Severe Guillain-Barré Syndrome Associated With *Campylobacter jejuni* Infection With Failure to Respond to Plasmapheresis and Immunoglobulin

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Guillain-Barré syndrome is a subacute inflammatory demyelinating polyradicular neuropathy of the peripheral nerves. It is characterized by varying degrees of weakness, sensory abnormalities, and autonomic dysfunction. The cause of Guillain-Barré syndrome is not completely understood, but it is believed to be a postinfectious autoimmune disorder, because approximately two thirds of all cases are preceded by an infection, such as those caused by human immunodeficiency virus, cytomegalovirus, Epstein-Barr virus, and *Campylobacter jejuni*. Occasionally Guillain-Barré syndrome has been reported to come after vaccinations of various types. *C jejuni* infection, thought to be the most common antecedent infection to Guillain-Barré syndrome and the only bacterial infection that regularly precedes it, has been implicated in 50 to 75 percent of all cases. Culture studies have proved that a high proportion of patients with Guillain-Barré syndrome have *C jejuni* infection in their stools at the time of the onset of neurologic symptoms as well.

We describe a case of Guillain-Barré syndrome associated with gastrointestinal *C jejuni* infection. This case not only highlights the clinical aspects of Guillain-Barré syndrome but also illustrates the severity of this neurologic syndrome and the lack of response to both plasmapheresis and immunoglobulin therapy.

**Case Report**

A 37-year-old man came to the hospital complaining of weakness in the lower extremities. Five days earlier he had developed nausea, vomiting, and diarrhea associated with fever and chills after eating a hamburger from a fast-food restaurant. The gastrointestinal symptoms subsided after 3 days but recurred 2 days later, at which time he consulted a physician, who prescribed an oral cephalosporin. His gastrointestinal symptoms did not resolve, and on the night before admission, he had returned to the emergency department complaining of inability to urinate. A urethral Foley catheter was inserted, and approximately 900 cc of urine was obtained. He was given 2 g of ceftriaxone intramuscularly and sent home with a diagnosis of neurogenic bladder and follow-up instructions to see a urologist. He was readmitted the next day, however, because he had become progressively weaker and was unable to walk.

When the patient was admitted 72 hours after being seen in the emergency department, he was paralyzed in all four limbs. He had no history of recent travel, exposure to toxins, recent immunization, or shellfish ingestion. His temperature was 101°F, blood pressure 120/58 mmHg, respiration 20/min, and pulse 67 beats per minute. Findings during the physical examination were essentially unremarkable except for obvious quadriplegia. He had grade 0/5 power in his upper extremities and grade 2/5 power in his lower extremities at the time of admission, and all deep tendon reflexes were absent.

Results of laboratory studies at the time of admission included a white blood cell count of 6700/μL with a normal differential (presumably as a result of previously administered antibiotics) and normal serum electrolytes. Antinuclear antibodies were negative. Thyroid-stimulating hormone levels were normal, as were findings from protein electrophoresis.

Stool cultures done at admission were positive for *C jejuni*, and the immunoglobulin (Ig) M and IgG *C jejuni* antibody titers by enzyme immunoassay were 10:2 SD. Cerebrospinal fluid recovered from a spinal tap had a total protein of 50 mg/dL, glucose 54 mg/dL, and a white blood cell count of 56 per high-powered field. There was no evidence of infection, either bacterial or viral. Findings on a computed tomographic scan and
magnetic resonance imaging of the brain and cervical spine were normal. Results of an electromyogram and nerve conduction studies showed loss of conduction velocity in multiple nerves in both the upper and lower extremities, which was consistent with Guillain-Barré syndrome.

Hospital Course
When he was admitted to the hospital, the patient was given a combination of erythromycin and ciprofloxacin, which was continued for 14 days. Although his gastrointestinal complaints resolved, he developed progressive respiratory paralysis requiring mechanical ventilation and intubation. His hospital course was complicated by nosocomial pneumonia, which was successfully treated. He required a tracheostomy about 3 weeks into his hospitalization and was weaned from the ventilator about 8 weeks after hospitalization.

