Bilateral mydriasis as the first manifestation of Miller Fisher syndrome

Rathnasiri KADV¹*, Senadeera Y¹, Karunathilaka S¹, Wijerathne A¹, Premasiri L¹

Abstract

Miller Fisher Syndrome (MFS) is a rare variant of Guillain-Barré Syndrome (GBS), characterised by a unique clinical triad of ophthalmoplegia, ataxia, and areflexia. MFS, which was first described in 1956 by Charles Miller Fisher, is frequently preceded by an infection, usually respiratory or gastrointestinal, and is believed to be triggered by an autoimmune reaction targeting peripheral nervous system components. However the MFS is further categorised into incomplete forms which can be present without the classical triad, such as acute ophthalmpopaesis, acute ataxic neuropathy, acute ptosis and acute mydriasis. We report a case of a 50-year-old man presenting with dilated and unresponsive pupils, which progressed rapidly to ophthalmoplegia, ataxia, and areflexia. Given the clinical history supported by the cyto-protein dissociation in cerebrospinal fluid, the patient was diagnosed to have MFS and successfully treated with intravenous immunoglobulin. This case underscores the importance of recognising atypical features of MFS, such as primary mydriasis, and highlights the variable clinical spectrum within the syndrome. Clinicians should maintain a high index of suspicion for MFS, particularly when faced with unusual neurological presentations, to ensure timely intervention and optimal patient outcomes.

Keywords: Miller Fisher syndrome, atypical MFS, bilateral mydriasis, Guillain-Barré syndrome, ophthalmoplegia

Introduction

Miller Fisher Syndrome (MFS) is a rare neurological disorder characterised by a distinct constellation of symptoms, including ophthalmoplegia, ataxia, and areflexia. First described by Charles Miller Fisher in 1956(1), MFS represents a variant of Guillain-Barré Syndrome (GBS), exhibiting unique clinical features and diagnostic challenges. The atypical variants of MFS include isolated ophthalmoplegia, ptosis, pupillary abnormalities, ataxia, etc.(2) The pathogenesis of MFS is thought to involve an autoimmune reaction targeting peripheral nerve components, often triggered by a preceding infections.(3) Despite advancements in our understanding of MFS, its variable clinical presentation and atypical features continue to pose diagnostic dilemmas for clinicians.

Case presentation

A 50-year-old man presented to the medical ward complaining of progressively worsening blurred vision and photophobia over the course of one day. Notably, he denied any symptoms of double vision. Upon examination, his pupils were dilated to 6 mm and showed poor response to both light and near stimuli. Fundal examination did not reveal any signs of papilledema, and his visual acuity was normal. Extraocular movements were normal. There was no evidence of any limb muscle weakness. However his deep tendon reflexes were diminished. He denied any recent drug ingestion, ophthalmological procedures or snakebite. There was no history of preceding respiratory tract infections or acute gastroenteritis. The patient was admitted for close monitoring.

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On the following day, he reported diplopia, and clinical examination revealed bilateral abduction limitations. Within a day, this condition rapidly progressed to complete ophthalmoplegia. Additionally, persistent mydriasis was noted, accompanied by the absence of both light and accommodation reflexes. Although the patient denied lower limb weakness, deep tendon reflexes in both upper and lower limbs were diminished. Furthermore, he complained of numbness in his hands without any associated sensory disturbances, along with slight ataxia in the absence of other cerebellar symptoms.

Considering the clinical history and presentation, Miller Fisher syndrome was considered as a potential diagnosis. Neuroimaging in the form of NCCT brain and MRI brain scans was performed to exclude intracranial space-occupying lesions. Treatment was initiated with intravenous immunoglobulin (IVIG) administration at a dose of 0.4g/kg/day. Nerve conduction studies yielded normal findings apart from subtle nonspecific f wave changes, and cerebrospinal fluid analysis revealed cyto-protein dissociation, characterised by an elevated protein level of 120 mg/dL with no pleocytosis. However, anti-GQ1b antibodies were not tested due to unavailability.

The patient’s condition significantly improved following IVIG therapy, supporting the diagnosis of Miller Fisher syndrome.

