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Miller Fisher Syndrome with Unilateral Ophthalmoplegia and White Matter Lesions: A Case Report and Review of the Literature

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Abstract **Case Report**

Miller Fisher syndrome (MFS) is a rare variant of Guillain–Barré syndrome classically characterized by the clinical triad of ophthalmoplegia, ataxia, and areflexia. It is an acute immune-mediated neuropathy that primarily affects the peripheral nervous system and is strongly associated with anti-GQ1b antibodies. The typical presentation involves rapidly progressive bilateral ophthalmoplegia; however, atypical or incomplete forms are increasingly recognized. These may include unilateral cranial nerve involvement or the absence of one or more components of the classical triad, which may complicate the diagnosis, particularly in the early stages. We report the case of a 43-year-old man who presented with acute binocular diplopia evolving over 15 days and associated with gait instability. Neurological examination revealed left-sided ptosis with impaired upward gaze, accompanied by diffuse areflexia and mild ataxia, while motor strength and sensory examination were normal. Brain magnetic resonance imaging demonstrated lesions in the right juxtacortical region and the left mesencephalic sulcus, initially raising suspicion of a central demyelinating disorder. Cerebrospinal fluid analysis showed albuminocytologic dissociation without pleocytosis or oligoclonal bands. Electroneuromyography demonstrated normal motor and sensory conduction studies with abolition of the H reflex. Serological testing revealed the presence of anti-GQ1b IgG antibodies, supporting the diagnosis of Miller Fisher syndrome. The patient was managed conservatively with close neurological monitoring and physiotherapy, leading to gradual clinical improvement and favorable recovery. Although MFS predominantly affects the peripheral nervous system, central nervous system involvement has occasionally been reported. Magnetic resonance imaging abnormalities are uncommon and usually involve the brainstem or cerebellum, whereas cerebral white matter lesions remain exceptionally rare. This case highlights an atypical presentation of Miller Fisher syndrome characterized by unilateral ophthalmoplegia associated with cerebral white matter lesions. It emphasizes the importance of careful clinicoradiological correlation and early serological testing for anti-GQ1b antibodies to avoid misdiagnosis and ensure appropriate management.

Keywords: Miller Fisher syndrome; anti-GQ1b antibodies; unilateral ophthalmoplegia; Guillain-Barré syndrome variant; diplopia; ataxia; areflexia; white matter lesions; brain MRI; peripheral neuropathy.

INTRODUCTION

Miller Fisher syndrome (MFS) is a rare variant of Guillain–Barré syndrome (GBS), classically characterized by the triad of ophthalmoplegia, ataxia, and areflexia [1]. It is an acute immune-mediated neuropathy that predominantly affects the peripheral nervous system and is strongly associated with anti-GQ1b antibodies [1]. The typical presentation involves rapidly progressive, bilateral ophthalmoplegia. However, accumulating evidence indicates that MFS may manifest in incomplete or atypical forms, including unilateral ophthalmoplegia, isolated cranial nerve palsies, or the absence of one or more components of the classical triad [1], [2]. Such presentations may obscure the diagnosis, especially in the early stages.

Brain MRI is usually normal in MFS. Nevertheless, occasional reports have documented central nervous system (CNS) abnormalities, most often involving the brainstem particularly the pons and medulla oblongata or the cerebellar peduncles, and more rarely the optic nerves [3]. In contrast, cerebral white matter involvement is exceedingly uncommon [4]. When present, these radiological findings may misleadingly suggest a primary demyelinating disorder of the CNS,

potentially delaying appropriate diagnosis and management.

Here, we describe a case of MFS revealed by unilateral ophthalmoplegia associated with cerebral white matter lesions, initially raising suspicion of a central demyelinating disease.

Case Presentation

A 43-year-old man, with no history of alcohol abuse, toxic exposure, or relevant personal or family medical conditions, was admitted for acute-onset binocular diplopia that had progressed over 15 days and was associated with gait instability. There was no history of preceding infection, recent vaccination, or systemic symptoms. Neurological examination revealed left-sided ptosis with impaired upward gaze **(Figure 1).** Pupillary reflexes were intact, and no additional involvement of the facial, bulbar, or other oculomotor nerves was noted. Motor strength was preserved in all four limbs, and deep tendon reflexes were diffusely absent. Sensory examination was normal. The patient initially consulted a neurologist who, given the unilateral nature of the ophthalmoplegia, requested brain imaging. Brain magnetic resonance imaging (MRI) demonstrated lesions in the right juxtacortical region and the left mesencephalic sulcus **(Figure 2).** Cerebrospinal fluid analysis revealed albuminocytologic dissociation, with elevated protein levels and a normal cell count no pleocytosis and no intrathecal synthesis of immunoglobulins, with negative oligoclonal bands. These results did not support a central inflammatory demyelinating process. A follow-up brain MRI has been planned to assess the evolution of the mesencephalic white matter abnormalities. Electroneuromyography demonstrated normal motor and sensory nerve conduction studies, with abolition of the H reflex **(Figure 3).** Serological testing for antiganglioside antibodies was positive for anti-GQ1b IgG, supporting the diagnosis of Miller Fisher syndrome with unilateral ophthalmoplegia.

