IgG anti-GQ1b positive acute ataxia without ophthalmoplegia

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Abstract

IgG anti-GQ1b antibody was present in a patient with acute ataxia and areflexia without ophthalmoplegia or elementary sensory loss. Sensory nerve conduction studies and somatosensory evoked potentials were normal, but postural body sway analysis showed dysfunction of the proprioceptive afferent system. The clinical presentation and laboratory results for this patient resemble those of Miller Fisher syndrome, except for the lack of ophthalmoplegia. This case may represent part of an IgG anti-GQ1b syndrome. (J Neurol Neurosurg Psychiatry 1999;67:668–670)

Keywords: ataxia; Miller Fisher syndrome, anti-GQ1b antibody

Miller Fisher syndrome is characterised by the clinical triad of ophthalmoplegia, ataxia, and areflexia.1 The IgG anti-GQ1b antibody often detected in patients with Miller Fisher syndrome may have a role in the pathophysiology of this ophthalmoplegia. Ganglioside GQ1b is expressed in the paranodal portion of human ocular motor nerves and is the possible target molecule in this disease.2 Moreover, an IgG anti-GQ1b positive case of acute ophthalmoplegia with areflexia but without ataxia has been reported as the clinical phenotype of this anti-GQ1b antibody syndrome.3

Ataxia is a regular feature of Miller Fisher syndrome, but the site of the lesion that causes it is not clear. Some studies based on clinical findings have suggested that peripheral nerve dysfunction is a possible peripheral mechanism,4,5 whereas others based on clinical findings or neuroimaging6 have suggested that a brainstem or cerebellar lesion may be responsible for the ataxia. A recent report on postural body sway analysis showed selective involvement of the proprioceptive afferent system in Miller Fisher syndrome.7 We describe a patient with acute ataxia and areflexia, but no ophthalmoplegia, associated with IgG anti-GQ1b antibodies. Clinical findings, electrophysiological studies, and postural body sway analysis suggest that this patient’s ataxia is very similar to that seen in patients with Miller Fisher syndrome.

Results

ANTIGANGLIOSIDE ANTIBODY ASSAY

An enzyme linked immunosorbent assay (ELISA), was performed as described previously8 with minor modifications. The patient’s serum obtained on day 7 had increased IgG antibody titres to GQ1b (1:2000) and GT1a (1:1000) but did not have detectable IgG or IgM antibody concentrations to the other gangliosides tested (GM1, GM1b, GM2, GM3, GD1a, GD1b, GD2, GD3, GT1b, GalNAc-GM1b, GalNAc-GD1a, fucosyl-GM1, fucosyl-GD1b, a galactosyl [α fucosyl] GM1, α galactosyl [α fucosyl] GD1b, GM1α, GT1a, GQ1b, sialosyl paragloboside, sialosyl lactosaminyl paragloboside, and sialated glucuronyl paragloboside). No IgM antibodies to GQ1b and GT1a were detected. Thin layer chromatography with immunostaining was done as described previously9 with minor modifications. In this test, the patient’s

Case report

A 35 year old Japanese man who had been in good health, experienced a flu-like syndrome with coughing, sputum, and a sore throat in early April 1998 during the time his child had an upper respiratory infection. His symptoms cleared in a week, but 1 week later, he developed unsteady gait as well as paraesthesia of the four distal limbs. An examination done 6 days after neurological onset showed obvious ataxia in all four limbs, as well as generalised areflexia. He denied diplopia, and his eye movements were normal. There was no evidence of other cranial nerve involvement. His muscle strength was normal, and there was no impairment of pinprick, touch, position, or vibratory sensation. Romberg’s sign was negative. He could walk only with assistance, and tandem gait was impossible.

His CSF on day 3 showed a protein concentration of 62 mg/dl with 1 lymphocyte/mm3. Brain CT showed no abnormalities. He received supportive care and gradually improved over the next 2 weeks without the use of plasma exchange or intravenous immunoglobulin treatment. A follow up examination 4 weeks after onset showed nearly complete clinical recovery from the ataxia and dysaesthesia, but the tendon reflexes were still hyporeactive.

Keywords: ataxia; Miller Fisher syndrome, anti-GQ1b antibody

References

1. The IgG anti-GQ1b antibody often detected in patients with Miller Fisher syndrome may have a role in the pathophysiology of this ophthalmoplegia. Ganglioside GQ1b is expressed in the paranodal portion of human ocular motor nerves and is the possible target molecule in this disease. Moreover, an IgG anti-GQ1b positive case of acute ophthalmoplegia with areflexia but without ataxia has been reported as the clinical phenotype of this anti-GQ1b antibody syndrome.

