CASE REPORT

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A Variant Guillain-Barré Syndrome with Anti-Ganglioside Complex Antibody

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Background: Recently, anti-ganglioside complex (GSC) antibodies were discovered among the various subtypes of Guillain-Barré syndrome. GSC is the novel glycoepitopes formed by two individual ganglioside molecules.

Case Report: We present a 36-year-old man with overlap Miller Fisher syndrome and acute bulbar palsy who had anti-GSC antibody that provided diagnostic robustness.

Conclusion: Anti-GSC testing could be considered important in patients who show atypical manifestation with negative antibody reaction against each constituent ganglioside.

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Key words: Guillain-Barre syndrome; Miller Fisher syndrome; Antibodies; Gangliosides

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INTRODUCTION

Anti-ganglioside antibodies are mostly found in Guillain-Barré syndrome (GBS) and its variants. Besides the progression of research on anti-glycolipid antibodies, the presence of these antibodies assist in the diagnosis of rare or unusual variants of GBS. Recently, anti-ganglioside complex (GSC) antibodies were discovered among some cases of GBS that do not have antibody against a single ganglioside. This could expand the phenotypic spectrum of GBS. The current case showed the diagnostic utility of anti-GSC antibodies in an atypical variant with Miller Fisher syndrome (MFS) overlap and acute bulbar palsy (ABP) which did not have significant antibody reactivity against each single ganglioside including GQ1b and GT1a.

CASE REPORT

A 36-year-old man was admitted with diplopia, oral paresthesia, dysarthria and gait disturbance 7 days after suffering from a common cold. On admission, the patient complained of paresthesia and pain on the upper back and limbs. Neurological examination revealed left medial rectus palsy, bifacial weakness, loss of taste sensation, dysphagia and dysarthria. Apart from vibration, pinprick,

temperature and proprioception were normal. Vibration sensation were impaired in the bilateral lower extremities. Motor strength was normal in extremities. Deep tendon reflexes were absent with the exception of bilateral trace biceps jerk. The patient was unable to stand without assistance due to severe gait ataxia.

Initial vital capacity was within normal limits (4 L). The nerve conduction study on limbs showed no significant concern, while blink reflex test suggested right facial nerve lesion. Brain magnetic resonance imaging also showed unremarkable finding except for maxillary sinusitis. Cerebrospinal fluid (CSF) analysis showed mild pleocytosis (white blood cell [WBC] count of 15/μL, poly 52%, lymphocyte 40% and a red blood cell count of 5/μL), normal glucose level of 62 mg/dL and mildly increase protein level of 66 g/dL. Extensive evaluation of infection causes (including blood culture, CSF culture, human immunodeficiency virus, herpes simplex virus, varicella zoster virus, syphilis, mumps, and acid-fast bacillus test) were unrevealing.

Ig (immunoglobulin) M and IgG anti-ganglioside antibody test using enzyme linked immunosorbent assay (ELISA) with acute stage serum against each single ganglioside GM1, GM2, GD1a, GD1b, GD3, GT1a, GT1b and GQ1b as described elsewhere showed only equivocal positive to IgG anti-GQ1b antibody.[1] Additional evaluation for the anti-GSC antibodies was performed on various subset of ganglioside complexes such as GM1/GT1a, GD1a/GT1a, GD1b/GT1a, GT1b/GT1a, GM1/GQ1b, GD1a/GQ1b, GD1b/GQ1b, GT1b/GQ1b based on the patient's main neurological problem. Each ganglioside was used with half amount of conventional single ELISA for complex study. The results were strongly positive to IgG anti-GM1/GT1a (3+), GM1/GQ1b (3+), GD1b/GQ1b (2+) and GD1a/GT1a (1+) (semi-quantitative titer using subtracted optical density [OD] decided as follows; OD 0.1-0.29 as 1+, OD 0.3-0.49 as 2+, OD 0.5-0.99 as 3+ and OD more than 1.0 as 4+). Under the clinical diagnosis of variant form of GBS, whose findings were overlap of MFS and ABP, the patient was subsequently treated with intravenous immunoglobulin (IVIg) (400 mg/day for 5 days). Even with the treatment, his neurological condition continued to worsen and showed more pronounced ophthalmoplegia, progressive limb weakness (Medical Research Council grade 3 in both upper extremities and 4 in both lower extremities) and the vital capacity decreased to 2 L. The nadir of the patient's signs and symptoms was reached by the 7th day in hospital. Three days after completing IVIg, his neurological condition started to improve rapidly. The patient was able to ambulate without assistance by the 10th day in hospital. His ocular symptoms had been the slowest to resolve 1 month after the symptoms onset.