Cerebrospinal fluid analysis showed no pleocytosis and no intrathecal synthesis of immunoglobulins, with negative oligoclonal bands. These results did not support a central inflammatory demyelinating process. A follow-up brain MRI has been planned to assess the evolution of the mesencephalic white matter abnormalities.The patient was managed conservatively with close neurological monitoring and physiotherapy, leading to a gradual and favorable clinical recovery.

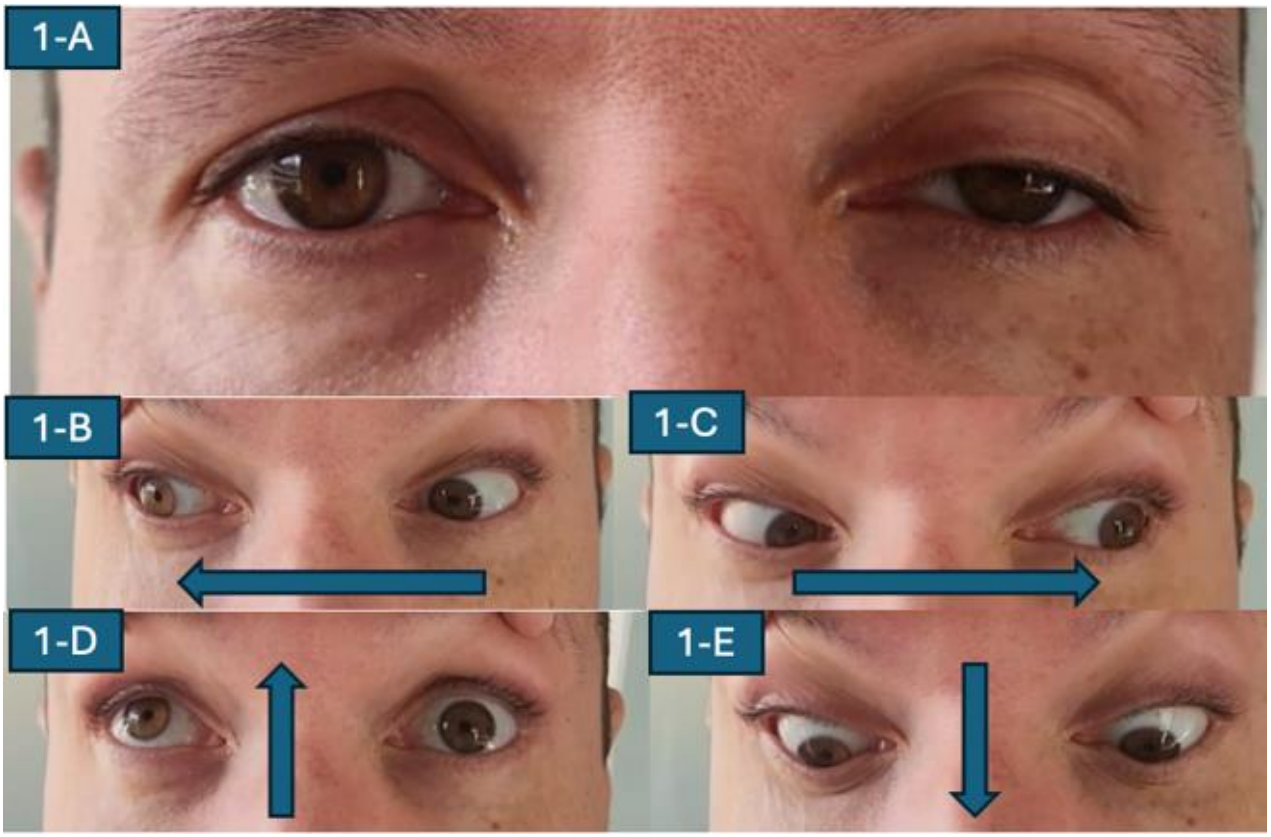

Figure 1: Examination of ocular movements in different gaze directions demonstrating impairment of ocular motility. A: In primary gaze, left ptosis is observed; Panels B–E demonstrate paralysis of upward gaze of the left eye on vertical and lateral gaze testing. The arrows indicate the directions of gaze examined during the clinical evaluation

