Neurology Asia 2026; 31(2) : 819 – 822

Anti-sulfatide IgG in Miller Fisher syndrome: Report of two cases

[1,2]Vishnu Prasad Rao *MD*, [1]Khoo Jia Jun *MBBS*, *[2]Shahidatul-Adha Mohamad *MD*, *MMed*, [3]Mahavishnu Sahadevan *MMed FEBN*, *[2]Yaakub Azhany *MMed, PhD*

[1]Department of Ophthalmology, Hospital Putrajaya, Putrajaya, Malaysia; [2]Department of Ophthalmology and Visual Science, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan; [3]Department of Neurology, Hospital Putrajaya, Putrajaya, Malaysia

Abstract

Anti-GQ1b IgG is the hallmark biomarker of Miller Fisher syndrome (MFS), an acute neuropathy characterized by ophthalmoplegia, ataxia and areflexia. In contrast, anti-sulfatide IgG is typically associated with chronic neuropathies, and its presence in acute presentations is uncommon. We report two female patients who presented with acute-onset giddiness, imbalance and diplopia. Initial examination showed gait ataxia, reduced reflexes and mild extraocular movement restriction, which progressed over the next few days to near complete ophthalmoplegia, consistent with classic MFS. Both patients had albuminocytologic dissociation on cerebrospinal fluid analysis. Serology showed isolated sulfatide-IgG positivity in the first case, and dual sulfatide-IgG and anti-GQ1b IgG positivity in the second. Both patients received intravenous immunoglobulin (IVIG) and showed marked clinical improvement. These cases suggest that anti-sulfatide IgG, although classically linked to chronic neuropathies, may also be detected in MFS, either alone or in combination with anti-GQ1b. Recognition of nonclassical antibodies may assist in identifying atypical or GQ1b-negative MFS-spectrum presentations and broaden the understanding of its immunological profile.

Keywords: Miller Fisher syndrome, anti-sulfatide IgG, anti-GQ1b, ophthalmoplegia, IVIG

INTRODUCTION

Miller Fisher syndrome (MFS) is classically defined by the triad of ophthalmoplegia, ataxia, and areflexia, with anti-GQ1b IgG detected in up to 85% of cases.[1] Anti-GQ1b is considered the principal biomarker across the GQ1b-spectrum disorders, including acute ophthalmoplegia, Bickerstaff brainstem encephalitis, and overlapping Guillain–Barré variants.[1-3]

In contrast, anti-sulfatide antibodies are traditionally associated with chronic immune-mediated neuropathies such as chronic inflammatory demyelinating polyneuropathy (CIDP), sensory ataxic neuropathy, and paraproteinemic neuropathies.[4] Their relevance in acute neuropathic presentations remains uncertain, and reported cases are uncommon.

We report two clinically classical MFS cases, one with isolated sulfatide IgG positivity and one dual-positive for sulfatide IgG and anti-GQ1b IgG, demonstrating the immunological spectrum of MFS and the diagnostic relevance of non-classical antibodies in GQ1b-seronegative MFS.

CASE REPORT

Patient 1

A 75-year-old woman with hypertension and diabetes mellitus presented with acute dizziness, diplopia and imbalance. On admission, she had mild ptosis on both eyes, mild restriction of extraocular movement and gait ataxia. Over the subsequent days, her condition progressively worsened to severe ptosis obscuring the visual axis, complete ophthalmoplegia (Figure 1A) and inability to stand without support. Deep tendon reflexes were diminished, but pupillary reflexes remained intact. The ice-pack test was

Address correspondence to: Shahidatul-Adha Mohamad, Yaakub Azhany Department of Ophthalmology and Visual Science, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan. Email: shieda@usm.my (Shahidatul-Adha Mohamad), azhany@usm.my (Yaakub Azhany)

Date of Submission: 27 November 2025; Date of Acceptance: 4 January 2026

https://doi.org/10.54029/2026kci

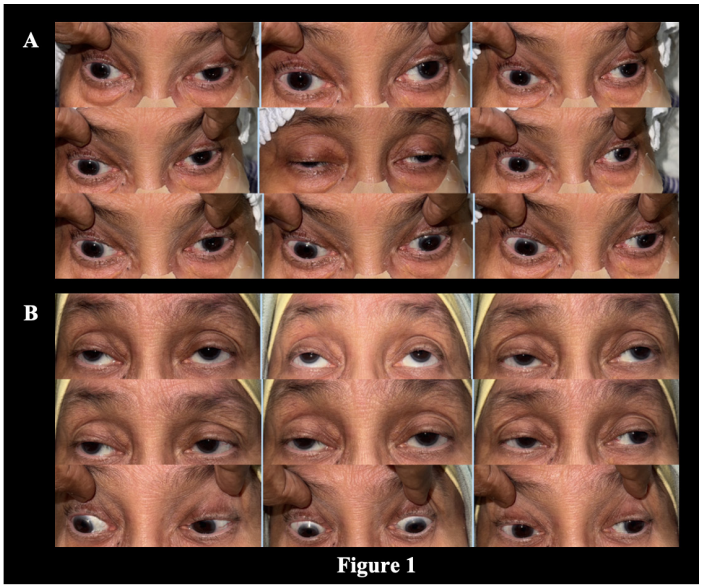

Figure 1. Nine-gaze photographs of Case 1. (A) Pre-treatment: bilateral, asymmetrical, severe ptosis with marked complex ophthalmoplegia in all gaze directions. (B) Post-treatment: partial improvement in extraocular motility after intravenous immunoglobulin therapy.