### Discussion

Dilated and unresponsive pupils may occur due to either the paralysis of parasympathetic function or the stimulation of sympathetic activity. Paralysis of the parasympathetic system is often triggered by anticholinergic medications such as scopolamine or atropine, or by conditions such as oculomotor nerve palsy resulting from brain stem issues, injury, vascular events, or localised nerve damage.(4) Conversely, sympathetic stimulation can arise from the use of sympathomimetic drugs like cocaine or amphetamines.

On presentation, our patient only had bilateral mydriasis and diminished reflexes. He denied any drug ingestion. So he was kept under observation. With the development of ophthalmoplegia associated with areflexia and ataxia, we narrowed down the differential diagnoses to Miller Fisher syndrome.

MFS is a rare variant of Guillain-Barré Syndrome (GBS), characterised by a unique clinical triad of ophthalmoplegia, ataxia, and areflexia, first recognized by James Collier in 1932. Later, it was described in 1956 by Charles Miller Fisher as a possible variant of Guillain-Barré syndrome.(1)

In the classic presentation of MFS, patients typically experience ophthalmoplegia, ataxia and areflexia or hyporeflexia. Limb weakness and hypersomnolence are typically absent. However incomplete forms of MFS may lack certain features. So the patients can

### Table 1 - Subtypes of Miller Fisher syndrome according to New diagnostic classification GBS classification group published in Vol. 10, Nature Reviews Neurology 2014

<table>
<thead>
<tr>
<th>Category</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classic Miller Fisher syndrome</td>
<td>Ophthalmoplegia, ataxia and areflexia/hyporeflexia, absence of limb weakness and hypersomnolence</td>
</tr>
<tr>
<td>Acute ophthalmoparesis</td>
<td>Ophthalmoplegia</td>
</tr>
<tr>
<td>Acute ataxic neuropathy</td>
<td>Isolated ataxia</td>
</tr>
<tr>
<td>Acute ptosis</td>
<td>Palsy without ophthalmoplegia or weakness</td>
</tr>
<tr>
<td>Acute mydriasis</td>
<td>Paralytic mydriasis</td>
</tr>
<tr>
<td>Bickerstaff brainstem encephalitis</td>
<td>Hypersomnolence, ophthalmoplegia and ataxia</td>
</tr>
<tr>
<td>Acute ataxic hypersomnolence</td>
<td>Hypersomnolence and ataxia</td>
</tr>
</tbody>
</table>
present with isolated ophthalmoparesis, acute ataxic neuropathy, acute ptosis and acute mydriasis, etc. (2) Subtypes of MFS with their clinical features are summarised in table 1. The presence of anti-GQ1b IgG antibodies would support the diagnosis.

The underlying pathophysiological mechanism of Miller Fisher syndrome is thought to be molecular mimicry. The immune system's activation of lipo-oligosaccharides (LOS) found on the membranes of some pathogens, most notably Campylobacter jejuni, which resemble gangliosides (GQ1b, GM1, and GD1a), would result in the formation of autoantibodies. If the antibody generated is GM1 or GD1b, the classic form of GBS with acute motor axonal neuropathy is produced, whereas GQ1b causes MFS. (3) GQ1b is a ganglioside found in paranodal myelin, namely in oculomotor nerves (III, IV and VI cranial nerves), dorsal root ganglia (DRG), and neuromuscular spindle fibres. (3) The location of the ganglioside explains the classical triad in MFS. (3) Serum IgG antibodies to GQ1b are commonly associated with Guillain-Barré Syndrome (GBS), whether the presentation is typical or atypical. These antibodies are particularly useful in diagnosing MFS, with a sensitivity of 85 to 90 percent. (5)

Tonic pupil in MFS was first described in 1977. (6) Later comprehensive literature reviews have described the association of fixed dilated pupils in cases of MFS. (7) Fixed dilated pupils are a result of involvement of the preganglionic parasympathetic pathway from Edinger-Westphal nucleus to the ciliary ganglion. Even though the exact pathophysiology is not known it is thought to be due to damage of the ciliary ganglion or short ciliary nerves caused by anti-GQ1b IgG antibodies. (6)

**Conclusion**

In summary, this case underscores the variable clinical presentation of MFS and the importance of recognising atypical features, such as primary mydriasis, in facilitating timely diagnosis and management.

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**References**


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