Rapidly Progressive Guillain-Barré Syndrome Following *Escherichia coli* Infection

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**Abstract**

Guillain-Barré Syndrome (GBS) is a prototype of post-infectious autoimmune disease. A 76-year-old woman was treated for a renal abscess and developed muscle weakness in all four extremities, 18 days after the onset of infection. She was diagnosed with GBS on the basis of acute flaccid paralysis, hyporeflexia, nerve conduction studies (reduced amplitude of compound muscle action potentials), and high titers of IgG antibodies to GM1 and GalNAc-GD1a. GBS rarely occurs after sepsis and this case represents the first report of rapidly progressive GBS following *Escherichia coli* urosepsis.

**Key words:** Guillain-Barré syndrome, *Escherichia coli*, GM1, GalNAc-GD1a, immunoabsorption

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**Introduction**

GBS, characterized by acute flaccid paralysis and areflexia, is a prototypical post-infectious autoimmune disease. Most GBS patients have gastrointestinal or upper respiratory symptoms 1-3 weeks prior to the onset of limb weakness. Motor strength usually reaches its nadir within 4 weeks (1). *Campylobacter jejuni* (C. jejuni), cytomegalovirus, and Epstein-Barr virus have all been implicated frequently in the pathogenesis of GBS. Here, we report a 76-year-old woman who developed rapidly progressive GBS with high titers of IgG antibodies to GM1 and GalNAc-GD1a, 18 days after sustaining urosepsis due to *Escherichia coli* (E. coli). GBS preceded by *E. coli* urosepsis has not been previously reported.

**Case Report**

A 76-year-old female presented with one week of fever reaching 38°C, accompanied by vomiting and frequent urination. Prior to that, she was in her usual state of health. She had a history of hypertension, idiopathic thrombocytopenia, and stroke.

On admission, her temperature was 39.1°C, heart rate was 119/min and blood pressure was 77/48 mmHg. Coarse crackles were heard bilaterally at the lung bases. A III/VI systolic ejection murmur, heard at the cardiac apex, did not radiate. Left-sided costovertebral angle tenderness was present. Her mental status was alert without neurological deficits. Deep tendon reflexes were preserved.

Urinalysis showed pyuria. Cultures of both urine and blood revealed *E. coli* sensitive to cephalosporins. Enhanced abdominal CT revealed a left renal abscess, but no hydronephrosis. She was treated with intravenous cephalosporin and gentamicin. Percutaneous drainage was not necessary.

She improved initially, but on hospital day 10, she developed symmetrical weakness of her lower extremities, which spread to her upper extremities over the next 24 hours. Muscle strength testing on the 11th hospital day revealed 2/5 strength in the arms, and 1/5 strength in the legs. Generalized hyporeflexia was present. Sensory abnormalities and ataxia were absent. Mental status was normal, and cranial nerves II-XII were intact. Vital signs were normal, and there was no respiratory compromise. Nerve conduction studies performed 24 hours after neurological deterioration revealed normal conduction velocities, but reductions in the amplitudes of compound muscle action potentials in the median, ulnar posterior tibial, and peroneal nerves.

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Serum obtained 2 days after the neurological onset was analyzed for IgG and IgM antibodies to gangliosides GM1, GM1b, GD1a, GalNAc-GD1a, GD1b, GT1a, and GQ1b by enzyme-linked immunosorbent assay as described elsewhere with minor modifications (2). Absorbance values at 492 nm were calculated by subtracting the optical densities (ODs) obtained for wells without antigen. Antibody titer was defined as the highest serum dilution at which the OD at 492 nm was 0.1 or more. Serum was considered positive if the titer was 500 or more. High titers of IgG antibodies to GM1 (1:16,000) and GalNAc-GD1a (1:64,000) (normal: less than 500) were detected.

Cerebrospinal fluid (CSF) obtained 20 days after the onset of neurological impairment revealed an elevated protein level (90 mg/dl), but a normal glucose level (62 mg/dl). Cell counts revealed 1 leukocyte/mm² (a monocyte) and no erythrocytes. No organisms were cultured from CSF. No organisms grew in cultures of stool or sputum.

