CASE REPORT

Late Presentation of Ataxia, Areflexia, and Electrophysiological Abnormalities as Part of Miller Fisher Syndrome: Case Report

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ABSTRACT

Miller Fisher syndrome (MFS) is characterised by the triad of ophthalmoplegia, ataxia, and areflexia. A case with external ophthalmoplegia and absence of ataxia and areflexia until the end of second week is presented. Electrophysiological findings became apparent after the third week and showed reduced amplitudes of sensory nerve action potentials and prolonged latencies of F with no evidence of conduction blocks. There was no response to intravenous immunoglobulin, but there was response to corticosteroids. This case may represent an atypical MFS with late presenting electrophysiological abnormalities. Corticosteroids can be a therapeutic option when intravenous immunoglobulin fails to control clinical symptoms.

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Introduction

Miller Fisher syndrome (MFS) was originally described in 1956 as a triad of total external ophthalmoplegia, ataxia, and loss of tendon reflexes.¹ Although the optimal treatment for Miller Fisher syndrome has yet to be established, the typical therapy includes intravenous immunoglobulin or plasma exchange. Continued controversy exists regarding the efficacy of steroids.

We report a case of a 7-year-old boy with clinical external ophthalmoplegia with late presentation of ataxia, areflexia, and electrophysiological abnormalities as part of Miller Fisher syndrome. Intravenous immunoglobulin failed to control clinical symptoms in this patient.

Case presentation

Two days after being hit on the head with a stone by one of his friends, a 7-year-old boy became dizzy and noticed blurred and double vision. At the same time, his mother noticed an inward deviation of his eyes. His symptoms on diplopia progressively increased,

and on the fourth day, the boy was referred to our hospital.

There was no history on a preceding viral prodrome. Examination found no ptosis, no lid retraction. Visual acuity and confrontation visual fields were normal, as were the optic fundi. The pupils were 4 mm in diameter and reacted normally to light. Biomicroscopy did not reveal any signs of inflammation. There was an asymmetric limitation of abduction to either side. Abduction was limited minus 3 in the right eye and minus 2 in the left. The eye movements did not improve with the doll's head manoeuvre. Adductions, supra- and infra-ductions of both eyes were normal. There was no nystagmus. Orthoptic examination revealed an esotropia of 12 prism dioptres (PD) at near that increased to 25 PD at far. The findings were compatible with bilateral sixth nerve palsy. All other cranial nerves were normal.²

A paediatric neurologist consulted the patient. On examination, he was conscious. He had normal limb power with normal deep tendon reflexes and flexor plantar responses. Limb and gait ataxia were absent, and the cerebellar examination was normal. He had

no distal symmetrical impairment of vibration. Meningeal irritation signs were absent.

Routine blood tests were normal. Cerebrospinal fluid examinations showed white cell count $<1/\text{mm}^3$ (normal: $<5/\text{mm}^3$), protein 0.3 g/L (normal: 0.15–0.45 g/L), and glucose contents of 40 mmol/L (simultaneous blood glucose of 83 mmol/L). Serology for *Brucella*, *Salmonella*, *Mycoplasma*, *Chlamydia*, TORCH (toxoplasmosis, other [syphilis, varicella-zoster, parvovirus B19], rubella, cytomegalovirus [CMV], and herpes), and Epstein-Barr virus (EBV) revealed no abnormality. Hepatitis B surface antigen and human immunodeficiency virus (HIV; enzyme-linked immunosorbent assay [ELISA]) were negative. Cerebrospinal fluid examinations for herpes simplex virus, varicella-zoster virus, enterovirus, and adenovirus were also negative.

Cranial magnetic resonance imaging (MRI) with contrast did not demonstrate a central nervous system lesion or cranial nerve enhancement. Also, MRI of the orbits did not show enlargement of the extraocular muscle bellies (excluding thyroid eye disease).

The boy returned back to our clinic 10 days later. The mother reported an increase in diplopia and poor balance since the day before. Bilateral eyelid retraction (without lagophthalmus) was present. Horizontal gaze limitation had increased and reached a nearly symmetric minus 4 limitation of abduction to either side. An elevation palsy of the right eye was now also added to the picture with accompanying mild upward gaze-evoked nystagmus (Figure 1). Examination revealed an increase in esotropia 25 PD at near, which reached 35 PD at distance. Although the boy could not voluntarily elevate his right eye above the horizontal, his eye

moved fully during forced lid closure. Infraduction was spared in both eyes.

The patient was transferred to the regional neurosciences centre for further investigation where the patient was found to be ataxic on heel-to-toe walk and the deep tendon reflexes were absent. Dysautonomia was noted with hypohidrosis. The family refused to give consent to a repeat lumbar puncture. Tensilon test was negative. Nerve conduction studies (16 days after the onset of diplopia) showed normal motor conduction velocities, normal sensory action potentials (SNAPs), and normal F waves in upper and lower limbs. Distal latencies and compound muscle action potentials (CMAPs) were within normal limits with no evidence of conduction block. We were not able to ascertain the presence of anti-ganglioside GQ1b antibody, since it was not covered by social security system and the patient's financial position could not meet the demand.

