Infections in Oncology

CAMPYLOBACTER JEJUNI BACTEREMIA IN AN HIV-POSITIVE PATIENT WITH NON-HODGKIN’S LYMPHOMA

Charles Callahan, MD; John N. Greene, MD; Ramon L. Sandin, MD; Dawn Ruge, MT (ASCP); and Jeff Johnson, BS, MT (ASCP)

Department of Medicine, Division of Infectious and Tropical Diseases and Pathology, University of South Florida College of Medicine, and H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida

Introduction

Campylobacter is a micro-aerophilic, motile, nonspore-forming, comma-shaped, Gram-negative rod. Since 1974, it has been recognized as a pathogen with ubiquitous animal reservoirs. Routes for infection in developed countries typically involve consumption of milk, swine, or poultry. Signs and symptoms of infection include moderate to high fever, diarrhea (50% bloody), headache, abdominal pain, and nausea. The peak incidence occurs in the summer and early fall, and bacteremia most often occurs in the very young and the very old. While enteritis is more commonly caused by C. jejuni, bacteremia is more often due to C. fetus. In one survey, bacteremia was noted in only 24 of 6,402 C. jejuni isolates vs 22 of 35 C. fetus isolates. We report a case of C. jejuni bacteremia in an HIV-positive patient with non-Hodgkin’s lymphoma that was originally identified as Eikenella corrodens by a commercial automated identification system. The significance of virulence factors, host immunity, and identification methods for C. jejuni are also discussed.

Case Report

A 34-year-old HIV-positive man with non-Hodgkin’s lymphoma (diffuse large-cell type) presented with fever, chills, mild productive cough, lower abdominal pain, and fullness without diarrhea. He had recently received a second cycle of cyclophosphamide, doxorubicin, vincristine, and prednisone. Medications included 100 mg of prednisone per day and G-CSF once per day.

Physical examination revealed a temperature of 102.4°F. The pulse rate was 120 beats per minute, the respirations were 20 breaths per minute, and the blood pressure was 132/62 mmHg. The lungs were clear to auscultation, and no murmurs were noted on heart examination. The abdomen demonstrated mild distention and mild right upper-quadrant tenderness without rebound tenderness. Onychomycosis of the thumbnails and toenails was noted, but no stigmata of endocarditis was seen.

Laboratory data revealed a white blood cell count of 2,000/µL, a hemoglobin level of 7.9 g/dL, and a platelet count of 135,000/mm³. The CD-4 lymphocyte count was 188 cells/µL. The electrolytes and liver function tests were normal. A series of abdominal radiographs showed a normal bowel gas pattern without evidence of free air. Urine analysis showed no bacteriuria or pyuria, but there was moderate hematuria. No stool culture was obtained as diarrhea was not present.

On admission, fever reached a maximum of 104.2°F. Because he was febrile and neutropenic, intravenous piperacillin and tobramycin were administered. He remained febrile until the third hospital day, but his overall fever curve diminished, coinciding with the initiation of antibiotic therapy and G-CSF.

On the third day, the blood culture from admission was reported as being positive for Gram-negative rods, which were subsequently identified on the fifth day as E. corrodens in one set of culture bottles using the Vitek Gram-Negative Identification Card (GNI Card, Vitek Inc, St. Louis, Mo).

An echocardiogram noted normal left ventricular cavity size, wall motion, and contractility and valvular function was normal with no signs of vegetations. A small pericardial effusion and a normal Doppler study were observed. It was recommended that the patient receive 10 to 14 days of cefotaxime and tobramycin for treatment of a possible HACEK group endocarditis (Haemophilus spp, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, E. corrodens, and Kingella kingae).

On the seventh hospital day, the microorganism originally identified as E. corrodens was correctly identified as C. jejuni. The organism was a Gram-negative seagull-shaped bacterium that did not pit the agar or smell like Eikenella. It grew well on Campylobacter agar at 42°C and was hippurate positive. Two sets of repeat blood cultures and a fungal culture were sterile. Upon further questioning, the patient stated that he had eaten a "bad sausage" five days prior to admission but he denied recent foreign travel, pet contact, or consumption of unprocessed milk, untreated water, or poultry. After completing a week of intravenous antibiotics, he was discharged to take 500 mg of oral ciprofloxacin twice a day for 14 days. He recovered completely from this infection.

Discussion

Preclinical Studies

Serotyping of C. jejuni blood isolates correlates closely with stool isolates, indicating translocation of the organism from the gastrointestinal tract to the blood as the primary cause of bacteremia. Host immune factors play a role for the development of bacteremia in animal models. Symptoms of diarrhea are seen in neonatal calves at 72 hours after inoculation with C. jejuni, and bacteremia occurs within the first six hours. The RITARD (removable intestinal tie adult rabbit diarrhea) rabbit model demonstrated that 96% of rabbits inoculated with C. jejuni had bacteremia within 24 hours. IgG titers were elevated by day 28, and all rectal swabs were positive after 24 hours. At autopsy, there were inflammatory lesions with ulcerations and goblet-cell hyperplasia in the colon.
The likelihood of *Campylobacter* bacteremia is 1,000-fold greater for *C. fetus* than for *C. jejuni*, but there is no specific serological type of *C. jejuni* that predisposes an inoculant to bacteremia. One *in vitro* study employed a serum-resistant S-layer protein containing *C. fetus* strain (S) and a serum-sensitive S-layer protein lacking mutant strain (M). The S strain did not bind C3 and was resistant to opsonization. The M strain bound C3 and consumed C5 and C9, with a polymorphonuclear leukocyte kill rate of >99%. Immune serum restored killing of the S strain. Specific anticapsule antibodies are not necessary. It was proposed that the S-layer protein capsule interrupts the C5 convertase step and that phagocytosis of serum-resistant strains is Fc-receptor-mediated.