At the time he was hospitalized, the patient was initially treated with plasmapheresis and intravenous immunoglobulin. The plasmapheresis was repeated four more times after admission, and he received three more doses of intravenous immunoglobulin following his hospitalization. There was no demonstrable improvement in the patient’s neurologic status, however. Repeated nerve conduction studies yielded no new information. He was finally transferred to the rehabilitation unit, and 8 months into his hospitalization remained quadriplegic with no major improvement. Repeated C. jejuni IgG titers were 1:5 SD.

Discussion
The reservoir for most Campylobacter species has been animals, including both wild and domesticated (poultry, cattle, sheep, swine), which carry the organisms in their intestinal contents. The pathogen is highly susceptible to heating, but infections can be acquired by eating undercooked meat or through cross-contamination of kitchen utensils and surfaces. Poultry is the most important reservoir, and several studies indicate that 50 to 70 percent of sporadic infections are due to this source. Consumption of unpasteurized milk can also result in sporadic or epidemic cases, and untreated or improperly treated water has been a vehicle for several large outbreaks of infection.

Person-to-person transmission is rare, though there are a few exceptions. One is perinatal transmission from mother to child, presumably as a result of the infant’s passage through the birth canal; in these instances the mothers are not necessarily symptomatic. The second is transmission from infants or other persons who are incontinent of feces to their caregivers. There is little transmission between adults except among homosexual men.

In most developed countries Campylobacter infection occurs year-round, peaking in summertime. Men and women are infected at similar rates, although some evidence suggests women might be at a slightly higher risk. The highest age-specific attack rates are in young children, especially those younger than 1 year, but a second broad peak occurs in persons aged from 15 to 29 years. Infection is even more common in developing countries, where children often have 10 or more infections during the first 2 years of life. With age the attack rate decreases, and an increasing proportion of infections are clinically silent.

C. jejuni often causes acute febrile gastroenteritis with a prodromal period of 24 hours or less in which constitutional signs are predominant. The most common signs and symptoms during the intestinal phase are diarrhea, abdominal pain, and fever. The diarrhea can vary from a few loose stools to massive watery or grossly bloody stools.

Bacteremia, which is rarely observed in part because blood cultures often are not performed and because the organism is fastidious, is most common at the extremes of age and among immunocompromised hosts. Extraintestinal C. jejuni infection has been described as occurring in three major patterns. The first, transient bacteremia in a previously normal host, is often discovered by isolation from blood cultures days after the patient has recovered. Such patients generally need no treatment. The second is sustained bacteremia or seeding of an extraintestinal site accompanying the enteritis in a normal host. Responses to antimicrobial therapy and drainage procedures usually are good. Third, bacteremia or deep infection can occur in immunocompromised hosts. These infections tend to be prolonged or recurrent, and some are fatal. Some of the other common extraintestinal sites include the meninges, endovascular tissue including the heart valve, peritoneal fluid, and soft tissues, but numerous other sites have been reported as well.

Nonsuppurative complications of C. jejuni infections include reactive arthritis in persons posi-
tive for human leukocyte antigen (HLA)-B27, hepatitis and interstitial nephritis, a truncal macular rash, and Guillain-Barré syndrome.

The first case of C. jejuni-associated Guillain-Barré syndrome was described in 1984; since then several other reports have been published. The organism is described as a gram-negative bacteria of the genus Campylobacter and of related genera. This species appears to colonize frequently in the gastrointestinal tracts of humans, other mammals, and birds. The high incidence of C. jejuni infections and their propensity to invade tissue and induce inflammation are compatible with the role in the causation of Guillain-Barré syndrome.

