

SHORT REPORT

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.

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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 ophthalmoparesis 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,⁴⁻⁶ whereas others based on clinical findings⁷ or neuroimaging⁸ 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.⁹ 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.

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 hypoaffective.

Results

ANTIGANGLIOSIDE ANTIBODY ASSAY

An enzyme linked immunosorbent assay (ELISA) was performed as described previously¹⁰ 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, GM1 α , GT1 α , GQ1 α , sialosyl paragloboside, sialosyl lactosaminyl paragloboside, and sulphated glucuronyl paragloboside). No IgM antibodies to GQ1b and GT1a were detected. Thin layer chromatography with immunostaining was done as described previously¹¹ with minor modifications. In this test, the patient's

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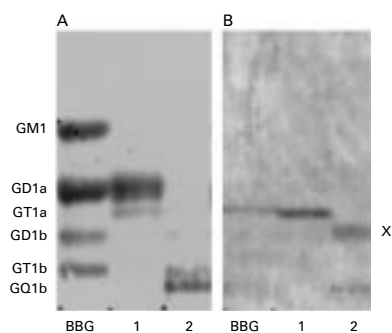
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Thin layer chromatography immunostaining. Plates were stained with (A) orcinol/sulphuric acid for hexose and with (B) IgG from the patient (dilution, 1:50). Lane 1, fraction containing GD1a and GT1a, which was separated from bovine brain ganglioside by Q-sepharose column chromatography. Lane 2, fraction enriched with GQ1b and GT1b prepared as above. BBG=bovine brain ganglioside mixtures; X=unidentified glycolipid.

serum reacted with GT1a and more weakly with GQ1b (figure).

ELECTROPHYSIOLOGICAL STUDIES AND POSTURAL BODY SWAY ANALYSIS

Nerve conduction studies, soleus H reflex studies, somatosensory evoked potentials (SEPs), and posturography were done on day 7. Nerve conduction studies showed normal sensory and motor nerve conduction, but soleus H reflexes were absent bilaterally. The SEPs recorded after median and tibial nerve stimulation using the recommended standards¹² showed that all the peak latencies were within normal limits. Body sway was measured with a G5500 posturograph (Anima Corp, Tokyo, Japan) as described elsewhere.⁹ The posturograph detected the centre of the body weight from the pressure of the feet on the board, and the total distance (mm) travelled in 20 seconds was calculated. Peak frequency of body sway was calculated by Fourier analysis using the computer program, Gravi Analyzer (Anima Corp, Tokyo, Japan). The patient had an abnormal increase in body sway while standing upright and a power spectrum sway peak at 1.0 Hz similar to that in patients with acute sensory ataxia or with Miller Fisher syndrome (data not shown).

Discussion

The major clinical manifestation of this patient was acute ataxia and areflexia associated with prior infection and increased CSF protein, which suggests a postinfection immune mediated neurological disorder such as Guillain-Barré or Miller Fisher syndrome. This patient was further characterised by the lack of elementary sensory loss, as well as the lack of ophthalmoplegia. Acute sensory neuropathy is one cause of sensory ataxia, but it is always associated with impairment of deep sensation that is proportional to the degree of ataxia.¹³

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 suggested dysfunction of the proprioceptive afferent system.

Posturography provides another means of analysing peripheral nerve and cerebellar functions: patients with cerebellar ataxia had a specific power spectrum peak frequency of body sway at 3 Hz,¹⁴ 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 muscle spindle afferents.⁹ This patient actually had the same pattern as that found in Miller Fisher syndrome. Some cases of acute ataxic neuropathy without weakness or elementary sensory loss are reported to be an ataxic form of Guillain-Barré syndrome,^{16, 17} but antiganglioside 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.³ The author suggested an "IgG anti-GQ1b syndrome" which includes acute ophthalmoparesis without ataxia, Miller Fisher syndrome, Bickerstaff's brainstem encephalitis, and Guillain-Barré syndrome with ophthalmoplegia.³ Isolated acute ataxia without 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 ophthalmoparesis without ataxia, despite the presence of anti-GQ1b antibodies, is unknown. Predisposition for a particular 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 patient's serum showed the presence of IgG antibodies 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 oropharyngeal palsy.¹⁹ On the other hand, this patient's serum did not react with any of the other gangliosides, such as b-series gangliosides (GD2, GD3, GD1b, and GT1b), that have been detected in patients with acute sensory 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 antibodies 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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