS manifestations and underscores the necessity of early antibody testing in unexplained autonomic or neurological symptoms.

Conclusion This report expands the phenotypic spectrum of pediatric MFS by demonstrating isolated bilateral mydriasis as a potential initial manifestation, clinicians evaluating pupillary dilation should consider MFS in differential diagnoses. Future studies should continue to explore the pathophysiological link between anti-GQ1b antibodies and isolated autonomic dysfunction in pediatric MFS.

Keywords Miller-Fisher syndrome, Pediatric neurology, Guillain-Barré syndrome, Anti-GQ1b antibodies, Case report

Introduction

GBS, the leading cause of acute flaccid paralysis globally [1], is an immune-mediated neuropathy classically characterized by rapidly progressive symmetric limb weakness and albuminocytological dissociation in cerebrospinal fluid [2–3]. Recognized subtypes include MFS, Pharyngeal-cervical-brachial weakness (PCB), and facial diplegia with paresthesias, each defined by distinct clinical patterns. While IVIG and plasma exchange remain cornerstone therapies [2], timely diagnosis relies on recognizing variable phenotypic presentations.

MFS, accounting for 5% of GBS cases, classically manifests as a triad of ophthalmoplegia, ataxia, and areflexia

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[4]. However, incomplete forms, such as acute isolated ophthalmoparesis or ataxic neuropathy, expand its diagnostic spectrum. Notably, pupillary abnormalities like mydriasis and light-near dissociation, though rare, correlate strongly with anti-GQ1b antibodies [5–6]. These antibodies target gangliosides enriched in ocular motor nerves and autonomic pathways, with cross-reactivity to GT1a potentially disrupting sympathetic innervation of the iris [7]. Such mechanisms may underlie atypical autonomic features, including bilateral mydriasis, in MFS. Beyond core symptoms, relevant case series describe diverse neurological accompaniments, including facial palsy, dysarthria and convergence insufficiency, underscoring MFS's heterogeneous nature [8]. Therapeutic alignment with GBS protocols, including IVIG, accelerates recovery in most patients.

We present a diagnostically challenging pediatric case of MFS manifesting solely as acute bilateral mydriasis with absent light reflexes, devoid of ophthalmoplegia, ataxia, or areflexia. Initial evaluations excluded toxic, metabolic, and structural etiologies, while empirical therapies proved ineffective. Serological confirmation of anti-GQ1b IgM/IgG and anti-GT1a IgG antibodies established an MFS diagnosis, with rapid symptom resolution following IVIG. This case highlights three critical insights: First, isolated autonomic dysfunction may herald MFS in children. Second, antibody testing is pivotal in atypical presentations. Third, pupillary abnormalities warrant consideration of immune-mediated neuropathies even without classic neurological signs. By expanding the recognized phenotype of pediatric MFS, this report urges clinicians to integrate ganglioside antibody profiling into the workup of unexplained mydriasis.

Case presentation

Chief complaints

A 7-year-old girl presented with painless bilateral mydriasis and absent light reflexes persisting for 7 days.

History of present illness

One week prior to presentation, the patient experienced a mild upper respiratory infection that resolved after treatment. During a routine ophthalmology follow-up for previously diagnosed amblyopia (detected one year earlier), bilateral pupil dilation (7 mm diameter) with complete loss of light and accommodation reflexes was noted. The patient denied ocular pain, visual disturbances, diplopia, ptosis, or systemic symptoms (e.g., limb weakness, ataxia, dysphagia). Initial head CT and neurological evaluations by ophthalmology were unremarkable, prompting observation. Persistent mydriasis without progression led to referral for further workup.

Past medical and family history

Ocular history: Stable amblyopia under surveillance; no prior pupillary abnormalities or use of mydriatic agents (e.g., tropicamide).

Medical history: Fully immunized, including COVID-19 vaccine; no chronic illnesses or medications.