The patient was designated as atypical Miller Fisher syndrome and received a course of intravenous immunoglobulin treatment (IVIg) of 400 mg/kg/day for 5 days. On no improvement of symptoms of ophthalmoplegia, nerve conduction studies were repeated. Repeat electromyographic studies revealed axonal polyneuropathy with polyphasic, high-amplitude, and long-duration muscle action potentials (MUAPs), especially on tibialis anterior muscle. Any evidence of demyelinating neuropathy (i.e., long conduction velocities, long distal latencies, and conduction block) was absent. The F latency of median nerve was 21.55 ms (normal values for 7-year-olds: 23–27.6 ms). Sensory nerve conduction studies of the limbs revealed reduced amplitudes of SNAPs. The

Figure 1. External ophthalmoplegia, spared depression.

Figure 2. Follow-up at two months after intravenous immunoglobulin and pulse steroid: normal ocular movements.

amplitudes of SNAPs of median nerve ($15 \mu\text{V}$ [26 ± 9.4], sural nerve ($10.5 \mu\text{V}$ [26.7 ± 6.5]), and peroneal nerve ($1.65 \mu\text{V}$ [8.5 ± 4.19]) were reduced.

The patient received 30 mg/kg/day pulse methyl prednisolone for three days. Oral steroid administered afterwards was ceased slowly in one month.

At the end of two weeks, autonomic dysfunction improved, external ocular movements returned, and ataxia decreased. Follow-up at two months showed normal ocular movements and no ataxia (Figure 2).

Discussion

In Miller Fisher syndrome, paresis of the extraocular muscles progresses to complete bilateral ophthalmoplegia within one to two weeks, accompanied by areflexia, sensory disturbance, and ataxia; a varying combination of other cranial nerve signs may also be present.^{3–5} These clinical signs are preceded by signs of upper respiratory tract infection in 56–76% of the patients.

The development of an acute nearly total ophthalmoplegia and preservation of motor strength led us to consider a clinical pre-diagnosis of MFS. However, this definite diagnosis was doubted in the absence of ataxia and the preservation of deep tendon reflexes during the first two weeks; also, it was not supported by the cerebrospinal fluid (CSF) examinations. Areflexia and ataxia developed after the second week, and the patient was designated clinically as having atypical MFS, but nerve

conduction studies, 16 days after the onset of diplopia, still showed normal motor conduction velocities, normal sensory action potentials, and normal F waves. As the family did not give consent to a second CSF analysis, albuminocytological dissociation could not be assigned. The definitive diagnosis of MFS could not be made without detecting electrophysiological abnormalities, which became apparent only after the 22nd day of the onset of diplopia.

Perhaps the most interesting and useful result relates to the response to steroid treatment. MFS is a predominantly axonal inflammatory neuropathy. Our observation in this case and a review of the literature suggest that there may be a small group of patients in whom corticosteroid treatment, possibly because of anti-inflammatory and/or immunosuppressive action, may be a therapeutic option when intravenous immunoglobulin fails to control clinical symptoms.^{6–8} Nevertheless, in this context, it is worth considering whether the improvement in this patient could be accounted for by a delayed response to intravenous immunoglobulin or spontaneous improvement or response to steroids.

The role of the anti-ganglioside GQ1b antibody in the pathogenesis of MFS was recognised in the early 1990s.^{9–11} MFS is associated with the presence of anti-GQ1b antibodies in the serum over 80% of patients. We were not able to show the presence of anti-GQ1b antibodies. Also, the characteristic albuminocytological dissociation in the CSF, which appears usually from the second week, could not be assigned. These are the two important

limitations of our study. Although electrophysiological abnormalities vary in MFS, reduced sensory nerve action potentials are characteristic. In this case, reduced amplitudes of sensory nerve action potentials and prolonged latencies of F waves were interpreted as criteria for diagnosis of MFS.

The question of whether the development of Miller Fisher signs is or is not related to a mild head injury remains open in this case. A mild head injury in theory might trigger a molecular mimicry, and once this is established, an inflammatory autoimmune response may occur and disrupt both peripheral and cranial nerve function, leading to the characteristic neurological findings of Miller Fisher syndrome.

In conclusion, this case may represent a spectrum of atypical MFS with an absence of ataxia and areflexia by the end of second week, accompanied by normal electrophysiological findings until the end of third week, which was unresponsive to intravenous immunoglobulin but corticosteroids. This reinforces the importance of considering Miller Fisher syndrome normally accompanied by electrophysiological abnormalities in the differential diagnosis of a patient presenting with bilateral ophthalmoparesis without this manifestation. Corticosteroids can be a therapeutic option when intravenous immunoglobulin fails to control clinical symptoms.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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