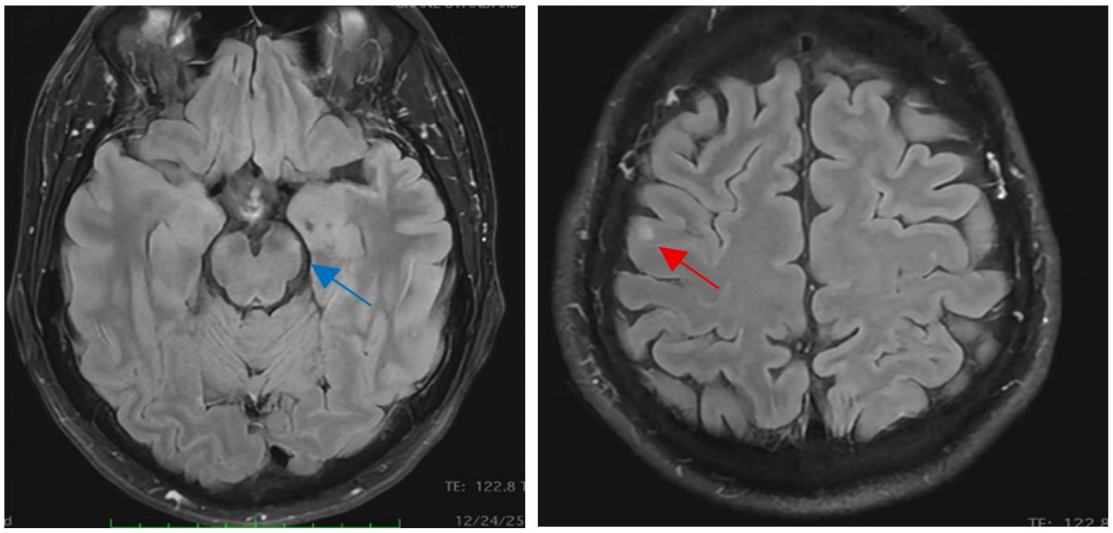

Figure 2: Brain MRI showing lesions located in the right juxtacortical region (red arrow) and in the left mesencephalic sulcus (blue arrow)

DISCUSSION

Classic Miller Fisher syndrome (MFS) is defined by the triad of ophthalmoplegia, ataxia, and areflexia; however, atypical presentations including unilateral involvement, isolated cranial nerve palsies, or incomplete forms are increasingly recognized [1], [2]. The pathogenesis of anti-GQ1b antibody syndromes is closely linked to antecedent infections through molecular mimicry [5]. Nevertheless, most patients have no identifiable preceding pathogen, suggesting that host-specific factors such as genetic susceptibility and variations in blood–nerve barrier integrity may significantly influence clinical expression. Unilateral external ophthalmoplegia has been reported in approximately 27–31% of cases and the most frequently published cases are summarized in **Table 1** [2]. The mechanisms underlying this lateralization remain incompletely understood but may involve heterogeneous ganglioside distribution or localized barrier disruption. These atypical presentations pose a diagnostic challenge, as isolated third nerve palsy frequently leads clinicians to initially consider vascular or compressive etiologies, potentially delaying accurate diagnosis.

Table 1 : summary of patients with unilateral ophthalmoplegia due to anti-GQ1b anti body syndrome.

Author	Age / Sex	Preceding illness	Ptosis	Neuro-ophthalmologic findings (EO)	Deep tendon reflex	Ataxia	CSF (cells / protein mg/dL)	MRI findings	Treatment	Prognosis
Susuki et al.	35/M	Cough, sore throat	Left	Left horizontal and vertical	Absent	+	Normal / 56	Normal	None	Recovery within 3 months
Vanden et al.	12/M	Asymptomatic Chlamydia pneumoniae	No	Left abduction	–	–	Normal / 97	Normal	None	Partial recovery within 1 month
Yuki et al.	26/F	Sore throat	No	Left abduction	–	–	0 / 24	Abducens nerve enhancement	NA	NA
Yuki et al.	32/M	None	No	Left abduction	Decreased	–	1 / 41	Normal	NA	NA
Yuki et al.	26/F	URI	No	Left abduction and adduction	Decreased	–	2 / 34	Normal	NA	NA
Yuki et al.	35/M	URI	No	Left abduction and downward gaze	–	–	3 / 51	Normal	NA	NA