Family history: No neuroimmunological or autoimmune disorders reported.

Physical examination

Vitals: Afebrile (36.8 °C), normotensive (92/53 mmHg), and hemodynamically stable.

General: Alert, interactive, with normal cognition and speech.

Ocular: Bilateral fixed mydriasis (right: 7.0 mm, left: 7.5 mm) unresponsive to light or accommodation; preserved convergence reflex (Fig. 1). Extraocular movements full, no ptosis or diplopia. Visual acuity 1.0 bilaterally; funduscopy and intraocular pressure (12 mmHg) normal.

Neurological: Cranial nerves intact; normal muscle tone/strength (grade V throughout), gait, and coordination. Physiological and deep tendon reflexes (knee, Achilles) normoactive. No meningeal signs or pathological reflexes.

Systemic: Cardiorespiratory and abdominal exams unremarkable.

Laboratory examinations

Routine panels: Complete blood count, electrolytes, renal/hepatic function, thyroid studies, inflammatory markers (CRP), and autoimmune serology (ANA) within normal limits.

Provocative testing: Neostigmine challenge negative; 1% pilocarpine failed to induce pupillary constriction.

Neurophysiology: Normal nerve conduction studies (sensory/motor) and electroencephalography.

Imaging examinations

Unremarkable cranial/orbital MRI, chest CT, and ocular ultrasound. Ophthalmologic examination showed bilateral pupil dilation and loss of light reflex (Fig. 2).

Preliminary diagnosis

Isolated bilateral mydriasis of undetermined etiology.

Further diagnostic workup

Empirical therapies (3-day mannitol, acyclovir, dexamethasone [0.3 mg/kg/day], and 5-day B vitamins) yielded partial improvement, as evidenced by pupil dilation to 6 mm and diminished light reflexes (to 5–5.5 mm on light exposure). The etiology of pupil dilation and loss of light reflex remained elusive, and imaging studies revealed no intracranial space-occupying lesions,