negative, making myasthenia gravis unlikely. Cerebrospinal fluid (CSF) analysis showed elevated protein of 0.65 g/L with no pleocytosis, consistent with albuminocytologic dissociation. Serology demonstrated isolated sulfatide IgG positivity, while anti-GQ1b, anti-AChR and anti-MuSK antibodies were negative. Infective screening including viral serologies, Mycoplasma and syphilis serology was also negative. Brain MRI was unremarkable. She was treated with intravenous immunoglobulin (IVIG) at 0.4 g/kg/day for 5 days and showed improvement (Figure 1B). By four weeks, she had fully recovered.

Patient 2

A 42-year-old woman presented with acute vertigo, diplopia and unilateral ptosis. Examination revealed a mild left abduction deficit, truncal ataxia and unsteady gait. Over the subsequent days, she progressed to "frozen eye", consistent with complete ophthalmoplegia (Figure 2A) and was unable to stand unaided. Reflexes were globally reduced. Brain MRI was unremarkable apart from an incidental non-compressive pituitary lesion. CSF analysis showed elevated protein of 1.38 g/L without pleocytosis. Serology demonstrated dual positivity for sulfatide IgG and anti-GQ1b IgG. Routine infective workup (viral panels, Mycoplasma, syphilis and HIV) was negative. She received IVIG for 5 days with marked clinical improvement (Figure 2B). At follow-up, her extraocular movements had returned to baseline, and her gait instability had resolved.

DISCUSSION

Our two cases demonstrate sulfatide IgG positivity in clinically classical MFS. Although sulfatide IgG is traditionally associated with chronic immune-mediated neuropathies[2,5], its detection in patients with the acute neuropathies such as classic MFS has been infrequently reported. While anti-GQ1b IgG remains the widely recognized immunological hallmark of MFS and related spectrum disorders[1], its absence in a subset of clinically typical presentations, including one of ours, highlights the need to consider additional or alternative immune targets such as sulfatide.

The significance of sulfatide IgG in MFS has not been well characterized, largely because sulfatide testing is not routinely included in serological panels for the syndrome. As a result, its prevalence in MFS remains uncertain, and under-recognition is plausible. The identification of sulfatide IgG in a clinically typical but GQ1b-seronegative MFS patient raises the possibility that sulfatide-directed immune responses may account for a subset of seronegative MFS presentations. In the dual-positive patient,

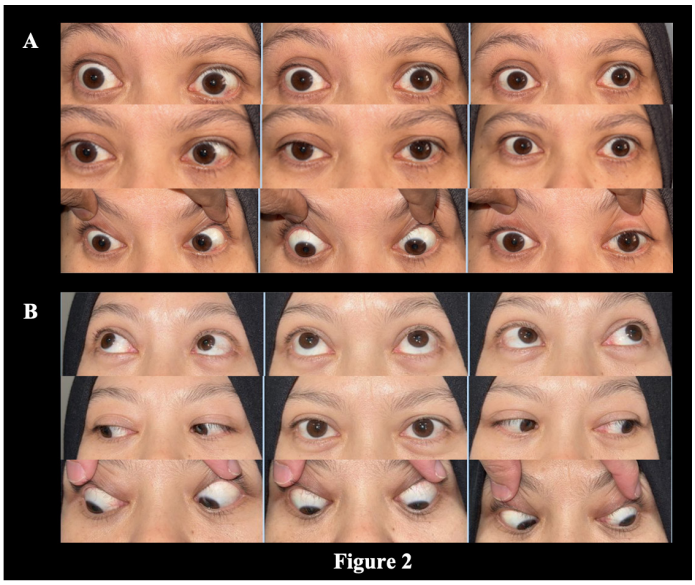

Figure 2. Nine-gaze photographs of Case 2. (A) Pre-treatment: complex ophthalmoplegia with frozen eye appearance. (B) Post-treatment: full recovery of ocular motility following intravenous immunoglobulin therapy.

sulfatide IgG may represent a modifying or ancillary antibody that influences the breadth or severity of the phenotype. Although the precise pathogenic importance of sulfatide IgG remains to be defined, the consistent clinical and cerebrospinal fluid features in both cases suggest that sulfatide positivity in MFS warrants attention rather than dismissal. A comparison between the clinical and immunopathological characteristics of anti-GQ1b and anti-sulfatide antibodies in MFS spectrum disorders is summarised in Table 1.

