# A case of ocular myasthenia gravis and Miller-Fisher syndrome

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## INTRODUCTION

Ophthalmoplegia is a common manifestation of myasthenia gravis (MG). The clinical course of MG may fluctuate but other concurrent disorders can also result in deterioration of ocular palsy, such as thyroid disease and febrile illnesses. The authors report a patient with a much rarer problem.

## DISCUSSION

The chance of Miller-Fisher syndrome (MFS) and MG occuring in the same patient is extremely small, but this case illustrates that an unrelated illness might produce clinical deterioration masquerading as worsening of a chronic condition.

Characterized by ophthalmoplegia, ataxia, and areflexia (Miller-Fisher, 1956), MFS is considered a rare clinical variant of Guillain–Barré syndrome (GBS) accounting for no more than 10% of cases. In series from Japan (Mori et al, 2001) and Taiwan (Lyu et al, 1997), and from the authors' observation (unpublished data, 2001), MFS is more common in Orientals at around 20% of all GBS cases. Within its spectrum are:

- Pure MFS, defined as the classical triad in the absence of significant limb weakness
- Acute ophthalmoparesis, a post-infectious syndrome characterized by ophthalmoplegia without ataxia
- An overlapping MFS and GBS with limb weakness on top of predominating ocular features.

Bickerstaff's brainstem encephalopathy (BBE), which consists of ophthalmoplegia, ataxia, and central involvement with pyramidal signs or impairment of consciousness, is also regarded as a variant of MFS (Newsom-Davies, 1997). MFS usually runs a benign clinical course; almost all patients recover to normal functional status (Mori et al, 2001).

Antiganglioside antibodies are associated with GBS. Where clinical usefulness is concerned, anti-GQ1b antibody is particularly relevant because of its exceptional sensitivity and specificity for MFS. Mori et al (2001) reported the largest series of MFS, and anti-GQ1b antibody was positive in 89% of tested cases. It is undetected in other neurological or autoimmune diseases, including MG. Besides MFS, anti-GQ1b antibody is also found in GBS with ophthalmoplegia, acute ophthalmoparesis, and BBE. It seems to be an exclusive marker for acute inflammatory polyradiculoneuropathies or related conditions with ocular palsies.

These disease entities, now collectively termed 'anti-GQ1b immounoglobulin-G antibody syndrome' (Odaka et al, 2001), are believed to share a common immune aetiology with anti-GQ1b antibody assuming a central pathogenic role. Nevertheless, this is still speculative and the exact disease mechanism is not fully understood. GQ1b ganglioside concentrates at the paranodal regions of the ocular motor nerves (Chiba et al, 1993), but direct antibody binding to GQ1b epitopes cannot explain all the features of these syndromes.

In-vitro experiments using mouse hemidiaphragm demonstrated that neuromuscular transmission blockade can be induced by acute-phase MFS sera,

## CASE REPORT

A 40-year-old Chinese man with myasthenia gravis presented to the emergency department with worsening of ocular symptoms and the authors were asked for an opinion. He first presented 7 years ago with diplopia and ptosis that were responsive to edrophonium. His acetylcholine receptor antibody titre was elevated at 0.8 optical density unit (ODU) (laboratory reference <0.43 ODU), although repetitive nerve stimulation study did not produce a significant motor potential decrement. He improved with regular pyridostigmine (40 mg three times a day) but there was still mild ptosis and limited abduction of his left eye.

His condition did not change in the last few years. For the current presentation, he had progressive deterioration of ocular movements over 1 week. Physical examination showed complete ophthalmoplegia bilaterally, partial ptosis of the left eye and absent pupillary light reflex in the right. Intravenous edrophonium 10 mg produced minimal improvement in right eye abduction.

On further questioning, he also complained of numbness of his extremities, difficulties in fine hand functions, and unsteadiness while walking. He recalled a flu-like illness 2 weeks before the neurological symptoms. All his tendon reflexes were unobtainable and he had an ataxic gait. There was no demonstrable limb or facial weakness. Cerebrospinal fluid analysis showed increased protein concentration at 1.33 g/litre (reference range 0.12–0.6 g/litre) with total cell count of $<1\times10^6$/litre. Anti-GQ1b antibody level was elevated at 43 enzyme immunoassay (EIA) Units (reference range <10 EIA). Nerve conduction studies only showed marginal reduction of F-wave persistence in the upper limbs. Magnetic resonance imaging of his brain revealed no abnormalities.

Miller-Fisher syndrome (MFS) was diagnosed. He was treated with three sessions of plasmapheresis. His symptoms started to improve over the next week and he subsequently made a full clinical recovery. Moreover, he was completely free from his myasthenia gravis-related ophthalmoplegia in the following 2 months. Pyridostigmine was later recommenced when his baseline symptoms returned.

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IgG, or monoclonal anti-GQ1b immounoglobulin-M (Roberts et al, 1994; Buchwald et al, 2001). The relevance of these findings in Miller-Fisher and related syndromes is yet to be determined. **HM**


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