SHORT REPORT

Miller Fisher-Guillain-Barré overlap syndrome with enhancing lesions in the spinocerebellar tracts

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Abstract

The site of lesions in Miller Fisher syndrome, especially those causing ataxia, has been controversial. A 50 year old man with features of Miller Fisher syndrome in whom MRI showed enhancing lesions in the spinocerebellar tracts at the level of the lower medulla is reported. Peripheral involvement of cranial nerves was also indicated by an abnormal blink reflex and by clinical manifestations: complete external ophthalmoplegia, bilateral peripheral facial weakness, convergence disturbance, absence of Bell's phenomenon, oculoccephalic, and oculovestibular reflex. Abnormal lesions on MRI disappeared and the blink reflex became normal with clinical improvement. The case is regarded as Miller Fisher-Guillain-Barré overlap syndrome, a postinfectious allergic reaction involving both peripheral nerves in the cranium and neuraxis in the spinocerebellar tract. The lesions in the spinocerebellar tracts are responsible for cerebellar ataxia in this syndrome.

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Since the first description by Miller Fisher,¹ nosology of the syndrome of ophthalmoplegia, cerebellar ataxia, and areflexia (Miller Fisher syndrome) has been controversial. At one extreme, proposals have included a peripheral disturbance as a variant of Guillain-Barré syndrome and the other, brainstem lesions including Bickerstaff encephalitis.² Recently, antibodies against ganglioside GQ1b was reported to be strongly associated with Miller Fisher syndrome,^{3,4} yet the pathophysiology remains unresolved. We encountered a patient with features of Miller Fisher syndrome whose MRI showed enhancing lesions in the spinocerebellar tracts and the results of blink reflex study indicated peripheral facial nerve disturbance.

Case report

A 50 year old man developed fever, which

lasted for a week, and acute onset of double vision, followed by bilateral ptosis, gait ataxia, nausea, and vomiting. On admission to Sumitomo Hospital on 13 November 1993 neurological examination disclosed severe ophthalmoplegia, bilateral ptosis, areflexia, and moderate cerebellar ataxia in all limbs and the trunk. He was alert and fully oriented and showed a normal mental state. There was no sign of meningeal irritation. Pupils were midsized and round, but poorly reactive to light. Optic fundi, visual acuity, and fields were intact. Bell's phenomenon, oculoccephalic reflex, and oculovestibular reflex were not evoked. Other cranial nerves were intact. Speech was not dysarthric and there was no limb weakness. Deep tendon reflexes were absent in all limbs and plantar responses were flexor. He complained of acroparaesthesia but sensory modalities were normal. Gait was wide based and ataxic. Cranial CT was normal. Laboratory studies showed a normal complete blood cell count, no inflammatory reaction, and normal renal and liver function, electrolytes, chest radiographs, and ECG. Lumbar puncture yielded clear CSF containing 3 normal lymphocytes/ml and raised protein (70 mg/dl). Serological screening for *Campylobacter jejuni/coli*, herpes simplex virus type 1, varicella zoster virus, and Epstein-Barr virus were all negative. During the next three days, his condition worsened, with complete external ophthalmoplegia and ptosis, dysphagia, and weakness of the tongue. On 17 November he had bilateral peripheral facial paresis and mild limb weakness. Axial T1 and T2 weighted MRI were normal. After injection of gadolinium DTPA, T1 weighted axial MRI showed enhancing lesions in the lateral lower medulla on both sides, consistent with the anterior and posterior spinocerebellar tracts (figure). A diagnosis of Miller Fisher syndrome was made and methylprednisolone (1000 mg/day) was given intravenously for three days, and plasma exchange was performed. Weakness of the tongue improved shortly after plasma exchange. Facial and limb weakness showed gradual recovery over the next three months. Diplopia, ophthalmoplegia, ptosis, and ataxia began to regress about six weeks after admission, and showed complete recovery within three months from the onset. Anti-GQ1b antibody titre was not measured in the acute

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(A) Precontrast axial T1 weighted image (TR/TE: 500/18) showing normal appearance of the medulla oblongata at the level of the decussation of pyramids (I). Postcontrast axial T1 weighted image showing lateral medullary enhancement on both sides (arrows) (II). (B) Anatomical scheme indicating the spinocerebellar tract at the level of decussation of pyramids. Shaded area represents the enhanced lesion on our patient's MRI. a = Anterior spinocerebellar tract; b = posterior spinocerebellar tract; c = pyramid; d = decussation of pyramid; e = spinal root of accessory nerve.

stage and was normal three months after onset. Abnormally enhancing lesions on MRI regressed after three months and disappeared completely six months after onset.

Conventional nerve conduction studies in the right median and tibial nerves showed normal amplitude, wave form, and conduction velocity in both motor and sensory studies; F waves from the same nerves showed a normal response. Brainstem auditory evoked potentials showed a normal appearance and latency. Blink reflexes showed bilateral delay in direct response R1 and R2 waves. These abnormalities had recovered at the study performed three months after onset.

