Anti-GQ1b antibodies; from discovery to recent research

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Miller Fisher syndrome (MFS) is characterized by the triad of ophthalmoplegia, ataxia, and areflexia. It shares several features with Guillain-Barre syndrome (GBS); acute and self-limited clinical course, frequent presence of antecedent infection, and albuminocytological dissociation in cerebrospinal fluid. Therefore it is considered as a variant of GBS. In 1992, we reported that anti-GQ1b IgG antibody is specifically and frequently (more than 90%) present in the acute-phase sera from patients with MFS. Further examinations revealed that anti-GQ1b antibodies are also detected in the acute-phase sera of GBS with ophthalmoplegia and/or ataxia, "atypical MFS" (ophthalmoplegia without ataxia or ataxia without ophthalmoplegia of acute post-infectious self-limited clinical course), and Bickerstaff's brainstem encephalitis, which has clinical characteristics of MFS and central nervous system involvement. On the other hand, this antibody is never detected in sera from patients with other diseases such as multiple sclerosis and myasthenia gravis even when they have ophthalmoplegia or ataxia.

Anti-GQ1b antibodies may cause ophthalmoplegia by binding to the paranodal myelin of cranial nerves innervating extraocular muscles. Binding of anti-GQ1b antibodies to a subset of neurons in the dorsal root ganglia and muscle spindles may be associated with the development of ataxia. In addition, the inhibitory effect of anti-GQ1b antibodies on neuromuscular transmission was shown in the mouse diaphragm model. We found that GBS patients with anti-GQ1b antibodies more frequently need artificial ventilation than antibody-negative patients. Therefore, presence of anti-GQ1b antibody is a marker predictive of mechanical ventilation in GBS.

Recently, we found antibodies with specificity to a mixture of two ganglioside antigens in the sera of some GBS patients and named such antibodies as antiganglioside complex antibodies. Anti-GQ1b antibodies also can be classified into at least three types; GQ1b-specific, enhanced by the addition of GM1 (GQ1b/GM1 complex- specific), enhanced by the addition of GD1a (GQ1b/GD1a complex-specific). Gangliosides form clusters as rafts in the plasma cell membrane. Interaction of two gangliosides may create new epitopes with conformational changes. Anti-ganglioside-complex antibodies may bind to the new epitopes in ganglioside clusters in the neuronal membrane. To study the pathogenetic roles of anti-GQ1b antibodies, it is necessary to consider environment surrounding GQ1b molecule in the plasma cell membrane.