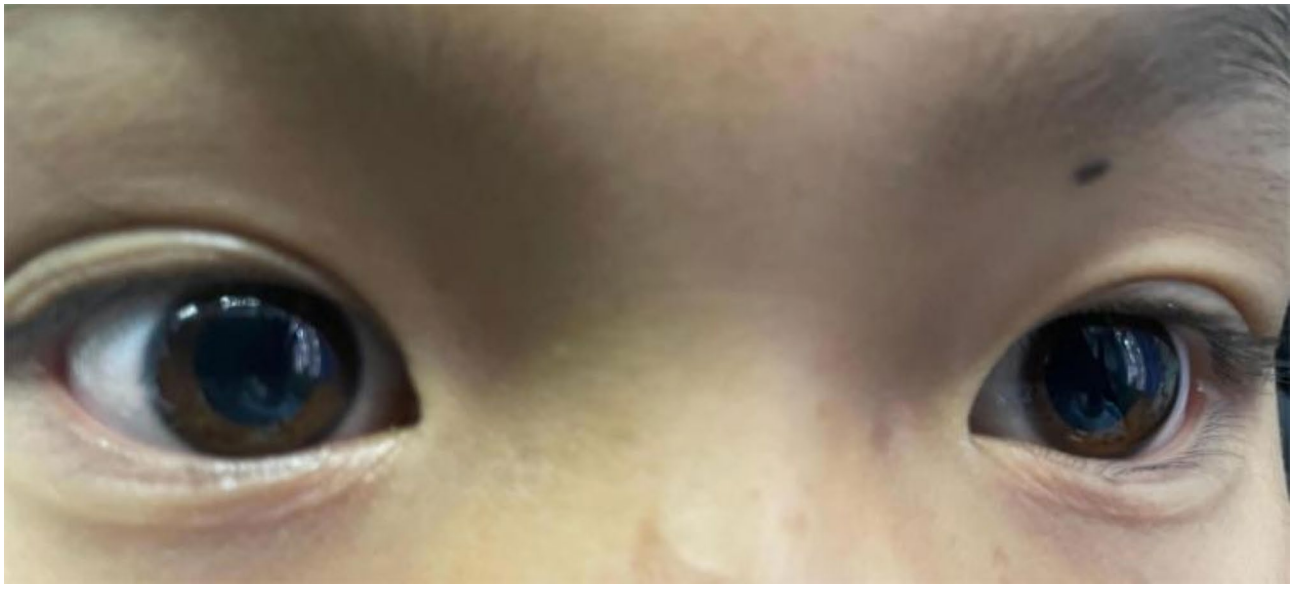

Fig. 1 Bilateral pupillary dilation in bright light - an atypical presentation of a child with MFS seen in the clinic

increasing suspicion of an immune-mediated pathology. Subsequent CSF analysis showed no albuminocytological dissociation and was antibody-negative. Serum anti-GQ1b (IgM/IgG) and anti-GT1a (IgG) antibodies were positive, and the assay was performed by western blotting.

Final diagnosis

Miller-Fisher Syndrome subtype presenting with isolated bilateral mydriasis.

Treatment

IVIG 400 mg/kg/day for 5 days.

Outcome and Follow-Up

Post-treatment: Pupil diameter normalized to 3–4 mm with restored light reflexes within 5 days.

6-month follow-up: Sustained resolution without recurrence or development of classic MFS features.

Discussion

MFS is a rare neuroimmune disorder that is considered a subtype of GBS. Typical manifestations of MFS include ophthalmoplegia, ataxia, and areflexia. Still, they vary and include acute ocular muscle paralysis without ataxia and acute ataxic neuropathy without ocular muscle paralysis. In addition, nystagmus and pupillary dilation may be present, which can be particularly challenging to diagnose and manage, especially in pediatric cases. Although a case of MFS with gait abnormalities and dilated pupils in a 3-year-old girl has been reported in the literature [9], cases of pediatric MFS with only dilated pupils have not been documented.

About the completeness of the case, additional information about the family history and early symptom development contributed to a better understanding. The patient's family history did not include a significant genetic predisposition to neurologic disease. Early symptoms included mild headache and malaise that preceded the pupil abnormality by one week, which may be indicative of early neurologic involvement in MFS [10].

In terms of the diagnosis of the case, the results of the 1% pilocarpine drop test in this case are significant. Adie's pupil has mostly unilateral onset, is sensitive to the 1% pilocarpine drop test, and is negative for anti-GQ1b antibodies. Thus, the negative result in this case helps to rule out Adie's pupil and supports a neurogenic origin for the pupillary abnormality. This result, combined with other clinical and laboratory evidence, further supports MFS as the underlying cause of the patient's bilateral pupillary dilation. A review of the literature revealed that Lee et al. had reported four patients with MFS, all of whom had bilateral pupillary dilation, which manifested as pupil dilation and unresponsiveness to light stimulation, which is similar to the symptoms of the present case. This review suggests that in atypical cases, detecting anti-GQ1b antibodies can help identify MFS early [11]. In other unexplained ocular neurological disorders, serum search for anti-GQ1b antibodies may be helpful for diagnosis, especially in young patients [12]. Therefore, we performed a serum immunologic examination, which showed positive serum anti-GQ1b and anti-GT1a antibodies, suggesting that the diagnosis of MFS should be considered. However, it is equally important to carefully differentiate between other diseases positive for anti-GQ1b antibodies, including Bickerstaff Brainstem