DISCUSSION

Clinical manifestations such as MFS, pharyngeal-cervical-brachial variant and ABP are varied in acute immune mediated polyneuropathy including GBS and GBS variants.[2,3] Therefore, clinical history and neurologic examination may have limited diagnostic utility when the patients has atypical presentation or overlapping symptoms.

Electrophysiological study has a central role for differential diagnosis and shows evidence of nerve conduction abnormalities. However, the electrical abnormality may be insufficient for definite diagnosis for the first 2 weeks of GBS contraction.[4,5] Like other diagnostic marker, serum anti-ganglioside antibody assay facilitate the diagnosis of GBS and have wide recognized clinical significance.[1,6] Although, test results are not always available at the time of diagnosis, anti-ganglioside antibodies are able to provide a better understanding of pathophysiology and diagnostic relevance. However, antibodies to gangliosides are not present in the sera of approximately 40-50% of the patients with GBS.[1,7] Recent studies have demonstrated that the ganglioside mixture consisting of two different gangliosides in sera among the patients with GBS.[7-9] Kaida et al.[9] reported that antibodies to a GSC may affect the function of axon or Schwann cell through binding to clustered epitopes of glycosphingolipids in the plasma membrane. Therefore, they may induce nerve conduction failure and severe disability in patients with GBS.

In presenting this case, initial symptom were those of

ABP that shares features with either the MFS or ABP. IgG anti-GQ1b antibody is specifically associated with MFS, and anti-GT1a antibody without GQ1b reactivity is essential for the occurrence of bulbar palsy in patients with GBS. However, the patient's serum IgG binds strongly to GSCs such as GM1/GT1a, GM1/GQ1b, GD1b/GQ1b and GD1a/GT1a, but only equivocally to GQ1b. Previous studies reported that IgG antibodies to at least one GSC including anti-GM1/GQ1b, GM1/GT1a, GD1b/GQ1b, GD1b/GT1a are present in 41% of MFS and 28% of GBS with ophthalmoplegia accompanying sensory dysfunction.[6] Additionally, antibodies to GD1a/GQ1b, GD1a/GT1a, GT1b/GQ1b, GT1b/GT1a are present in 6% of MFS and 19% of GBS with ophthalmoplegia.[6] Therefore, anti-GSC antibodies in present study seem to be associated with clinical symptoms overlapping MFS and ABP.

Since the patients showed fever and CSF pleocytosis, present case had additional diagnostic difficulties. For pleocytosis on CSF (polymorphonuclear granulocytes 50%) an alternative diagnosis should be considered. Many viral infections and CNS demyelinating disease such as acute disseminated encephalomyelitis can clinically mimic GBS. However, Wong et al.[10] reported that the prevalence of mild pleocytosis (WBC 6-50/μL) was approximately up to 26% of GBS and 11% of MFS. At this point, pleocytosis on CSF in the present case does not preclude the diagnosis of variant GBS.

In summary, we present a rare case of a variant GBS with pleocytosis who have complex anti-ganglioside antibody that help a diagnostic robustness. Further studies are needed to clarify the relationship between complex anti-ganglioside antibodies and characteristic phenotypes.

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