CASE REPORT

Anti-GQ1b-Negative Miller Fisher Syndrome with Acute Areflexic Mydriasis and Cholinergic Supersensitivity

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ABSTRACT

Miller Fisher syndrome is a rare variant of Guillain-Barré syndrome and it is characterised by ophthalmoplegia, ataxia, and areflexia. Pupillomotor involvement occurs in approximately half of the patients with the disorder. The authors report a patient with acute areflexic mydriasis, external ophthalmoplegia, areflexia, and ataxia. Although the pupils were unreactive to light and near stimuli, administration of 0.1% pilocarpine resulted in marked miosis, suggesting cholinergic supersensitivity. Antibodies against GM1, GD1b, and GQ1b were negative. This is the first report of acute areflexic mydriasis with cholinergic supersensitivity in anti-GQ1b-negative Miller Fisher syndrome.

KEYWORDS: anti-GQ1b; cholinergic supersensitivity; Miller Fisher syndrome; mydriasis

INTRODUCTION

Acute onset of ophthalmoplegia, ataxia, and areflexia characterises Miller Fisher syndrome (MFS), an immune-mediated neuropathy associated with anti-GQ1b antibody.¹ Internal ophthalmoplegia develops in almost half of the patients with MFS.^{1,2} Pupillary response to light and near stimuli varies and light-near dissociation and cholinergic supersensitivity may be found.^{1,3,4}

We report a patient with acute bilateral mydriasis, unresponsiveness to light and accommodative stimuli, and cholinergic supersensitivity, associated with external ophthalmoplegia, areflexia, and ataxia. An informed consent was obtained from the patient.

CASE REPORT

A 36-year-old woman presented with a 5-day history of acute onset of double vision, photophobia, and

gait unsteadiness. The patient denied any antecedent infection or vaccination.

On admission, neuro-ophthalmological examination revealed symmetrically mydriatic pupils (6.0 mm OD and 6.0 mm OS in room light), unresponsive to light and near stimuli (Figure 1). Accommodation was impaired. Ocular movements of both eyes were limited in all directions except downward gaze (Figure 2). Funduscopic examination revealed normal findings. An eye drop test was performed with 0.1% pilocarpine. The administration of the solution to the right eye induced marked miosis (Figure 3). Vermiform movements of the pupils were not observed.

Systemic neurological examination showed that the strength of the facial muscles as well as the upper and the lower limbs muscles was normal. A gait ataxia was present. Deep tendon reflexes were absent with bilateral flexor plantar responses. There was no evidence on history nor examination of involvement of sensory, respiratory, and autonomic systems nor of sphincter functions.

Nerve conduction studies revealed impersistence or absence of the median, ulnar, peroneal, and the posterior tibial F waves as well as the posterior tibial H reflexes. Motor and sensory nerve conduction studies were within normal limits. The diagnosis of botulism was excluded by electrophysiological studies.

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There were no abnormal findings in routine laboratory data, including complete blood cell count, C-reactive protein, urine analysis, serum levels of glucose, electrolytes, liver enzymes, urea, creatinine, protein, calcium, magnesium, phosphate, thiamin, vitamin B12, folate, and thyroid hormones. Erythrocyte sedimentation rate was elevated (64 mm/h). Tests for antinuclear antibody, complements 3 and 4, and rheumatoid factor were either negative or within normal limits. Serological tests were negative for HIV, syphilis, and hepatitis B and C viruses. Cerebrospinal fluid (CSF) analysis showed normal glucose level, increased level of total protein (205 mg/dL, normal range 10–40 mg/dL), and 16/mm³ mononuclear leucocytes. CSF culture and cytology revealed no pathological findings. Electrocardiogram and chest X-ray were normal. Magnetic resonance (MR) images of the brain and the orbits and brain MR angiography were normal. Stool analysis for *Campylobacter jejuni* was negative. Serological testing for anti-GQ1b, GM1, and GD1b antibodies was negative.

The patient was treated with 0.4 g/kg/day intravenous immunoglobulin over 5 days. After the treatment, the diameter of the pupils decreased to 3 mm in room light and the pupils began to react slowly to light and near stimuli without segmental movements. During hospitalisation, ocular movements and ataxia also substantially improved, but in a more gradual fashion. The

patient was followed up in our outpatient clinic after 4 weeks of hospitalisation. Six weeks after disease onset, the patient became symptom-free. At that time, neurological examination showed no pathological findings except for slightly diminished deep tendon reflexes. A second CSF analysis revealed a slightly increased protein level (47 mg/dL), normal glucose level, and no cells. During 6 months of observation, no relapses were observed.