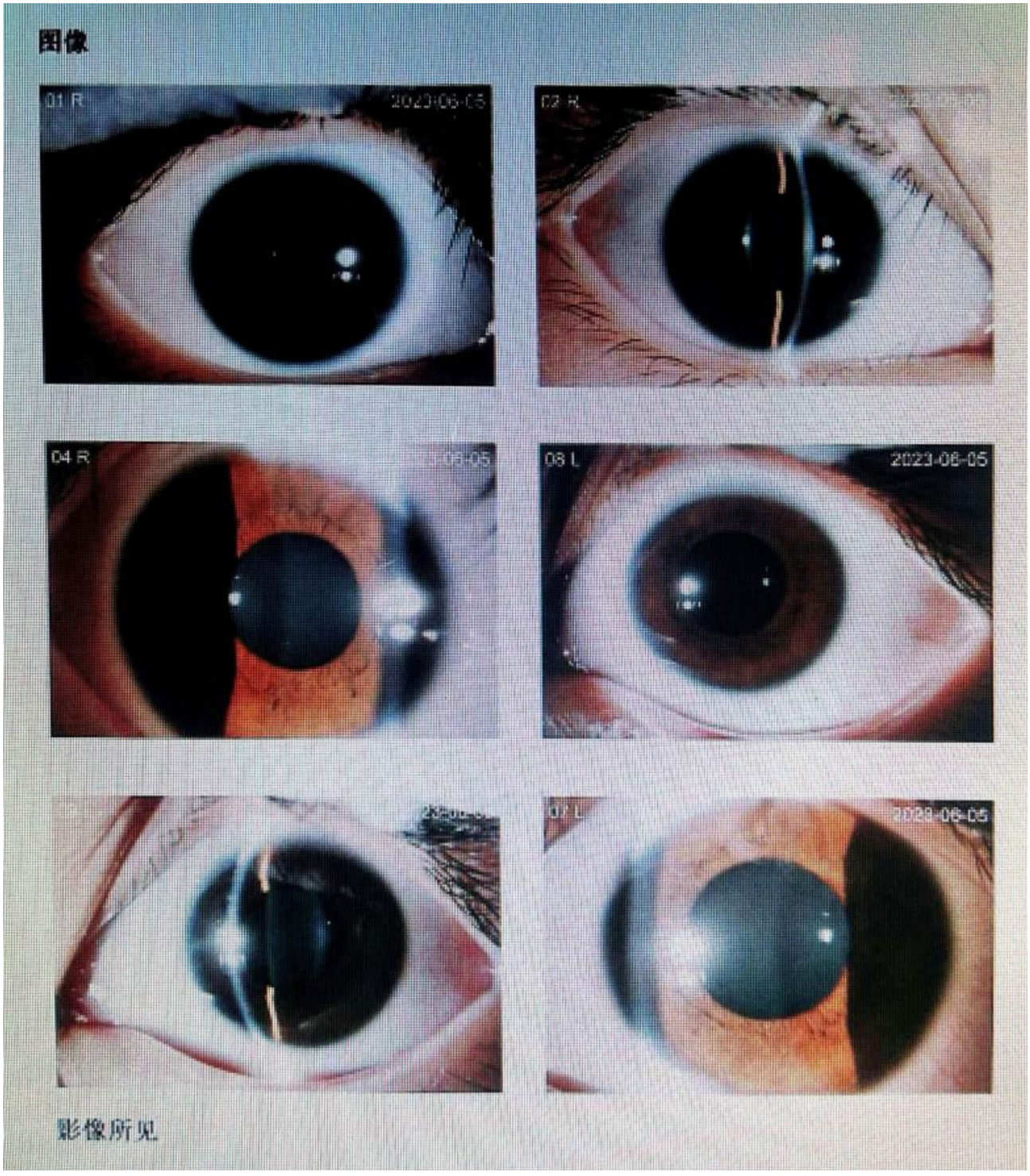

Fig. 2 Ophthalmologic examination showed bilateral pupil dilation and loss of light reflex

Encephalitis (BBE) and PCB. In this case, the child had no typical clinical manifestations other than bilateral pupil abnormalities, such as dysphagia, limb weakness, and sensory deficits. Therefore, BBE and PCB were not considered at the time. Despite the absence of abnormalities on imaging, an extensive immunological and neurological examination ruled out other possible diagnoses, such as central nervous system infection or tumor.

