

Miller Fisher Syndrome - A Case Report

Miguel Pires, Joana Monteiro, Sonia Chan, Luisa Pinto

Centro Hospitalar de Leiria

Introduction

Miller Fisher Syndrome (MFS) is a rare variant of GBS (Guillain-Barre Syndrome). It involves both adults and children and its mostly a clinical diagnosis. It comprises a classic triad of ophthalmoplegia, ataxia and areflexia which all develop over a period of few days. This triad was first described by James Collier in 1932 and it was subsequently reported as a variant of GBS by Charles Miller Fisher in three clinical cases in 1956¹.

MFS is a geographically variable variant of GBS observed in about 1% to 5% of all GBS cases in Western countries, yet up to 19% and 25% in Taiwan and Japan respectively². There is a male predominance at a ratio of 2:1 and a mean age of 43.6 years, although cases of MFS have been reported in all age groups².

Unlike the classic ascending weakness/paralysis that is characteristic of GBS, neurological deficits follow a top down pattern in MFS, starting with diplopia in the eyes; caused by external ophthalmoplegia—the most common presenting symptoms^{2,4}. In a clinical series of 50 consecutive cases of MFS in Japan it was discovered that 78% of cases presented initially with diplopia, 46% with ataxia, and 34% with both. Other abnormalities reported, albeit less frequently, were limb dysesthesia; blepharoptosis; face, bulbar, and pupillary palsies; mild (grade 4) motor weakness; and micturition disturbance².

As in GBS an antecedent infectious illness can be identified. Upper respiratory infection is the most commonly described prodromal entity followed by gastrointestinal illness³. *Campylobacter jejuni* and *Haemophilus influenzae* have been the most commonly implicated pathogens. Other pathogens, including *Mycoplasma pneumoniae* and *Cytomegalovirus*, have been associated too.

An acute onset is typical of MFS, beginning with neurologic symptoms approximately 8-10 days (range of 1-30) following the antecedent illness^{2,5}. The disease then progresses until a clinical nadir is reached approximately 6 days (range of 2-21) after the initial neurologic symptoms². The recovery period is marked by gradual improvement and often resolution of symptoms; although rarely, serious complications such as respiratory failure or cardiac arrhythmia (that are common in GBS, with 30% of cases requiring ventilator support) have been reported⁵.

The following case presents key clinical features of MFS. Familiarity with this rare syndrome will clue the clinician to consider MFS in patients presenting with areflexia, ataxia, and ophthalmic symptom.

Keywords: Areflexia. Ataxia. Guillain-Barré syndrome. Miller Fisher. Ophthalmoplegia.

Palabras clave: Arreflexia. Ataxia. Síndrome de Guillain-Barré. Miller Fisher. Oftalmoplejía.

Case report

Male, 55-year-old, presented to the emergency department (ED) with headache, difficulty in vision and unsteadiness in walking for 5 days. There were no complaints of unconsciousness, convulsion, speech problems, hearing defects, vertigo, tinnitus, dysphagia or hoarseness of voice. There were no complaints of motor weakness elsewhere in the body, sensory symptoms or bowel or bladder symptom.

He had a history of bipolar disease and alcoholism, but he was not taking any medication.

Upon physical examination hypertension was present (174/130 mmHg). Other vital signs were in the normal range. The patient had normal higher function. Neurological examination revealed marked ophthalmoplegia with severe decreased movements on lateral, medial and upward gaze. The pupils were bilaterally equal, semi-dilated and not reacting to light or accommodation. There was no ptosis. Decreased visual acuity in both eyes (Right eye 20/50 and Left eye 20/10 on Snellen's chart). The visual field and fundus both were normal. Rest of the cranial nerves were normal to examination. A global areflexia was present, and muscle strengths testing was normal. Sensory examination was normal. The finger nose test and the knee heel test were normal. Dysidiadochokinesia was absent. Romberg's sign was negative. The gait was ataxic and broad based but possible with a cane.

Patient was admitted for further investigation and treatment.

On the second day of hospital admission the patient developed bilateral ptosis and eye movements were restricted in all direction. No change in muscle strength but patient was unable to walk.