2. Ataxia is a regular feature of Miller Fisher syndrome, but the site of the lesion that causes it is not clear. Some studies based on clinical findings have suggested that peripheral nerve dysfunction is a possible peripheral mechanism, whereas others based on clinical findings or neuroimaging have suggested that a brainstem or cerebellar lesion may be responsible for the ataxia. A recent report on postural body sway analysis showed selective involvement of the proprioceptive afferent system in Miller Fisher syndrome. We describe a patient with acute ataxia and areflexia, but no ophthalmoplegia, associated with IgG anti-GQ1b antibodies. Clinical findings, electrophysiological studies, and postural body sway analysis suggest that this patient’s ataxia is very similar to that seen in patients with Miller Fisher syndrome.

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Discussion

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that is proportional to the degree of ataxia.

In this patient, normal sensory nerve action

potentials and SEPs indicated that most of the

afferent nerve fibres were intact, whereas the

results of the postural body sway analysis and

the bilateral absence of the soleus H reflex sug-

gested dysfunction of the proprioceptive affer-

ent system.

Posturography provides another means of

analysing peripheral nerve and cerebellar func-

tions: patients with cerebellar ataxia had a spe-

cific power spectrum peak frequency of body

sway at 3 Hz,16 whereas patients with sensory

ataxia (tabes dorsalis) had a peak at about 1.0

Hz.15 Moreover, patients with Miller Fisher

syndrome are reported to have a 1.0 Hz peak

on posturography despite intact peripheral

sensory nerve action potentials and SEPs,

indicative of selective involvement of the mus-

cle spindle afferents.9 This patient actually had

the same pattern as that found in Miller Fisher

syndrome. Some cases of acute ataxic neu-

ropathy without weakness or elementary sen-

sory loss are reported to be an ataxic form of

Guillain-Barré syndrome,16 17 but antiganglio-

side antibodies and postural body sway were not

examined in those patients.

Although our patient did not present with

ophthalmoplegia, the clinical and laboratory

findings suggest that our case is a variant form

of Miller Fisher syndrome. Yuki reported cases

of isolated acute ophthalmoparesis without

ataxia but with IgG anti-GQ1b antibodies,

another possible variation of Miller Fisher

syndrome.1 The author suggested an “IgG

anti-GQ1b syndrome” which includes acute

ophthalmoplegia without ataxia, Miller Fisher

syndrome, Bickerstaff’s brainstem encephalitis,

and Guillain-Barré syndrome with ophthalmoplegia.1 Isolated acute ataxia with-

out ophthalmoplegia but with IgG anti-GQ1b

antibodies may be among the clinical variants

of this syndrome. The reason for the lack of

ophthalmoplegia in our case and the lack of

ataxia in cases of acute ophthalmoplegia with-

out ataxia, despite the presence of anti-GQ1b

antibodies, is unknown. Predilection for a par-

ticular region may be caused by factors such as

the extent and intensity of damage to the

blood-nerve barrier and local activation of

inflammatory cytokines or complements.

Antiganglioside antibody assays of this pa-

tient’s serum showed the presence of IgG anti-

bodies to GQ1b and GT1a, a situation commonly described in Miller Fisher

syndrome;2 Guillain-Barré syndrome with

ophthalmoplegia,2 Guillain-Barré syndrome

without ophthalmoplegia,18 and acute orophary-

genaeal palsy.19 On the other hand, this

patient’s serum did not react with any of the

other gangliosides, such as b-series ganglio-

sides (GD2, GD3, GD1b, and GT1b), that

have been detected in patients with acute sen-

sory neuropathy.11 Ataxic neuropathy with

anti-GQ1b antibodies has been reported,11 20–23

but those patients had sensory ataxia with

elementary sensory loss, and they had other

b-series antiganglioside antibodies. Moreover,

the isotype of the anti-GQ1b antibodies was

IgM not IgG,11 20–23 and some of those patients

had a chronic clinical course.20–22

Our case suggests that IgG anti-GQ1b anti-

bodies are present in acute ataxic neuropathy

despite the absence of ophthalmoplegia or
elementary sensory loss. Postinfection Miller Fisher syndrome-type ataxia without ophthalmoplegia, such as acute ophthalmoparesis without ataxia, may represent a variant Miller Fisher syndrome and may be a part of the “IgG anti-GQ1b syndrome”. Further investigation of the clinical phenotypes of anti-GQ1b positive neurological disorders should clarify the pathophysiological role of this antibody.

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