It has been found that molecular mimicry is a key factor in the pathogenesis of MFS. The mechanism suggests that antigens of certain pathogens have similar molecular structures to those in the host's neural tissues, which

leads to a misdirected attack by the immune system on its own neural tissues [13]. In this case, the patient had a history of antecedent infections of the respiratory tract; therefore, molecular mimicry may be a potential mechanism for the pathogenesis of this patient. It has been reported that molecular mimicry is likewise considered as one of the major pathogenic mechanisms in COVID-19-related MFS cases [14–15]. It is noteworthy that pediatric MFS patients have a higher incidence of autonomic symptoms and a lower rate of anti-GQ1b antibody positivity [16]. In future studies, the molecular mechanisms and immunological pathways of MFS should be further explored, especially the role of anti-GQ1b antibodies in pediatric MFS and their interrelationship with other immune mediators.

In terms of treatment, IVIG, a well-established therapy for treating immune-related diseases, was used according to the MFS guidelines [10]. The efficacy of immunoglobulin is demonstrated by symptomatic improvement and pupil normalization, which highlights its suitability as a primary treatment. In the present case, the treatment regimen of IVIG was effective, and the child's symptoms improved dramatically after treatment. Recurrence of MFS is rare, and the prognosis is primarily favorable; in the present case, there was no sign of recurrence.

However, there is still a gap in the understanding of this MFS subtype. In the present case, the patient had only symptoms of pupillary dilation without ophthalmoplegia. The mechanism of this phenomenon has not been fully elucidated, but studies have suggested some possible hypotheses. Which may be related to differences in the distribution and function of gangliosides in different nerve fibers or differences in individual immune responses. Anti-GQ1b antibodies, which are abundantly expressed in the actinic, synovial, and abducens nerves, may affect the nerve conduction function by binding to the ganglioside GQ1b, leading to abnormal pupillary responses [17–18]. In this case, the light reflex and accommodation reflex was absent, but convergence reflexes were present, suggesting that autoimmune attack selectively targeted parasympathetic fibers in the ciliary ganglion. The selective involvement of parasympathetic fibers with preservation of somatic motor function may be related to the differential expression of GQ1b gangliosides in autonomic and somatic nerve endings. Previous studies have found that anti-GQ1b antibodies bind primarily to the presynaptic membrane of nerve endings, interfering with the release of acetylcholine and thereby causing a block in nerve conduction, a process that may block the release of acetylcholine required for light reflexes. In contrast, somatomotor fibers expressed lower levels of GQ1b, which may be the underlying mechanism behind this phenomenon and may explain the absence of ophthalmoplegia in this patient [19–20]. The preservation of the vergence reflex suggests that central integration and somatomotor function were not impaired, highlighting the multifocal nature of immune damage in the MFS variant. Furthermore, it has been shown that anti-GQ1b antibodies may lead to neuroinflammation and demyelination through activation of the complement system, which in turn affects neurological function [21]. Future studies should continue to explore the pathophysiological link between anti-GQ1b antibodies and isolated autonomic dysfunction in pediatric MFS.

Albuminocytological dissociation is one of the typical manifestations of GBS and its subtypes, characterized by elevated protein levels in the CSF and normal or mildly elevated cell counts [22]. This dissociation is more common in patients with GBS, but its frequency is more time-dependent [22]. In MFS, CSF protein cell dissociation may not be evident, especially in the early stages of the disease [2]. In this case, the child's CSF did not show typical albuminocytological dissociation, which may be related to disease course, manipulation, or the heterogeneity between MFS and GBS. These issues still need to be further explored in future studies.