DISCUSSION

The clinical manifestations of our patient were suggestive of the diagnosis of MFS, although she reported no antecedent infection. Table 1 shows the differential diagnosis of the patient. Brainstem diseases and botulism, which may mimic the clinical picture, were excluded by neuroimaging and electrophysiological studies. Electrodiagnostic evidence of polyradiculopathy and elevation of protein level in the CSF supported the diagnosis. Although there was a mild pleocytosis in the CSF, extensive investigations regarding infectious disorders including syphilis and human immunodeficiency virus (HIV), revealed no abnormal findings. Rauschka et al.⁵ reported that although the typical finding is albuminocytological dissociation with no or few (i.e., <5 cells/mm³) leucocytes in the CSF, with exclusion of mimicking infectious or malignant disorders in a typical clinical context, pleocytosis is not a criteria of exclusion in Guillain-Barré syndrome.

Ophthalmoplegia is the most characteristic finding in MFS.^{1,2,6} In addition to the involvement of the extraocular muscles, internal ophthalmoplegia develops in approximately 50% of patients with MFS.^{1,2,7} In our patient, pupillomotor palsy was more prominent than the paresis of the extraocular muscles and it resolved in a significantly shorter time, suggesting an independent mechanism of pupillomotor involvement in MFS, as previously proposed.³

FIGURE 1 The pupils were symmetrically mydriatic (6.0 mm OD and 6.0 mm OS in room light) and unresponsive to light and near stimuli.

FIGURE 2 Adduction and adduction (a), (b), and supraduction (c) movements of the eyes were limited; infraduction movement (d) was unaffected.

FIGURE 3 An eye drop test with 0.1% pilocarpine to the right eye induced marked miosis.

Light-near dissociation and cholinergic supersensitivity may develop in patients with MFS.³ Keane⁴ reported two cases of MFS with cholinergic supersensitivity and light-near dissociation. The author proposed that aberrant reinnervation of the iris sphincter muscles denervated following a postganglionic parasympathetic lesion by the fibres to the ciliary muscles caused the pupillary findings.^{4,6,8} Nitta et al.³ also reported four patients with MFS presenting with mydriatic pupils unreactive to light stimuli. As two of the patients with light-near dissociation had cholinergic supersensitivity, whereas the other two patients responding neither light nor the near stimuli did not, the authors postulated that cholinergic supersensitivity might be associated with light-near dissociation and both may occur due to denervation of iris sphincter muscles.³

Although our patient exhibited cholinergic supersensitivity suggesting a postganglionic parasympathetic lesion causing tonic pupil, other characteristic findings of tonic pupil such as light-near dissociation, vermiform iris movements, or a prominent delay of redilation of the pupils were not observed during the course of the disease. Furthermore, pupil hypersensitivity was present from the onset of the symptoms, excluding the possibility of reinnervation of the iris sphincter muscle. The transient nature of the findings is also against a tonic pupil, which is a permanent disorder. Therefore, reinnervation of a denervated iris sphincter muscle seems unlikely in our patient. Indeed, cholinergic supersensitivity may also develop due to preganglionic parasympathetic lesions.⁹

A distinctive feature of our patient was the absence of anti-GQ1b antibody. Up to 95% of the patients have anti-GQ1b immunoglobulin G (IgG) antibodies during the acute phase of MFS, owing to the high specificity and sensitivity, these antibodies are useful to confirm the diagnosis; however, a negative result does not exclude the diagnosis.^{1,10} To the best of our knowledge, acute areflexic mydriasis showing cholinergic supersensitivity has not been reported in anti-GQ1b-negative MFS before.

In conclusion, in the case of acute bilateral areflexic mydriasis, which poses a diagnostic challenge to the

TABLE 1 The diagnoses considered and excluded by serological, microbiological, and electrophysiological methods in the patient.

Botulism
Stroke
Brainstem encephalitis
Carcinomatous meningitis
Lymphomatous meningitis
Hepatitis viruses infections
HIV infection
Syphilis
Paraneoplastic syndromes

clinician, the diagnosis of MFS should be considered even in the absence of serum anti-GQ1b antibody. Presence of cholinergic supersensitivity in the absence of light-near dissociation suggests that these two processes may be independent, at least in some of the patients with MFS.

Declaration of interest: The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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