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Anti-ganglioside Autoantibody in a Regional Variant of Guillain-Barrė Syndrome

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Guillain-Barre syndrome (GBS) is an immune-mediated peripheral polyneuropathy characterized by acute onset of symmetrical limb weakness and areflexia. Patients with typical GBS have greater *leg than arm* weakness with "ascending" progression. Some, however, have muscle weakness only at the oropharynx, neck, and proximal upper limb muscles, a "descending" pattern of weakness appearing as the illness progresses. Ropper[1] proposed that such patients had a variant of GBS, "pharyngeal-cervical-brachial weakness (PCB)". *Elsewhere* we confirmed by statistical analysis that PCB is a distinct clinical variant of GBS[2].

Gangliosides, important constituents of the plasma membrane, comprise a family of sialic acid-containing glycolipids that are concentrated mainly in the nervous system. In the last decade, autoantibodies against gangliosides have been shown to increase in sera during the acute phase of GBS. The presence of anti-ganglioside antibody is closely related to certain GBS variants. Serum IgG anti-GQ1b ganglioside antibody often is present in Miller Fisher syndrome (MFS)[3], a variant of GBS with the triad of ophthalmoplegia, ataxia, and areflexia. IgG anti-GM1 ganglioside antibody is present in the pure motor variant[4]. A patient with PCB-like symptoms who had anti-GT1a and anti-GD1a IgG antibodies has been reported[5], but which antibody is associated with this PCB variant was not clarified. We assumed that the former antibody is specific for PCB because the latter also is detected in the pure motor variant[6].

We made a prospective search of PCB patients and found 1 with PCB[7]. As expected, this patient had high IgG anti-GT1a antibody titer, as did most patients with MFS. An absorption study, however, showed that the IgG anti-GT1a antibody in the PCB patient was not absorbed by GQ1b ganglioside, whereas the antibody in the MFS patients was. The frequency of positive IgG anti-GT1a antibody did not differ in patients with and without bulbar palsy, a cardinal sign of PCB.

These findings indicate that IgG anti-GT1a antibodies, which do not cross-react with GQ1b, are specific to PCB and provide a diagnostic marker for it. It is important to differentiate PCB from botulism and myasthenia gravis, which have similar clinical features, as plasmapheresis is required treatment for PCB patients. Because IgG anti-GM1b antibody also is present in some PCB patients[8], we should routinely test for serum anti-GT1a and anti-GM1b IgG antibodies in order to select the most efficacious treatment.

GBS is considered a postinfectious disease, and *Campylobacter jejuni*, a leading cause of acute diarrhea, is an antecedent infectious agent in one-third of GBS patients[9]. There is molecular mimicry between the lipopolysaccharides of *C. jejuni* and gangliosides of human nerve tissue[10], and its existence has been hypothesized as being a critical factor in

the onset of GBS. GT1a- and GM1b-like structures are present in both human peripheral nerve and certain strains of *C. jejuni*. Interestingly, most of our PCB patients had a history of gastrointestinal illness before the onset of neurological symptoms. I speculate that the molecular mimicry between *C. jejuni* lipopolysaccharides and nerve tissue gangliosides functions in the induction of anti-GT1a and anti-GM1b IgG antibodies, thereby causing muscle weakness in the region where these epitopes are concentrated. It is necessary to determine the distribution of GT1a and GM1b gangliosides in the human nervous system.

References

1) Ropper, A.H.: Unusual clinical variants and signs in Guillain-Barre syndrome. *Arch. Neurol.*, **43** : 1150-1152, 1986.
2) Koga, M., Yuki, N. and Hirata, K.: Oropharyngeal palsy in Guillain-Barré and Fisher's syndromes is associated with muscle weakness in the neck and arm. *J. Neurol. Neurosurg. Psychiatry*, **66** : 254-255, 1999.
3) Chiba, A., Kusunoki, S., Shimizu, T. and Kanazawa, I.: Serum IgG antibody to ganglioside GQ1b is a possible marker of Miller Fisher syndrome. *Ann. Neurol.*, **31** : 677-679, 1992.
4) Visser, L.H., van der Meche, F.G.A., van Doorn, P.A., Meulstee, J., Jacobs, B.C., Oomes, P.G., Kleyweg, R.P. and the Dutch Guillain-Barre study group: Guillain-Barre syndrome without sensory loss (acute motor neuropathy) : a subgroup with ' specific clinical, electrodiagnostic and laboratory features. *Brain*, **118** : 841-847, 1995.
5) Mizoguchi, K., Hase, A., Obi, T., Matsuoka, H., Takatsu, M., Nishimura, Y., Irie, F., Seyama, Y. and Hirabayashi, Y.: Two species of antiganglioside antibodies in a patient with a pharyngeal-cervical-brachial variant of Guillain-Barre syndrome. *J. Neurol. Neurosurg. Psychiatry*, **57** : 1121-1123, 1994.
6) Yuki, N., Yoshino, H., Sato, S., Shinozawa, K. and Miyatake, T.: Severe acute axonal form of Guillain-Barre syndrome associated with IgG anti-GD1a antibodies. *Muscle Nerve*, **15** : 899-903, 1992.
7) Koga, M., Yuki, N., Ariga, T., Morimatsu, M. and Hirata, K.: Is IgG anti-GT1a antibody associated with pharyngeal-cervical-brachial weakness or oropharyngeal palsy in Guillain-Barre syndrome ? *J. Neuroimmunol.*, **86** : 74-79, 1998.
8) Koga, M., Yuki, N. and Hirata, K.: Antiganglioside antibody in patients with Guillain-Barre syndrome who show bulbar palsy as an initial symptom. *J. Neurol. Neurosurg. Psychiatry*, **66** : 513-516. 1999.
9) Koga, M., Yuki, N., Takahashi, M., Saito, K. and Hirata, K.: Close association of IgA anti-ganglioside antibodies with antecedent *Campylobacter jejuni* infection in Guillain-Barre and Fisher's syndromes. *J. Neuroimmunol.*, **81** : 138-143, 1998.
10) Yuki, N., Taki, T., Inagaki, F., Kasama, T., Takahashi, M., Saito, K., Handa, S. and Miyatake, T.: A bacterium lipopolysaccharide that elicits Guillain-Barre syndrome has a GM1 ganglioside-like structure. *J. Exp. Med.*, **178** : 1771-1775, 1993.