C. jejuni infection has been implicated in 50 to 75 percent of all cases of Guillain-Barré syndrome. The first line of evidence supporting Campylobacter infection as a trigger of Guillain-Barré syndrome is anecdotal reports. The second line of evidence is serologic surveys that have found anti-C. jejuni antibodies in serum from patients with Guillain-Barré syndrome, a finding consistent with recent infection. Finally, culture studies have proved that a high proportion of patients with Guillain-Barré syndrome have C. jejuni in their stools at the time of onset of neurologic symptoms. In addition, neurologic symptoms have been reported to be more severe and more likely to be reversible when Guillain-Barré syndrome is preceded by C. jejuni infection.

The combination of recent C. jejuni infection and positive antigangliocytie GM1 heralds a poor prognosis. The risk of developing Guillain-Barré syndrome after infection with Campylobacter is actually quite low. The Centers for Disease Control and Prevention estimates there are 1000 cases of C. jejuni infection per 100,000 population per year. National Center for Health Statistics hospital discharge data documented 7874 cases of C. jejuni infection in the United States in 1995; therefore, it is possible that 30 percent of Guillain-Barré syndrome cases are preceded by C. jejuni infection. The risk of developing Guillain-Barré syndrome might be higher after infection with C. jejuni type O:19. Of 12 C. jejuni isolates from Japanese Guillain-Barré syndrome patients, 10 yielded the type O:19. This O:19 type represents less than 2 percent of C. jejuni isolates from patients who had uncomplicated enteritis in Japan.

The treatment of Campylobacter-associated Guillain-Barré syndrome continues to remain problematic. In a study that compared intravenous immunoglobulin with plasma exchange, the two treatments were comparable; in fact, intravenous immunoglobulin might be slightly superior to plasma exchange. The use of plasmapheresis and immunoglobulin is based on the ability of immunoglobulin therapy to reduce the need for mechanical ventilation and the number of treatment complications. In addition, studies of treatment with plasma exchange show there might be related fluctuations in disease severity in about 10 percent of the patients. This finding has also been supported by a study by Vriesendorp and colleagues, who noted that 6 patients in the plasma exchange group and 8 in the immunoglobulin group had variations in their clinical course. In both groups the patients responded to repeated treatments.

Plasma exchange also has been found to decrease the need for hospital care, and the cost savings were greater than the cost of therapy. In this particular trial, the median time until the recovery of independent locomotion, a reasonable time for hospital discharge, was 14 days less in the immunoglobulin-treatment group than in the plasma-exchange group. In addition, the median time of intubation was 7 days less than in the immunoglobulin group, reflecting a similar decrease in days spent in the intensive care unit.

C. jejuni is susceptible in vivo to a variety of antimicrobial agents, including macrolides, tetracyclines, quinolone, the aminoglycosides, Chloramphenicol, and nitrofurantoin. Fewer than 5 percent of human C. jejuni isolates in the United States are resistant, but Campylobacter coli, Campylobacter cinaedi, and those isolates from developing countries more often are. Nearly all patients recover fully from the enteric Campylobacter infections, whether spontaneously or after antimicrobial therapy. In developed countries there have been occasional deaths, especially in elderly or immunocompromised patients. In developing countries a great number of infections very early in life until immunity supervenes probably contributes to the high morbidity and mortality rates associated with diarrheal diseases. Developing a vaccine for such populations is, therefore, a worthwhile goal. In developed countries avoiding under-
cooked or uncooked animal products is an important preventive measure.

This case highlights several interesting features of Guillain-Barré syndrome and *C. jejuni* infection. From an epidemiologic standpoint it appears to be a classic case: it occurred in a man (male to female ratio is 3:1), it occurred during the autumn season, and paralysis began within 1 week of the gastrointestinal disease. The patient was seropositive for *C. jejuni*, both IgM and IgG (positive stool cultures occur in 50 to 75 percent of the patients). The *C. jejuni* was found to be sensitive to the antibiotics used, yet the disease continued to progress despite appropriate antibiotics, plasmapheresis, and intravenous immunoglobulin. Finally, despite treatment with plasmapheresis and the immunoglobulin therapy, the patient remained quadriplegic 8 months later.

**References**