Yuki et al.	18/F	Fever, headache	No	Right horizontal and vertical	Decreased	–	0 / 30	Normal	NA	NA
Mori et al.	47/M	Fever and cough	Left	Left adduction and vertical	–	–	Normal / 80	Normal	Prednisolone + IVIG	Recovery within 28 days
Smith et al.	32/M	Mild coryzal illness	Left	Left horizontal and vertical	Absent	+	Normal / normal	Normal	Conservative	Recovery within 5 weeks
Lee et al.	30/M	URI	No	Right adduction and vertical	NA	–	0 / 57	Normal	NA	Recovery within 3 months
Lee et al.	27/M	Diarrhea	No	Right vertical	NA	–	0 / 23	Normal	NA	Lost to follow-up
Lee et al.	53/M	URI	Left	Left adduction and vertical	NA	–	0 / 34	Normal	NA	Recovery within 3 months
Present case	43/M	None	Left	Left vertical gaze palsy	Absent	+	Normal / elevated protein	Normal	Conservative	Favorable recovery

MFS predominantly affects the peripheral nervous system (PNS), yet central nervous system (CNS) involvement has been reported in several cases. The brainstem and cerebellum are the most frequently affected sites, with occasional involvement of the optic nerves or spinocerebellar tracts [3]. Large series indicate that MRI-detectable CNS lesions are rare, occurring in approximately 1% of MFS patients and typically involving the midbrain, cerebellum, or middle cerebellar peduncle. Cerebral white matter involvement remains exceptional, with only isolated cases described (Table 2)[6]. The pathophysiology of CNS lesions in MFS remains speculative and may include antibody-mediated demyelination, shared antigenic targets between the peripheral and central nervous systems, or localized disruption of protective barriers [6] .Experimental and clinical data suggest that peripheral nerve antigens can induce CNS lesions and that demyelination may persist longer in the CNS than in the PNS due to less favorable conditions for axonal repair.

Table 2: Comparative summary of reported cases

References	**Present case**	**Xu and Liu [4]**	**Tezer et al. [3]**	**Echaniz-Laguna et al. [7]**	**Urushitani et al. [8]**
Age	43	37	54	42	50
Sex	M	M	M	F	M
Initial symptoms	Diplopia, left ptosis, unsteady gait, ataxia	Diplopia, unsteady gait, dizziness, left eyelid ptosis, distal numbness	Vertigo, diplopia, dysphagia, unsteadiness	Diplopia, unsteadiness, lower limb weakness	Diplopia, bilateral eyelid ptosis, ataxic gait, nausea, vomiting
Albumino-cytological dissociation	Yes	No	No	Yes	Yes
CSF OCB	Negative	Not reported	Negative	Negative	Not reported
NCS	abolition of the H reflex	Abnormal	Abnormal	Abnormal	Normal
Antibodies profile	Anti-GQ1b positive	Negative	Not tested	Negative	Not tested
MRI findings	Brain MRI showing lesions located in the right juxtacortical region and in the left mesencephalic sulcus	Multiple juxtacortical, subcortical and deep white matter lesions	Lesions in pons, medulla oblongata, cerebellar peduncle	Lesions in cerebral white matter, brainstem, cerebellum	Enhancing lesions in spinocerebellar tracts (lower medulla)
Treatment	IV methylprednisolone	IVIG (1 course)	IVIG (1 course) + acyclovir	IV methylprednisolone	IV methylprednisolone + plasma exchange
Outcome	Favorable recovery	Complete recovery after 60 days	Complete recovery after 6 months	Complete recovery after 40 days	Complete recovery after 3 months

In our case, a mesencephalic lesion was identified and could potentially account for the oculomotor deficit; however, the clinical pattern limited to unilateral ptosis and impaired upward gaze was more

anatomically consistent with involvement of the superior division of the oculomotor nerve at its orbital bifurcation. In the presence of concomitant ataxia and areflexia, this clinico-anatomical correlation favored a diagnosis of Miller Fisher syndrome rather than a primary central lesion, underscoring that neuroimaging abnormalities, while informative, should never supersede careful clinical examination.

Clinicians should therefore maintain a high index of suspicion for anti-GQ1b antibody syndromes in patients presenting with acute unilateral ophthalmoplegia, as early serological testing can facilitate prompt diagnosis and avoid unnecessary investigations[6]. Available evidence suggests that the prognosis of unilateral ophthalmoplegia associated with anti-GQ1b antibodies is generally favorable. Recovery occurs with both conservative management and immunotherapy, including corticosteroids or intravenous immunoglobulin, and spontaneous resolution is common [6].

CONCLUSION

This case highlights an atypical presentation of Miller Fisher syndrome manifested by unilateral ophthalmoplegia associated with uncommon cerebral MRI lesions. Although MFS is classically considered a peripheral immune-mediated neuropathy, this observation supports the notion that central nervous system abnormalities may occasionally occur and should not exclude the diagnosis when the clinical picture is suggestive. Careful clinico-radiological correlation remains crucial to avoid misdiagnosis and to ensure appropriate management. Further studies are needed to better elucidate the mechanisms underlying atypical neuroimaging findings and clinical lateralization in anti-GQ1b syndromes.

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