Laboratory testing revealed normal complete blood count, comprehensive metabolic panel, thyroid stimulating hormone, and cardiac markers. Urine toxicology screens were negative for common substances of abuse. There was no elevation in erythrocyte sedimentation rate, C-reactive protein, or creatine kinase; HIV and RPR serologies were negative. On note, laboratory investigations for some of the more commonly implicated pathogens in MFS (*Campylobacter jejuni*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, or *cytomegalovirus*) were not undertaken. A lumbar puncture was performed and revealed cytoalbuminologic dissociation in the CSF with normal cell counts and an elevated protein count of 131.0 mg/dL.

Nerve Conduction Velocity (NCV) study showed mixed demyelinating (both motor and sensory) polyneuropathy, with an H-reflex detected. Contrast enhanced brain magnetic resonance imaging did not reveal areas of contrast enhancement or parenchymal abnormalities. Based on clinical presentation of ataxia and areflexia, and history of alcohol abuse, there was a concern for Wernicke's encephalopathy and the patient was started on intravenous thiamine (500mg every 8 hours). A rapid response was expected; however, this was not observed. The other two main competing diagnoses were an atypical presentation of GBS or MFS. Tests were ordered to look for antibo-

Correspondencia: joanasofiamonteiro@gmail.com

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dies that would support or refute each of these diagnoses. Meanwhile, decisions to start further treatment were made because the patient didn't improve. The intravenous thiamine was discontinued, and the patient was treated with intravenous immune globulin (IVIg) for seven days to treat for possible MFS. Serum antibody test results were positive for GQ1b IgG and the diagnosis of MFS was confirmed. The nadir of the patient's symptoms was reached by day seven. Physical, occupational, and speech therapy specialists were working daily with the patient and he began to exhibit steady improvement. He was able to walk without assistance by the tenth hospital day and on the twelfth day he was discharged.

Discussion

MFS is known for the characteristic triad of ophthalmoplegia, ataxia, and areflexia. It is considered a variant of GBS, which is also known as acute idiopathic neuritis. An increasing body of evidence suggests that a rather wide range of neurological features may be present and significant overlap exists with other forms of GBS.

Berlit et al reviewed 223 cases of MFS: the first symptom was diplopia (38.6%) or ataxia (20.6%). Areflexia was present in 81.6% of cases. The cranial nerves other than III were involved in 127 cases (56.9%): cranial nerves VII (45.7%), IX and X (39.9%), and XII (13%) were involved. In 53 cases, tetraparesis occurred. Elevated CSF protein was present in 134 patients (64.4%). CSF findings were normal in 56 patients, and 18 patients had mild pleocytosis. The prognosis of MFS was good. Recovery occurred after a mean time of 10.1 weeks. Residual symptoms were present in 74 cases (33.2%), recurrence of MFS was reported in 7 patients, and 8 patients died⁶. Fross et al reported 10 patients with typical MFS electrophysiological abnormalities characteristic of axonal neuropathy or neuronopathy with predominant sensory nerve changes in the limbs and motor damage in the cranial nerves⁷.

The differential diagnosis of MFS includes Wernicke's encephalopathy and brainstem encephalitis, but these are associated with altered mental status. In addition, patients with Wernicke's encephalopathy usually have nystagmus, a feature not associated with MFS. Other entities to consider in the differential diagnosis of MFS are myasthenia gravis and other neuromuscular junction disorders.

Appropriate laboratory and clinical electrophysiological testing with repetitive nerve stimulation helps to differentiate MFS from a neuromuscular junction disorder⁸. The combination of absent or reduced sensory responses on clinical electrophysiology testing and elevated protein with a normal white blood

cell in CSF could lead to the diagnosis of MFS⁹. The diagnosis could be confirmed by positive anti-GQ1b antibody testing with a high level of sensitivity (well over 90% of patients with MFS have this antibody) and specificity. However, radiological imaging were unremarkable in most cases of MFS, lesions in the brainstem and spinocerebellar tracts had been reported in few patients¹⁰.

MFS is generally regarded as a self-limiting benign condition. All of 28 untreated MFS patients in the largest published case series returned to normal activities 6 months after the neurological onset. The respective median (range) periods between neurological onset and the disappearance of ataxia and ophthalmoplegia were reported as 32 (8-271) and 88 (29-165) days. However, cases progressing to respiratory failure and requiring mechanical ventilation have also been described, particularly in children. Other serious complications reported include coma, ballism, cardiomyopathy from dysautonomia, lactic acidosis, and pain⁵.

In conclusion, MFS is a clinical diagnosis with a classic triad (ataxia, areflexia and ophthalmoplegia) and the early recognition improves the outcome of this highly limiting patients' condition.

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