She was diagnosed with acute motor axonal neuropathy (AMAN). Daily immunoabsorption (TR-350 Immusorba® Asahi Medical, Tokyo, Japan) was begun 2 days after the onset of neurological symptoms. Treatment was complicated by hypotension, requiring intravenous fluid resuscitation and catecholamines; thus, immunoabsorption was performed only four times. Nerve conduction studies performed 9 days after the neurological events showed no improvement and muscle strength was hardly improved. At that time, intravenous immunoglobulin (0.4 g/kg) was administered daily for 5 doses. Her muscle strength fluctuated, but appeared to gradually improve. Three months after presentation, she could move from her bed to wheelchair, but no further improvement occurred.

**Discussion**

This case documents the development of post-infectious autoimmune polyneuropathy, which occurred after an infection that does not normally have this consequence. Our differential diagnosis included the critical illness polyneuropathy (3). Her onset of weakness was explosive, and her symptoms were more severe than typical GBS, but the history, physical examination and laboratory data were nonetheless compatible with GBS. Her ascending muscular weakness was notably symmetric, and albumino-cytologic dissociation was present in the CSF.

Two-thirds of patients with GBS have antecedent respiratory or gastrointestinal symptoms. GBS has been reported in the setting of systemic diseases such as sarcoidosis, systemic...
lupus erythematosus (SLE) and lymphoma (4). C. jejuni, cytomegalovirus and Epstein-Barr virus have been frequently implicated in the pathogenesis of GBS, as have Haemophilus influenzae, Mycoplasma pneumoniae, Herpes simplex, and Borrelia burgdorferi (Lyme disease) (5). Antecedent infection with E. coli or antecedent urinary tract infection has never been reported. Molecular mimicry is a mechanism by which infectious agents may trigger an immune response against autoantigens. Gangliosides are composed of glycosphingolipids with one or more sialic acids linked to the carbohydrate moieties. Anti-GM1 IgG antibody is positive in about 30% of GBS occurring after C. jejuni infection. Anti-GM2 IgM antibody is positive in 10% of GBS occurring after cytomegalovirus infection. Molecular mimicry has been found between human GM1 ganglioside and the lipooligosaccharide of C. jejuni isolated from a patient with AMAN (6).

E. coli is an enteric Gram-negative rod and a frequent cause of urinary tract infection. Like all gram-negative bacilli, the capsule of E. coli contains lipopolysaccharide (LPS). However, no data is available addressing the homology between E. coli LPS and the GM1 ganglioside and the GaINAc-GD1α ganglioside. Molecular mimicry is not proven with isolation of a microorganism and the positive infectious serology. Campylobacter coli infection was not the cause of GBS, though Campylobacter coli was isolated from two GBS patients with positive anti-GM1 and anti-GD1 IgG antibodies (7). Further study is needed to investigate the relationship between anti-GM1 and anti-GaINAc-GD1α IgG antibodies and E. coli.

The present patient developed AMAN with positive IgG antibody to GaINAc-GD1α and GM1. Anti-GM1, anti-GM1b, anti-GD1α and anti-GaINAc-GD1α IgG antibodies have been demonstrated in many studies to have a strong association with AMAN. The gangliosides GM1 and GD1b had been investigated frequently. Kusunoki et al reported that GaINAc-GD1α is another target molecule for serum antibodies in AMAN (8). GBS patients with positive IgG antibody to GaINAc-GD1α showed low amplitudes for the compound muscle action potentials, and normal to slightly decreased nerve conduction velocities. One immunohistochemical study revealed that anti-GaINAc-GD1α antibodies purified from anti-GaINAc-GD1α antibody-positive rabbit sera immunostained an inner part of compact myelin. Additional staining occurred on periaxonal-axolemma-related portions of the ventral roots (9). In another study, GalNAc-GD1α is localized specifically in ventral spinal roots, but not in dorsal spinal roots (10). Anti-GaINAc-GD1α IgG antibody is positive in about 10% of GBS, especially GBS following campylobacter infections. Antibody positive cases typically have an uncommonly severe, rapidly progressive course, with predominantly distal weakness and little sensory and cranial nerve involvement (11).

We report a case of a 76-year-old woman who developed rapidly progressive GBS with high titers of IgG antibodies to GM1 and GaINAc-GD1α, 18 days after sustaining urosepsis due to E. coli. This is the first report of rapidly progressive GBS following E. coli urosepsis.

References


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