

## A case of atypical Miller Fisher syndrome with negative anti-GQ1b immunoglobulin G and importance of H reflex

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### To the Editor

Miller Fisher syndrome (MFS) is characterized by ophthalmoplegia, ataxia and areflexia<sup>1</sup>. The disease is strongly associated with anti-GQ1b immunoglobulin (Ig)G antibodies<sup>2</sup>. The clinical diseases associated with anti-GQ1b IgG antibodies are diverse. Anti-GQ1b IgG antibodies have been found in cases with acute ophthalmoplegia without ataxia as well, and these patients have been designated as having atypical MFS<sup>3</sup>. Electrophysiological abnormalities in MFS include selectively or globally abnormal motor nerve conduction velocity, sensory nerve conduction velocity, F waves, and H reflex<sup>4</sup>. In some patients, absence of H reflex may be the sole abnormality in MFS<sup>5</sup>. Here, we report a patient with negative anti-GQ1b IgG antibodies who presented with diplopia. He also had areflexia despite no signs of weakness, and absence of H reflex was the sole electrophysiological abnormality.

A 14-year-old boy presented with a three-day history of binocular diplopia and easy fatigability. He had a history of upper respiratory tract infection one week before presentation. On examination, he was conscious. Muscle power and tone were normal, but with areflexia in lower limbs. Babinski sign was negative. There was no ataxia, and the cerebellar examination was normal. Bilateral esotropia in primary position and abducting nystagmus of internuclear ophthalmoplegia on bilateral horizontal gaze were present. Convergence was also limited, especially in the left eye. Pupils were reactive to light and normal in size. Visual field (confrontation) testing and optic disc were normal. The findings were compatible with bilateral sixth nerve and left medial longitudinal fasciculus involvement. All other cranial nerves were normal. Cranial and spinal magnetic resonance imaging revealed no abnormality. Cerebrospinal fluid examination was acellular with protein and glucose contents of 30 mg/dl and 60 mg/dl (simultaneous

blood glucose of 90 mg/dl), respectively. Cerebrospinal fluid IgG index was mildly elevated (0.88 [0.3-0.7]). Serology for Brucella, Salmonella, Mycoplasma, Chlamydia, TORCH, and Epstein-Barr virus (EBV) revealed no abnormality. Cerebrospinal fluid examinations for herpes simplex virus, varicella zoster virus, enterovirus, and adenovirus were also negative. Motor conduction nerve studies, sensory nerve conduction studies, and F waves were normal, but H reflexes were absent. Anti GM1, GQ1b, GD1b, GT1b, GD1a, GM3, and GM2 antibodies were negative. After intravenous immunoglobulin treatment, diplopia improved within one week, and reflexes, including H reflex, reappeared within two weeks.

Anti-GQ1b IgG antibody syndromes comprise a wide range of disorders including MFS, acute ophthalmoplegia associated with Guillain Barré syndrome, isolated ophthalmoplegia, and Bickerstaff brainstem encephalitis<sup>6</sup>. MFS is a variant of Guillain Barré syndrome, which is characterized by ophthalmoplegia, ataxia and areflexia. Motor strength is usually preserved. MFS is strongly associated with anti-GQ1b IgG antibodies, but some patients are negative for these antibodies<sup>4,6</sup>. The rate of positivity of anti-GQ1b IgG antibodies in patients with MFS is 85%<sup>7</sup>. Anti-GQ1b IgG antibodies have been found in patients with ophthalmoplegia without ataxia as well, and these patients are designated as having atypical MFS<sup>3</sup>. The negativity of anti-GQ1b IgG antibodies does not exclude the diagnosis of MFS. We also designated our case as atypical MFS because he presented with acute ophthalmoplegia without ataxia, and his motor strength was also preserved. Detailed examinations for ganglioside antibodies were also negative. Isolated absence of H reflex is an important electrophysiological finding in MFS<sup>5</sup>. The absence of H reflex points to a demyelinating event in proximal conduction by selective involvement of group 1a neurons. In MFS,

anti-GQ1b IgG antibodies lead to destruction of paranodal regions of oculomotor nerves and neurons of the dorsal root ganglia. The absence of H reflex has also been suggested to reflect a demyelinating process near the dorsal root ganglia because a dorsal root ganglion does not have a blood-nerve barrier<sup>8</sup>. Absence of this barrier permits circulating antibodies to reach the gangliosides of the dorsal root ganglia. Our patient had negative ganglioside antibodies, but there may be other antibodies affecting both the eyes and proximal nerve conduction. Another important finding in our case was the fast recovery of ophthalmoplegia and deep tendon reflexes after immunoglobulin treatment. In conclusion, this case may represent a spectrum of atypical MFS with negative ganglioside antibodies and fast recovery. Absence of H reflex may be an important diagnostic clue in

the examination of such cases.

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