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CASE REPORT

A Typical Presentation of Miller Fisher Syndrome: A Case Report and Review of Literature

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Abstract

Objective: Miller Fisher syndrome (MFS) is a well-recognized, but rare variant of Guillain-Barre syndrome (GBS) and is typically characterized by the classic triad of ophthalmoplegia, ataxia, and areflexia. Here we report a case with an atypical presentation of Miller Fisher syndrome that presented with an incomplete triad of ataxia and areflexia without ophthalmologia accompanied by mild proximal limb weakness and distal sensory involvement.

Clinical presentation: A 65-years-old Arab man presented with a 2 week history of acute onset progressive unsteadiness of gait, associated with headache and numbness in all four extremities. He had history of a recent upper respiratory tract infection 2 weeks prior to the onset of his symptoms. He also had been vaccinated for the influenza one month back. Clinical examination showed intact higher mental functions, normal cranial nerves including extra-ocular movements and optic fundi, mild proximal muscle weakness in the lower limbs and graded distal sensory impairment for pin prick and joint position sense. There was generalized areflexia. There was mild appendicular ataxia and definite gait ataxia. CSF analysis showed albumin cytological dissociation. Nerve conduction study revealed mixed (axonal and demyelinating) motor polyneuropathy severely affecting lower limb nerves and cranial nerves. Ganglioside Profile was negative for GM1 and GQ1b antibodies. He improved completely after being treated with five sessions of plasma exchange.

Conclusion: Miller Fischer syndrome should be considered in all patients who present with acute onset progressive ataxia, given its excellent response with treatment. A complete triad of ataxia, areflexia and ophthalmoplegia may not be present in all patients. High index of suspicion at presentation helps proper evaluation and early initiation of treatment to have excellent outcomes.

Introduction

Miller Fisher syndrome (MFS) is a well-recognized, but rare variant of Guillain-Barre syndrome (GBS) that is characterized by the classic triad of ophthalmoplegia, ataxia, and areflexia [1]. The incidence of GBS is about 1 to 2 in 100,000 persons while MFS makes up only 1-7% of total GBS cases [2]. GBS typically presents as weakness and sensory abnormalities in the lower limb that progress upwards to effect the upper limb and cranial muscles. However, it is important to note that GBS is not a heterogenous disease and several variants exist with a myriad of different presenting symptoms [3]. MFS is a GBS variant that is usually not associated with limb weakness although presentations with limb weakness have been reported [4]. Ataxia is a typical feature of Miller Fisher syndrome, with central and peripheral sites implicated in its pathology. Studies analyzing the clinical findings have suggested peripheral nerve dysfunction as the putative mechanism [5] but neuroimaging in a few cases has suggested a central mechanism affecting the spino-cerebellar tracts instead [6]. It was hypothesized that the IgG anti-GQ1b antibodies have a role in the pathophysiology of the ophthalmoplegia seen in patients with MFS but cases with isolated ataxia without ophthalmoplegia have also been reported in anti GQ1b positive patients [13, 10].

Incomplete variants of MFS, where one or more components of the triad are not present, exist and this may result in diagnostic confusion for many treating physicians. Here we report of one of these atypical MFS cases with an incomplete triad that presented with ataxia and areflexia without ophthalmologia accompanied by mild proximal limb weakness and distal sensory involvement.

Case presentation

A 65-year-old Arab male, known case of hypertension, chronic kidney disease and ischemic heart disease with a regular smoking habit presented with a 2 week history of acute onset progressive unsteadiness of gait, with swaying to either sides, associated with headache and numbness in all 4 extremities. Upon presentation to the hospital, the patient was unable to ambulate independently. There was no history of diplopia, blurring of vision, facial weakness, dysphagia or dysarthria. He denied any urinary or bowel symptoms.

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He had history of a recent upper respiratory tract infection 2 weeks prior to the onset of his symptoms. He also had been vaccinated for the influenza one month back.

Clinical examination showed intact higher mental functions, normal cranial nerves including extraocular movements and optic fundi. Motor system examination revealed hypotonia in lower limbs, mild proximal muscle weakness in the lower limbs and graded distal sensory impairment for pinprick and joint position sense. There was generalised areflexia and plantar reflex was flexor bilaterally. There was mild appendicular ataxia with definite gait ataxia. There were no signs of meningeal irritation.

Investigations

Routine blood investigations including blood counts and liver function tests were normal. Renal function tests revealed elevated Creatinine and blood urea. The creatinine clearance was 20 mL/min. CSF analysis showed WBC count <5, Protein 162, Glucose 69, CL 124, Lactic acid 1.6, IGG 26.89. CSF Albumin 964, IGG 235, CSF/Serum Albumin ratio 23.2. Oligoclonal bands were detected in the CSF and serum indicating a systemic immunoreaction. No malignant cells were present in the CSF. CSF Culture was negative. PCR for Enterovirus, Herpes virus 1, 2, 6 &7, and Varicella Zoster Virus were all negative. Serum vitamin B1 and B12 levels were within normal range.

