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## Case report

# Progressive subacute Miller-Fisher syndrome successfully treated with plasmapheresis

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## ABSTRACT

**Background:** Miller-Fisher Syndrome (MFS) is a rare acute polyneuropathy composed of the clinical triad of ataxia, areflexia and ophthalmoplegia, with a monophasic, self-limited course and spontaneous improvement.

**Case report:** The authors present a 65-year-old man with Miller-Fisher syndrome consisting of bilateral ophthalmoplegia, trigeminal and facial nerve palsy, mild ataxia and peripheral neuropathy. The disease had a progressive, subacute course within 3 months. A high titer of anti-GQ1b antibodies was detected. As a result of plasmapheresis, complete recovery was achieved.

**Conclusions:** The presented case was atypical in its clinical course and treatment. It could support the theory of the continuity between MFS, Bickerstaff brainstem encephalitis (BBE), and Guillain-Barré syndrome (GBS).

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## 1. Introduction

Miller-Fisher Syndrome (MFS) is a rare acute polyneuropathy composed of the clinical triad of ataxia, areflexia and ophthalmoplegia. The presence anti-ganglioside GQ1b (anti-GQ1b) antibodies in serum is a powerful diagnostic marker of MFS. This syndrome is typically characterized by acute onset, a monophasic, and self-limited course with spontaneous improvement. Recovery from MFS is good, usually without any residual deficits [1,2].

The authors present an unusual MFS case with a subacute, and progressive course, with polycranial nerve palsy. Clinical

recovery with a significant lowering of anti-GQ1b antibody titer was achieved after plasmapheresis.

## 2. Case report

A 65-year-old man, without any significant medical history, developed diplopia, left trigeminal nerve palsy, and a mild headache one month after an upper respiratory infection. Brain CT and MRI with contrast were within normal limits. Two months later progressive ocular disturbances with right ptosis, severe headache in the right frontal area which was not responsive to analgetics, and an unsteady gait occurred. Neurological examination revealed hyperaesthesia in the first

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branch of the right trigeminal nerve, bilateral ophthalmoplegia with minimal pupil reaction to light, right ptosis, mild ataxia and diminished tendon reflexes, ataxic gait on the wide base. Three weeks later he developed left peripheral-type facial palsy. All the time he had a severe headache, burning and itching of the face, sleep disturbance, anxiety and mild agitation.

The immunological study was positive for anti-GQ1b antibodies (1:1280, normal value < 1:160). Serologic analysis of antibodies against other gangliosides (GM1, GD1b), auto-antibodies (ANCA, ANA, PANCA, CANCA, cardiolipin, anti-DNA, ENA,  $\beta$ 2-glycoprotein), neuro-oncological antibodies, anti-GAD, anti-MAG, anti-myelin, anti-unmyelinated nerve fibers, and anti-neuroendothelium were negative. Borrelia burgdorferi, hepatitis viruses C and B, HIV and VDRL tests were also negative. In the cerebrospinal fluid a mild protein level elevation was seen with a normal number of cells.

A nerve conduction study showed a slight, axonal, mainly sensory neuropathy. Neurographic examination of the left facial nerve revealed lowering of the amplitude with slight prolongation of the conduction time (frontal muscle – 0.35 ms/cm, orbicularis oculi muscle – 0.37 ms/cm, orbicularis oris muscle – 0.37 ms/cm). EMG from orbicularis oculi muscle showed neurogenic changes. A repetitive nerve stimulation test was negative. An EEG showed diffuse slow activity, single delta waves with a slightly higher amplitude over both temporo-parietal areas. The latencies of left BAEP's waves III and V, and inter-peak latencies I-III and I-V were delayed. A brain MRI with gadolinium revealed enhancement of the left facial nerve with no brainstem abnormalities.

The patient underwent five sessions of plasma exchange. After this treatment the clinical improvement was observed. Three months later the patient had no neurological deficit, EEG was normal, and the anti-GQ1b antibody titer was significantly lower (1:320).

### 3. Discussion

An analysis of MFS cases showed that its occurrence is seasonal, predominating in spring (March to May), in most cases after respiratory symptoms (76%), and the median time of improvement is 4–6 days (range 2–21 days) after the neurological onset [1–3]. In our patient the beginning of the disease was in April, a month after the upper respiratory infection, but his neurological symptoms progressed within three months. He had a mild headache, left oculomotor and trigeminal nerve palsy. Two months later he developed a severe headache, unstable gait, bilateral ophthalmoplegia, and one month later left facial nerve palsy occurred. In MFS patients the median interval between neurological onset and the beginning of recovery, usually without immunological treatment, is about 12–15 days [1,2]. In our patient complete neurological improvement was observed more than three months after the onset, and exclusively after the immunological treatment. According to Mori et al. [2], plasmapheresis has no beneficial effect in MFS patients, it even worsens facial palsy.

Headache is not a common symptom in MFS. Friedman and Potts [4] suggested that headache might be caused by antibody-mediated effects on the trigemino-vascular pain

pathway. The hyperaesthesia, burning and itching of the face could indicate trigeminal nerve impairment.

In most MFS cases neuro-images are unremarkable. In some patients lesions of the brainstem, dorsal root ganglia, lumbosacral roots and the posterior column of the spinal cord were seen in MRI. In a few cases trochlear, abducens and oculomotor nerve enhancement has been found in MR scans [2,5]. We observed a similar enhancement of the left facial nerve. Although we did not reveal any brain changes in MRI, mild behavioral disorders, abnormal EEG and BAEP could indicate central nervous system involvement in our patient.

Our findings could support the hypothesis of the continuity between MFS and BBE. The presence of anti-GQ1b antibody syndrome is proposed to associate MFS, BBE and GBS, known as an “anti-GQ1b antibody syndrome” [1–3].

The presented case is atypical because of its subacute and progressive course, and improvement exclusively after the immunological treatment. The clinical course, and the result of diagnostics, could support the theory of the continuity between MFS, BBE, and GBS.

### Conflict of interest

None declared.

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None declared.

### Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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