Antiganglioside Antibodies in Guillain-Barré Syndrome

Gangliosides are glycolipids which contain sialic acid in their carbohydrate portion. There are diverse molecular species determined by the carbohydrate sequence of gangliosides. Gangliosides are rich in the nervous system, localized on the cell surface membrane, and are considered to be involved in the cell-cell interaction, neuritogenesis, synaptic transmission, etc. Each ganglioside molecule is known to have a unique distribution in the nervous system.

See also p 607.

Guillain-Barré syndrome (GBS) is an acute monophasic polyneuropathy usually subsequent to an infectious episode. Frequent elevation of antiganglioside antibodies in the acute phase sera from patients with GBS has recently been reported by several research groups (1). Albuminocytological dissociation (Elevated total protein and normal cell count) in cerebrospinal fluid has been used as a laboratory marker for diagnosis of GBS. However, this finding often cannot be detected within one week after the neurological onset. In contrast, the titer of antiganglioside antibodies in GBS serum is maximum in the sample obtained earliest after the neurological onset and decreases in association with clinical improvement. Those antibodies therefore may be elevated in response to the stimulation to the immune system at the time of the preceding infection and can be used as a useful diagnostic marker for GBS, although negative antibody assay does not rule out the diagnosis of GBS. In addition, considering that gangliosides are cell surface molecules rich in the nervous system, antiganglioside antibodies may be directly involved in the pathogenetic mechanisms. Many factors, both humoral and cellular, may play roles in the pathogenetic mechanisms of GBS (1). Among them, antiganglioside antibodies may serve as factors to determine the distribution of the damage by binding to the respective ganglioside antigens that have unique localization.

The best example is the anti-GQ1b IgG antibody. Frequent elevation of this antibody in the acute phase sera from patients with Miller Fisher syndrome (MFS), which is a variant of GBS with triads of ophthalmoplegia, ataxia and areflexia, was first reported by Chiba et al (2) and later confirmed by other groups. The elevation of IgG anti-GQ1b antibody was also found in the acute phase sera from patients with GBS with ophthalmoplegia; generalized motor-dominant polyneuropathy and ophthalmoplegia (3). Moreover, it was found in acute post-infectious monophasic ophthalmoplegia without ataxia or areflexia, and in cases with the clinical features of MFS and central nervous system involvement. IgG anti-GQ1b antibody is not elevated in the other immunological or neurological diseases, even when there is ophthalmoplegia as in multiple sclerosis and myasthenia gravis. Thus, the elevation of serum IgG anti-GQ1b antibody is most closely associated with acute ophthalmoplegia due to such pathogenetic mechanisms as underlying GBS. This association can be explained by the unique localization of GQ1b. An immunohistochemical study has shown that GQ1b antigenic epitope is localized in the paranodal regions of the extramural portion of the cranial nerves innervating extraocular muscles (oculomotor, trochlear, and abducens nerves), but not in those of the other cranial and peripheral nerves (3). The total ganglioside fractions from the above three cranial nerves showed a higher proportion of GQ1b than those from the other cranial and peripheral nerves. Taken together, IgG anti-GQ1b antibody may play an important role in the pathogenesis of ophthalmoplegia by specifically binding to the paranodal regions of the cranial nerves innervating extraocular muscles.

As the distribution of each ganglioside varies greatly from species to species, an effective animal model of autoimmune neuropathy with antiganglioside antibody is difficult to establish. Induction of experimental sensory ataxic neuropathy has recently been reported by sensitizing rabbits with GD1b ganglioside, which is localized in primary sensory neurons both in humans and in rabbits (4).

Irie et al studied the relationships between the elevation of antibody against gangliosides and the clinical features of GBS using multivariate analysis (5). They confirmed a close association between IgG anti-GQ1b antibody and ophthalmoplegia. They also showed that the presence of anti-GM1 antibody is associated with prodromal diarrhea, which may reflect the preceding infection by Campylobacter jejuni (Cj). Antibody against Cj may cross-react with GM1 in those cases, since the lipopolysaccharide of Cj has been reported to have a GM1-like structure (6). On the other hand, while the association of anti-GM1 antibody and motor disturbance was shown, no relationship between anti-GM1 antibody and the prolonged disability nor the axonal damage was found. Since this has been an issue of controversy, their statistical analysis may be of importance.

Molecular species of gangliosides that are recognized by the acute phase GBS sera are quite varied and have recently been increasing in number. They include such minor components as GalNAc-GD1a and GM1b (7). Further investigation is needed to reveal which antibodies are actually involved in the pathogenetic mechanisms and what part they play. It should give us an important lead to the development of a more effective and specific therapy for GBS.
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References


