Rare Recurrence of Miller Fisher Variant of Guillain Barré

Jessica Rakonza, MD
Virginia Mason Medical Center, Seattle, WA

BACKGROUND

Guillain Barré syndrome (GBS) is an acute immune-mediated polyneuropathy, typically with a preceding infection. Its clinical presentation is classically characterized by progressive, ascending muscle paralysis; but it is a heterogeneous condition with variable presentations. Miller Fisher syndrome (MF) is a variant of GBS characterized by ophthalmoplegia, ataxia, and areflexia and represents approximately 10% of GBS cases in the United States and Europe and 20% in Asia. The incidence of MF is approximately 1 in 1,000,000.[1] There is limited data about the incidence of recurrence or the risk factors that may predispose certain patients.

This case of MF recurrence presented with acute, atypical symptoms that rapidly progressed to the point of requiring intensive care. But early detection and initiation of appropriate treatment resulted in the avoidance of life-threatening complications.

Subtypes and variants	IgG autoantibodies to
Guillain–Barré syndrome	
Acute inflammatory demyelinating polyneuropathy	None
Facial variant: Facial diplegia and paresthesia	None
Acute motor axonal neuropathy	GM1, GD1a
More and less extensive forms	
Acute motor–sensory axonal neuropathy	GM1, GD1a
Acute motor-conduction-block neuropathy	GM1, GD1a
Pharyngeal–cervical–brachial weakness	GT1a > GQ1b >> GD1a
Miller Fisher syndrome	GQ1b, GT1a
Incomplete forms	
Acute ophthalmoparesis (without ataxia)	GQ1b, GT1a
Acute ataxic neuropathy (without ophthalmoplegia)	GQ1b, GT1a
CNS variant: Bickerstaff's brain-stem encephalitis	GQ1b, GT1a

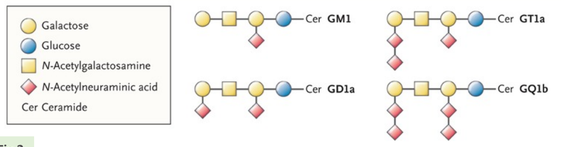

Fig 2

Antibodies associated with variants of Guillain Barré syndrome and their ganglioside structures.[3]

Fig 1a

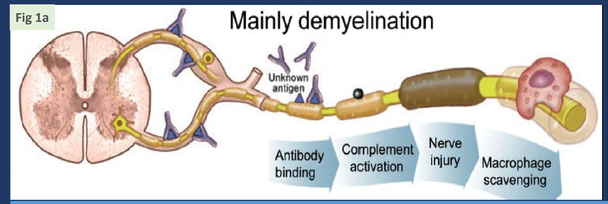

Fig 1b

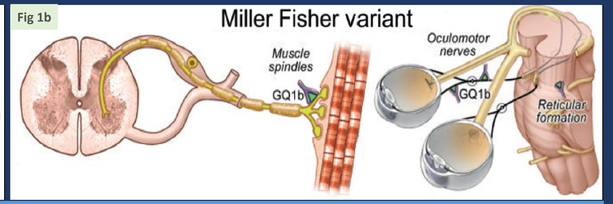

Fig 1a,b[4]: Pathogenesis of GBS is believed to be due to cross-reactivity of immunoglobulins formed in response to preceding infection with components of peripheral nerves, including myelin sheaths and axonal elements. Both cellular and humoral immune responses lead to macrophage-mediated demyelination. In the Miller Fisher variant, the characteristic presence of ophthalmoplegia is believed to be due to an antibody against the GQ1b ganglioside concentrated at the neuromuscular junction between the cranial nerves and ocular muscles. 70-90% patients will present with a positive GQ1b antibody. GQ1b is a ganglioside located at the neuromuscular junction between the cranial nerves and ocular muscles. 70-90% of Miller Fisher patients will test positively for anti-GQ1b on ELISA.[2]

CASE DESCRIPTION

Patient was a 51-year-old man with prior history of Miller Fisher (MF) variant of Guillain Barré syndrome in 2009 who was initially admitted to the hospital for an acute gout flare. Overnight after admission, he reported mild dysphagia, slurred speech, a nasal voice, and a feeling of right-sided lid lag. Examination in the morning was remarkable for a notably nasal voice, mildly limited lateral and upward gaze bilaterally, and absent deep tendon reflexes in the lower extremities. Speech therapy evaluation confirmed oral-pharyngeal phase dysphagia.

CT Head and MRI Brain were negative. LP was performed, CSF studies were unremarkable. Antibodies for Miller Fisher and Myasthenia Gravis were sent out, and empiric treatment with IV immunoglobulin was initiated. His course rapidly progressed with worsening of his dysphagia and dysphonia with new development of diplopia, ptosis, and numbness in his hands and feet. On hospital day 4, he developed autonomic instability with bradycardia and had an acute drop in his negative inspiratory force. He was transferred to the CCU and plasma exchange therapy (PLEX) was initiated. His symptoms gradually improved after three treatments, and his labs returned with a highly-positive Anti-GQ1b titer of 1:12,800, confirming recurrence of MF.

He ultimately completed seven PLEX treatments before discharge. At discharge, he had returned to a regular diet, but with ongoing diplopia, foot numbness, and persistent right-sided lid lag. On outpatient Neurology follow up three months after discharge, his only remaining deficit was mild diplopia at the extremes of lateral gaze.

DISCUSSION

Little is known about the incidence of MF recurrence, patterns of timing or severity of recurring symptoms, or potential risk factors that might predispose certain patients to having future episodes. This patient's presentation was initially not thought to be suggestive of Miller Fisher and other entities such as Myasthenia Gravis (MG) were favored over a recurrence of his MF. This was partially because of the atypical presentation, but also because of the rarity of recurrences.

This case was a reminder that although GBS and its variances are most classically monophasic, recurrences, while extraordinarily rare, can occur. It was also an exercise in building a differential based on initially vague neurologic symptoms and ordering appropriate serology. And while it is important to establish a definitive diagnosis, it should not delay initiation of treatment, which is critical to prevent progression to life-threatening muscle weakness and dysautonomia.

Serum Test	Result
Acetylcholine Receptor Ab	<15% inhibited
ACh Receptor (Muscle) Binding Ab	0.00 nmol/L
Muscle Specific Kinase Autoantibody	0.00 nmol/L
Ganglioside GQ1b antibody	**1:12,800 titer**

List of antibodies sent for our patient to test for MG versus MF. Results confirming Miller Fisher recurrence with high anti-GQ1b titer.

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