Table 1: Comparative features of anti-GQ1b and anti-Sulfatide antibodies in GBS/MFS

Feature	Anti-GQ1b IgG	Anti-Sulfatide IgG
Primary antigen	Ganglioside GQ1b (sialylated glycolipid)	Sulfatide (sulfated galactocerebroside)
Anatomical distribution	Highly expressed in cranial nerves III, IV, VI; dorsal root ganglia; cerebellum	Widely expressed in Schwann cell membranes, compact myelin, paranodes
Classical clinical associations	Miller Fisher syndrome; acute ophthalmoplegia without ataxia; Bickerstaff brainstem encephalitis; GBS overlap	Chronic neuropathies: CIDP, sensory ataxic neuropathy, paraproteinemic neuropathy
Acute presentations	Common and well-established (ophthalmoplegia, MFS, GBS variants)	Rare *emerging reports of acute ophthalmoplegia and GBS-like presentations
Prevalence in MFS	70–90% of cases	Very rare; sporadic case reports
Serological pattern	IgG dominant, highly disease-specific	IgM or IgG; less specific, broader neuropathy associations
Pathophysiology	Complement-mediated injury at cranial nerves and nodes of Ranvier	Binding to Schwann cell myelin → demyelination/nodal dysfunction
Response to IVIG	Excellent, rapid recovery	Limited data; emerging evidence suggests favourable outcomes
Prognosis	Excellent; full recovery in weeks to months	Variable; acute cases so far recover well with treatment

Sulfatide is a major glycolipid component of peripheral nerve myelin, particularly within Schwann cell membranes, where it plays a critical role in maintaining paranodal structure and axoglial integrity.[2,5,6] Antibodies directed against sulfatide have been implicated in demyelinating neuropathies, and conduction failure.[5] The presence of sulfatide IgG in both of our clinically classical MFS patients, isolated in one case and coexisting with anti-GQ1b IgG in the other—suggests that sulfatide-directed immune responses may contribute to the pathophysiology of MFS. It may act as a primary pathogenic target, contribute to a broader immune activation that is not mediated by GQ1b[4,6,7], or serve as a modifying antibody in dual-positive cases. Although the exact mechanism is unclear, the detection of sulfatide IgG in classical MFS underscores the importance of evaluating non-classical antibodies, particularly when anti-GQ1b serology is negative.

Both of our patients demonstrated favorable recovery to IVIG, consistent with expected outcomes in MFS. The similar therapeutic response observed in both patients, despite differing antibody profiles, reinforces the value of early immunotherapy irrespective of the specific serological pattern. IVIG remains the preferred treatment, while plasma exchange may be considered in severe cases or when IVIG is contraindicated or ineffective.[1] Corticosteroids, however, have not shown benefit in classical MFS and are not routinely recommended.

These cases expand the immunological understanding of MFS and highlight the potential diagnostic relevance of non-classical antibodies, particularly in GQ1b-seronegative presentations. Further studies are needed to determine the prevalence, specificity and prognostic implications of sulfatide IgG in MFS and to clarify whether it represents a primary pathogenic target, a secondary immune marker or a modulatory antibody within the broader landscape of immune-mediated cranial neuropathies.

In conclusion, sulfatide IgG may be detected in classical MFS presentations, either in isolation or alongside anti-GQ1b. Its presence in our cases supports broader immunological spectrum within MFS, particularly in GQ1b-seronegative cases. Early recognition and timely administration of IVIG remain essential for favorable outcomes.

DISCLOSURE

Ethics: Written informed consent for publication of clinical data and images was obtained from both patients.

Financial support: None

Conflict of interest: None

REFERENCES

1. Noioso CM, Bevilacqua L, Acerra GM, et al. Miller Fisher syndrome: an updated narrative review. Front Neurol 2023; 14:1250774. DOI: 10.3389/fneur.2023.1250774
2. Ji X, Zhu J, Li L, Yang X, Zhou S, Cao L. Anti-sulfatide antibody-related Guillain–Barré syndrome presenting with overlapping syndromes or severe pyramidal tract damage: a case report and literature review. Front Neurol 2024; 15:1360164. DOI: 10.3389/fneur.2024.1360164
3. Snyder LA, Rismondo V, Miller NR. The Fisher variant of Guillain-Barré syndrome (Fisher Syndrome). *J Clin Neurol* 2009; 29(4):312-4. DOI: 10.1097/WNO.0b013e3181c2514b
4. Roggenbuck D, Delmont E, Reinhold D, Schierack P, Conrad K, Boucraut J. Autoimmune peripheral neuropathies and contribution of antiganglioside/sulphatide autoantibody testing. Mediterr J Rheumatol 2020; 31(1):10-8. DOI: 10.31138/mjr.31.1.10
5. Roggenbuck JJ, Boucraut J, Delmont E, Conrad K, Roggenbuck D. Diagnostic insights into chronic-inflammatory demyelinating polyneuropathies. Ann Transl Med 2018; 6(17):337. DOI: 10.21037/atm.2018.07.34
6. Willison HJ. Anti-ganglioside antibodies in peripheral nerve pathology. Methods Mol Biol 2018:173-88. DOI: 10.1007/978-1-4939-8552-4_7
7. Noioso CM, Pecoraro A, Acerra GM, et al. Expanding horizons in anti-GQ1b antibody syndrome: Recognizing atypical and overlap forms. J Mental Health Dis 2025; 5(1):15-21. DOI: https://doi.org/10.33696/mentalhealth.5.031