Discussion

Considerable attention has been given to the pathophysiology of Miller Fisher syndrome, yet controversy still exists. In 1956, Miller Fisher regarded it as "a variant of Guillain-Barré type of polyneuropathy in which limb involvement was minimal or absent".¹ Most authors are proponents of the peripheral hypothesis. Indeed, normal MRI has been shown in patients with active Miller Fisher syndrome,⁵⁻⁷ no involvement of the brainstem or cerebellum has been found in necropsy cases,^{8,9} and peripheral nerve disturbance has been shown by electrophysiological studies.^{10,11} By contrast, Al-Din *et al.*, the first proponents of a central origin in 1982, argued that disturbance of consciousness and internuclear ophthalmoplegia could not be explained by peripheral lesion, and regarded Miller Fisher syndrome as a variant of brainstem encephali-

tis (Bickerstaff encephalitis).² Later, Al-Din proposed that Miller Fisher syndrome was a postinfection hypersensitive or allergic reaction in the neuraxis primarily in the brainstem, similar to the pathophysiology in the peripheral nervous system in Guillain-Barré syndrome.¹¹ Another hypothesis, by Meienberg and Ruffel, was that inflammation confined to the subependymal areas around the aqueduct and fourth ventricle causes Miller Fisher syndrome.¹² Many reports support the central hypothesis by showing abnormal findings on MRI—for example, in the midbrain,^{2,13,14} medulla oblongata,² and posterolateral brainstem peduncular area around the fourth ventricle.¹⁵

In our patient, clinical and electrophysiological findings strongly suggested peripheral nerve involvement in the cranium. Complete external ophthalmoplegia, lack of Bell's phenomenon, absence of doll's eye phenomenon and oculovestibular reflex, and convergence disturbance could exclude internuclear^{14,16,17} as well as supranuclear ocular palsy. The facial nerve palsy was also of a peripheral pattern clinically and the result of the blink reflex study showed the same pattern as in Guillain-Barré syndrome, hereditary motor sensory neuropathy type 1, and diabetic neuropathy,¹⁸ indicating peripheral involvement of both facial nerves. Therefore our patient definitely showed accompanying peripheral nerve involvement in the cranium. Precedent infection and increased protein in the CSF indicated an allergic postinfectious demyelination. In addition, normal brainstem auditory evoked potentials exclude such diffuse processes as brainstem encephalitis.

Ataxia is the most controversial manifestation in the Miller Fisher syndrome. Fisher reluctantly interpreted it as a manifestation of an unusual and unique disturbance of the peripheral neurons.¹ Ropper and colleagues postulated a disparity between proprioceptive information from muscle spindles, and kinesthetic information from joints and other proprioceptors.⁵ Landau *et al.* supported Fisher's concept by showing ataxia in Guillain-Barré syndrome, with severe peripheral motor and afferent impairment.⁶ On the contrary, proponents of a central origin have suggested the cerebellar pathway in the brainstem² including the dentatofugal pathways within the midbrain¹⁴ and roof of the fourth ventricle,¹² as the site of lesions causing cerebellar ataxia. Reports of radiographic abnormalities have implied that the primary lesion site for cerebellar ataxia is located in brainstem.^{2,13,15} We obtained brain MRI focusing on the brainstem with 3 mm slice thickness, and the post-contrast image showed abnormal areas around both spinocerebellar tracts; the midbrain, pons, and cerebellum were all intact. Regression of the MRI abnormalities with clinical improvement was evident and there was no detectable enhancement in the brainstem in healthy controls.¹⁹ Our MRI findings indicated that the origin of ataxia in our patient was localised inflammatory change in the spinocerebellar tracts. Limb

ataxia without cerebellar dysarthria can be explained by these lesions. Several authors postulated that secondary degeneration of these tracts causes ataxia in Miller Fisher syndrome.^{20,21} Involvement of the spinal peripheral nerve was not detected, however, by nerve conduction studies and F wave investigation in our case. Thus postinfection allergic inflammation localised to the spinocerebellar tracts is a reasonable hypothesis. Although similar lesions have not previously been reported on MRI, routine views without contrast material may have overlooked the localised lesion. Furthermore, most previous reports included findings on CT, from which it is difficult to detect small lesions in the brainstem.

Our data are insufficient to explain the areflexia. Nevertheless, normal results in the nerve conduction and F wave studies cannot exclude mild proximal spinal root involvement. Unfortunately, we had no opportunity to obtain somatosensory evoked potentials and H reflex, which might have been helpful. Further studies on this point are needed.

The diagnosis in our patient was Miller Fisher-Guillain-Barré overlap syndrome caused by a postinfectious autoimmune reaction involving cranial peripheral nerves, brainstem, and possibly proximal spinal roots. Ataxia is probably due to lesions in the spinocerebellar tracts. Previous reports must be examined carefully to determine whether they meet the criteria of Miller Fisher syndrome fully. Cases with lesions in the brainstem were not consistent with classic Miller Fisher syndrome, because patients showed various degrees of disturbance of consciousness, severe peripheral nerve involvement, or pleocytosis in the CSF. We believe that patients with disturbance of consciousness and partial ophthalmoplegia should not be diagnosed as Miller Fisher syndrome, even if they have a triad of ophthalmoplegia, areflexia, and ataxia with benign prognosis. Brainstem encephalitis may present with ophthalmoplegic ataxia with areflexia, but should be distinguished from Miller Fisher syndrome. Patients with severe

limb weakness should also be excluded, respecting Fisher's description in which "limb involvement was minimal or absent".

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