This case highlights the rarity and clinical significance of pediatric pupillary abnormalities in pediatric MFS and emphasizes the importance of prompt diagnosis and treatment. Differences in the clinical presentation of pediatric and adult MFS necessitate a tailored diagnostic and therapeutic approach to pediatric cases. In conclusion, this case emphasizes the need for clinical vigilance, timely evaluation, and intervention when encountering acute pupillary dilation and advocates continued research into the pathogenesis and treatment of this rare subtype of MFS.

However, this study has some limitations. First, only one case was reported in this study, and the sample size was too small to allow extensive validation and generalization of MFS's clinical manifestations, diagnostic methods, and therapeutic effects. Second, lacking long-term follow-up data, it is impossible to determine whether the patient will develop delayed symptoms or long-term complications, and we will continue to pay attention to the patient's long-term prognosis. Third, electromyography (EMG) findings are significant in MFS, but for some reason, the patient's family did not agree to perform EMG, which should be performed in subsequent studies. Fourth, the impact of environmental exposure and dietary habits on the disease diagnosis was not analyzed in detail during the diagnostic process, and attention should be paid to the relevant elements in subsequent studies to rule out other possible etiologies more comprehensively.

Conclusion

This report expands the phenotypic spectrum of pediatric MFS by demonstrating isolated bilateral mydriasis as a potential initial manifestation, clinicians evaluating pupillary dilation should consider MFS in differential diagnoses. Future studies should continue to explore the pathophysiological link between anti-GQ1b antibodies and isolated autonomic dysfunction in pediatric MFS.

Abbreviations

MFS	Miller-Fisher syndrome
GBS	Guillain-Barré syndrome
IVIG	Intravenous immunoglobulin
CSF	cerebrospinal fluid
PCB	Pharyngeal-cervical-brachial weakness
BBE	Bickerstaff Brainstem Encephalitis
EMG	Electromyography

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Author contributions

Fq Y and Z T wrote the main manuscript text under the guidance of K L; Fq Y and Z T prepared the figures; Yh L and Y L helped to draft the manuscript. All authors have read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

Ethical approval for this study was obtained from the Medical Ethics Committee of Kunming Children's Hospital, with approval letter reference number IEC-C-008-A07-V3.0.

Consent to participate

Consent has been obtained from the patient and family.

Consent for publication

Informed written consent was obtained from the patient and her parents for publication of this report and any accompanying images.

CARE Checklist (2013)