**Clinical Observations**

While *C. fetus* bacteremia is common, *C. jejuni* bacteremia is rarely seen unless there are exacerbating factors that contribute to the host’s inability to defend itself against systemic infection. In one study of 33 cases of *C. jejuni* bacteremia, 36% of the patients were less than 1 year of age, 50% had an underlying disease, and 8 of 12 immunosuppressed patients died. Another series showed that 4 out of 5 cases had diarrhea, the single exception being an immunosuppressed patient. Another report of 10 cases revealed that 2 patients had agammaglobulinemia and 2 had undergone chronic corticosteroid treatment, with 6 out of 10 having an underlying comorbid disease. Yet another report included two deaths. One patient had a mixed histiocytic lymphoma, and the second had a diffuse lymphocytic lymphoma. Finally, a patient on chronic hemodialysis with systemic lupus erythematosus and IgM and IgA deficiencies was noted to have a 12-month history of recurrent *C. jejuni* bacteremia. Resolution of the infection coincided with increasing IgG antibodies.

*Campylobacter* has been isolated from the stools of homosexual men. *C. jejuni* infections have also been reported in HIV-positive patients. Four HIV-positive patients were noted to have persistent *C. jejuni* infections, but only 1 out of 4 was bacteremic. Total T4 cell counts were 50, 120, 50, and 121. These patients exhibited decreased specific anti-*Campylobacter* IgA, IgG, and IgM antibodies.

*Campylobacter* virulence factors may also exist. A study of *C. jejuni* and *C. coli* blood isolates showed that all extraintestinal strains had rough-type lipopolysaccharide profiles. There was an inverse relationship between total carbohydrate concentration and serum susceptibility. Unlike *C. fetus*, there was no correlation between serum susceptibility and protein concentration. *C. jejuni*-resistant strains may produce either more LPS or larger polysaccharide chains.

**Laboratory Considerations**

The low number of reported *C. jejuni* bacteremias may be caused in part by transient or early bacteremia, failure of the laboratory to adhere to fastidious growth requirements, or mistaken identification. Different blood culture systems may affect growth characteristics. The Roche Septic Check System detected both *C. jejuni* and *C. fetus* in a median of 2 days. The BACTEC aerobic system (Becton Dickinson, Inc, Towson, Md) detected *C. jejuni* and *C. fetus* in a median of 5 days and 3 days, respectively, whereas the anaerobic system took more than 10 days to detect *C. jejuni*. Host and virulence factors may account for the greater prevalence of *C. fetus* bacteremia, but the low rate of *C. jejuni* bacteremia may be partially caused by the method of culturing.

Emerging resistance to *Campylobacter* is being reported with increasing frequency. Single-drug resistance to tetracycline, doxycycline, erythromycin, or fluoroquinolones in *Campylobacter* isolates recovered from humans has been documented worldwide. However, multirub drug resistance is rare in *C. jejuni* with prolonged, severe, and relapsing enteritis. Our patient’s isolate readily responded to a beta-lactam antibiotic and an aminoglycoside without evidence of resistance.

Animal models support the theory that *C. jejuni* enteritis tends to be locally invasive and that bacteremia is transient, most often occurring at the beginning of an infection. *C. fetus* has a significantly higher rate of bacteremia than *C. jejuni* because *C. fetus* possesses a serum-resistant S-layer protein capsule. Serum-resistant *C. jejuni* bacteremia rarely occurs but may be caused in part by an increase in polysaccharide chains. Host factors play an important role in predisposing a patient to *C. jejuni* bacteremia.

**Conclusions**

When immunosuppressed patients are exposed to *C. jejuni*, their likelihood of developing bacteremia increases. A proposed mechanism for this likelihood is that enteric infections in a normal host cause, at most, a transient bacteremia. If a serum-resistant bacteremia occurs in a normal host, a sustained infection will occur. In an immunosuppressed patient, however, a sustained infection is likely to occur even with a serum-sensitive strain. With the onset of HIV, the prevalence of immunosuppressed patients has increased. Certain populations of HIV-infected individuals may be especially at risk of developing campylobacteremia, and they may not manifest the expected symptomatology. Vigilance must be maintained when dealing with these patients. Blood cultures must be obtained early, and these cultures need to be scrutinized by laboratory personnel using techniques that facilitate in making a correct diagnosis of *C. jejuni* bacteremia.

**References**