MRI Brain showed generalized cerebral atrophic changes of the brain in addition to periventricular leukoaraiosis suggesting chronic small vessel disease.

Nerve conduction studies showed prolonged distal latencies and conduction velocities with temporal dispersion and prolonged F latencies. CMAP amplitudes were mildly reduced. Sensory conduction showed prolonged onset latencies and conduction velocities. Blink reflex study showed prolonged R1 and R2 latencies. The overall electrophysiological data was conclusive with an acute predominantly demyelinating sensorimotor polyneuropathy.

Ganglioside Profile including Asialogangliosides: GM1, Ganglioside GM1, GM2, GD1a, GD1b, GQ1b (IgG, IgM) antibodies were negative (<30). Anti-Hu antibody was negative.

Treatment and Outcome

Five sessions of large volume plasma exchange (40ml/kg/day) was done on alternate days. Intravenous immunoglobulin was not considered in view of the patient's chronic renal failure. His regular medications for hypertension and ischemic heart disease were continued during his hospital stay. After plasma exchange, patient showed remarkable clinical improvement. His ataxia and numbness improved and he was able to walk independently within a week of initiation of therapy.

Discussion

Miller Fisher described the triad of ataxia, ophthalmoplegia and areflexia, as an atypical variant of acute inflammatory demyelinating polyneuropathy [1]. Although the cases he described did not have the ascending limb weakness which is characteristic of classical GBS. MFS was seen similar to classical GBS in which both present with areflexia, have albumin-cytological dissociation in CSF and have self-limiting course with spontaneous recovery within weeks of onset of symptoms. However other clinical manifestations with one of the components of the classical triad missing have been reported rarely.

Uluç Yiş et al reported a case with diplopia following upper respiratory tract infection and a clinical examination revealing areflexia and ophthalmoplegia but no ataxia and negative Antiganglioside antibodies [7]. Paine MA et al described a case of Miller Fisher syndrome with ophthalmoplegia and mild ataxia but no areflexia [8]. Garima Gupta et al described a case where only one of the components of the classical triad was present. The presentation included history of headache and double vision that was preceded by upper respiratory infection but the clinical examination revealed intact reflexes and normal gait. Masahiro Mori et al reported a case with acute ataxia and areflexia without ophthalmoplegia or sensory loss. Nonetheless, ganglioside profile was positive for Anti-GQ1b antibodies in both of these cases [9, 10].

Similarly other case reports were published highlighting additional neurological manifestations of MFS apart from the classical triad. These neurological manifestations included pupillary abnormalities, bulbar dysfunction, limb weakness, psychosis and involuntary movements [11, 12, 14, 15].

Taku Hatano et al described the case of a young woman with acute ataxia, areflexia and ophthalmoplegia, accompanied by psychosis and involuntary movements. Both psychosis and involuntary movements were atypical MFS symptoms [11]. Appiotti et al described polyneuritis cranial is like presentation with prominent bulbar symptoms along with ophthalmoplegia, ataxia and areflexia with positive Anti-GQ1b antibodies [12]. Kodali VU et al described a case with the classical triad in addition to limb weakness and distal sensory loss [4].

Yuki et al has postulated that that IgG anti-GQ1b antibodies are responsible for syndromes with ophthalmoplegia which includes acute ophthalmoplegia without ataxia, Miller Fisher syndrome, Bickerstaff's brainstem encephalitis, and Guillain-Barre syndrome with ophthalmoplegia [13]. However a case with isolated ataxia without ophthalmoplegia has been reported in a patient with positive anti-GQ1b antibodies [10]. Most reported cases of ataxic neuropathies were previously reported to have positive GD1b antibodies [14, 15]

Conclusion

Our case was unique with respect to clinical features and the ganglioside profile. Our patient had an incomplete triad with only ataxia and areflexia but no ophthalmoplegia. In addition, he had progressive proximal limb muscle weakness and distal

sensory abnormalities which is atypical for Miller Fischer syndrome. His CSF showed albumin-cytological dissociation and nerve conduction study showed demyelinating polyneuropathy; however his serum did not react to any of the gangliosides including GQ1b, GM1, GM2, GD1a and GD1b antibodies. Nevertheless, the patient had excellent response with plasma exchange with complete recovery.

Miller Fischer syndrome should be considered in all patients who present with acute onset of progressive ataxia, given its excellent response with treatment. A complete triad of ataxia, areflexia and ophthalmoplegia may not be present in all patients. High index of suspicion at presentation helps proper evaluation and early initiation of treatment to have excellent outcomes.

Statement of Ethics:

The patient gave written consent to share his case.

Conflict of Interest Statement:

The authors declare that they have no conflicts of interest to disclose.

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