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References

1. Shahrizaila N, Lehmann HC, Kuwabara S. Guillain-Barré syndrome. LANCET. 2021; 397 LANCET. https://doi.org/10.1016/S0140-6736(21)00517-1
2. van den Berg B, Walgaard C, Drenthen J et al. Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. NAT REV NEUROL. 2014; 10 NAT REV NEUROL. https://doi.org/10.1038/nrneurol.2014.121
3. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. LANCET. 2016; 388 LANCET. https://doi.org/10.1016/S0140-6736(16)00339-1
4. Jørgensen L, Vedeler CA, [Miller-Fisher. syndrome]. TIDSSKR NORSKE LAEGE. 2005; 125 TIDSSKR NORSKE LAEGE. PMID: 15909003IF: 1.2 Q2 NA.
5. Fleury V, Aqallal A, Lagrange E, et al. Acute bilateral mydriasis associated with anti-GQ1b antibody. J CLIN NEUROSCI. 2010. https://doi.org/10.1016/j.jocn.2009.06.030. 17 J CLIN NEUROSCI.
6. Fehmi J, Scherer SS, Willison HJ, et al. Nodes, Paranodes and neuropathies. J NEUROL NEUROSUR PS. 2018. https://doi.org/10.1136/jnnp-2016-315480. 89 J NEUROL NEUROSUR PS.
7. Chiba A, Kusunoki S, Obata H et al. Serum anti-GQ1b IgG antibody is associated with ophthalmoplegia in Miller Fisher syndrome and Guillain-Barré syndrome: clinical and immunohistochemical studies. NEUROLOGY. 1993; 43 NEUROLOGY. https://doi.org/10.1212/wnl.43.10.1911
8. Jung JH, Oh EH, Shin JH et al. Atypical clinical manifestations of Miller Fisher syndrome. NEUROL SCI. 2019; 40 NEUROL SCI. https://doi.org/10.1007/s10072-018-3580-2
9. Shaath DS, Scheidt AF, Stiff HA. Sudden-Onset bilateral mydriasis in a young Girl. JAMA OPHTHALMOL. 2023;141(JAMA OPHTHALMOL). https://doi.org/10.1001/jamaophthalmol.2023.2585.
10. Doets AY, Jacobs BC, van Doorn PA. Advances in management of Guillain-Barré syndrome. CURR OPIN NEUROL. 2018. https://doi.org/10.1097/WCO.0000000000000602. 31 CURR OPIN NEUROL.
11. Lee JH, Jang Y, Kim SJ, et al. Characteristics of pupil palsy in miller-fisher syndrome: case reports and review of the literature. NEUROL SCI. 2021;42(NEUROL SCI). https://doi.org/10.1007/s10072-021-05157-7.
12. Caccavale A, Mignemi L. Acute onset of a bilateral areflexical mydriasis in Miller-Fisher syndrome: a rare neuro-ophthalmologic disease. J NEURO-OPHTHALMOL. 2000. https://doi.org/10.1097/00041327-200020010-00018. 20 J NEURO-OPHTHALMOL.
13. Koga M, Gilbert M, Li J, et al. Antecedent infections in fisher syndrome: a common pathogenesis of molecular mimicry. NEUROLOGY. 2005;64(NEUROLOGY). https://doi.org/10.1212/01.WNL.0000160399.08456.7C.
14. Poyraz T. Miller Fisher Syndrome Associated With COVID-19: A History of Molecular Mimicry and an Up-to-Date Review of the Literature. Cureus. 2023; 15 Cureus. https://doi.org/10.7759/cureus.43111
15. Poyraz T. Miller Fisher Syndrome Associated With COVID-19: A Child Case Report and an Up-to-Date Review of the Literature. Cureus. 2023; 15 Cureus. https://doi.org/10.7759/cureus.35656
16. Jang Y, Choi JH, Chae JH, et al. Pediatric miller fisher syndrome; characteristic presentation and comparison with adult miller fisher syndrome. J Clin Med. 2020. https://doi.org/10.3390/jcm9123930. 9 J Clin Med.
17. Yuki N, Hartung HP, Guillain-Barré. syndrome. NEW ENGL J MED. 2012; 366 NEW ENGL J MED. https://doi.org/10.1056/NEJMra1114525
18. Wanleenuwat P, Iwanowski P, Kozubski W. Antiganglioside antibodies in neurological diseases. J NEUROL SCI. 2020. https://doi.org/10.1016/j.jns.2019.116576. 408 J NEUROL SCI.
19. Willison HJ, Yuki N. Peripheral neuropathies and anti-glycolipid antibodies. Brain. 2002;125(BRAIN). https://doi.org/10.1093/brain/awf272.
20. Plomp JJ, Molenaar PC, O'Hanlon GM, et al. Miller fisher anti-GQ1b antibodies: alpha-latrotoxin-like effects on motor end plates. ANN NEUROL. 1999. https://doi.org/10.1002/1531-8249(199902)45:2%3C189::aid-ana9%3E3.0.co;2-t. 45 ANN NEUROL.
21. Kieseier BC, Mathey EK, Sommer C et al. Immune-mediated neuropathies. Nat Rev Dis Primers. 2018; 4 Nat Rev Dis Primers. https://doi.org/10.1038/s41572-018-0027-2
22. Fokke C, van den Berg B, Drenthen J, et al. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain. 2014;137(BRAIN). https://doi.org/10.1093/brain/awt285.

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