Miller Fisher Syndrome
A variant of Guillan Barré Syndrome

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1859
Jean Baptiste Octave Landry de Thézillat (1826-1865) published his observation on ‘ascending paralysis’ in the Gazette hebdomadaire de médecine et de chirurgie, 1859, 6: 472-474
1916
Guillain, Barré and Strohl (who did the original electrophysiological studies and whose name later is omitted from the syndrome), describe their observations of two soldiers with partial paralysis, reduced reflexes, raised CSF protein but without pleocytosis, followed by a quick recovery ‘possibly assisted by treatment with pork chops and claret’ in Bulletins et mémoires de la Société des Médecins des Hôpitaux de Paris. 1916, 40: 1459-1462
Dr. C. Miller Fisher (1913). Canadian neurologist who practiced most of his life at the Massachusetts General Hospital, Boston, MA.

His major interest was in defining the pathophysiological basis of stroke. This syndrome, named in his honor, was one he stumbled upon by his astute clinical observation but said, “he wasn’t really interested in it”.

GBS Definition

A variety of acute, acquired, immune-mediated, often self-limiting polyneuropathies

Usual clinical findings are

Weakness
Areflexia

History of an inciting event, such as a diarrheal illness or vaccination
Diagnostic Tests

CSF showing a raised protein without accompanying pleocytosis

Electrodiagnostic studies.
Guillain Barre Syndrome (GBS)

Acute inflammatory demyelinating polyneuropathy (AIDP):

Most common form of GBS and is the originally described form of GBS progressive over days to a week, symmetric muscle weakness with absent/decreased deep tendon reflexes. Arm, facial, respiratory and bulbar muscles can also be involved.
GBS Variant (AMAN)

Acute motor axonal neuropathy (AMAN): common in China and Mexico; immune response directed against axoplasm of peripheral motor nerves. Anti-GD3 Ab and anti-GD1a Ab present.
GBS Variants

Acute motor and sensory axonal neuropathy (AMSAN): also affects axons of sensory nerves; often incomplete recovery

Acute panautonomic neuropathy: rare, occasionally with encephalopathy. High mortality due to cardiac dysrhythmias
GBS Variant (BBE)

Bickerstaff’s brainstem encephalitis (BBE): ophthalmoplegia, ataxia, altered consciousness, hyperreflexia. Brain MRI shows brainstem hyperintensities
GBS Variant (MFS)

Miller Fisher Syndrome (MFS): is the most common GBS variant (accounting for 5-10% of GBS cases, with an incidence of roughly 1/1,000,000).

The three cardinal clinical findings are: Ophthalmoplegia, ataxia and areflexia.

There may also be facial weakness and bulbar weakness.
Differential Diagnosis

Brainstem vascular pathology (abrupt onset, impaired consciousness and involvement of motor and sensory tracts)

Wernicke’s encephalopathy

Myasthenia gravis
Differential Diagnosis

Carcinomatous meningitis

Sarcoidosis

Lyme disease

Botulism

Acute intermittent porphyria
Diagnostic Tests

As in GBS:

CSF analysis, elevated CSF protein with normal white cell count, (albuminocytologic dissociation)

CSF usually normal during the first few days of the illness, protein increasing usually after the first week, peak at around week 4;

CSF can be normal in MFS
Diagnostic Tests

Nerve conduction studies (NCS) as in GBS can be normal especially early in the illness.

Test for antibodies: Auto-antibodies against glycolipids.

Anti-GQ1b antibody is helpful in making the diagnosis of MFS.
Most common abnormal NCS

Reduction in the amplitude of muscle action potentials
Slow nerve conduction velocity
Conduction block in motor nerves
Prolonged distal latencies (reflecting distal conduction block)
Most common abnormal NCS

Prolonged or absent F-responses (indicating involvement of proximal parts of nerves and roots) and reflecting focal demyelination.

Delayed or absent H-reflex (confirming the loss of ankle jerks)
Anti GQ1b Antibody

Polyclonal anti-ganglioside Ab of IgM, IgA and IgG classes, found in serum of patient with acute MFS; sensitivity and specificity > 90% (IgG is measured for clinical diagnostic purposes)

Absence of Ab from normal/other disease control groups (but may be present in other GBS variants, such as GBS with ophthalmoparesis, Bickerstaff encephalitis, pharyngo-cervical brachial GBS)

Ab levels peak at presentation, rapid decay with clinical recovery
Anti GQ1b Antibody

Follows a variety of infections, including *Campylobacter jejuni*. Molecular mimicry between GQ1b and C. jejuni lipooligosaccharide seems to be central to pathogenesis (clinical pattern of restricted muscle involvement likely due to patterns of ganglioside expression within specific muscle groups). Some researchers doubt pathogenicity of this antibody.
Anti GQ1b Antibody

Studies underway to identify GQ1b Ab target: this appears to be presynaptically in the neuromuscular junction

Of this antibody in MFS vs association only
Treatment

No control trials to study effect of established treatments for GBS, i.e. plasma exchange or IVIG, in patients with MFS.
Observational Studies

Suggest a generally good prognosis
Japanese study suggesting slightly faster improvement of symptoms after treatment with IVIG but time to symptom resolution similar in IVIG, plasma exchange and control groups
Treatment & Prognosis

Some MFS patients may have swallowing or respiratory problems or develop arm or leg weakness or autonomic instability and in this setting IVIG may be beneficial.

Time to recovery with often complete symptom resolution is in the region of 8-12 weeks.
References

Whonamedit.com

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