Combined Treatment with Oral Kanamycin and Parenteral Antibiotics for a Case of Persistent Bacteremia and Intestinal Carriage with *Campylobacter coli*

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Abstract

*Campylobacter coli* (*C. coli*) is a rare pathogen of bacteremia, but in immunocompromised hosts, *C. coli* occasionally causes bacteremia which can be refractory to antibiotic treatment. We report a case of *C. coli* bacteremia in a patient with X-linked agammaglobulinemia. Bacteremia relapsed repeatedly in spite of treatment with combined intravenous antibiotics. *C. coli* was observed in the biopsy specimens from the intestinal mucosa, suggesting intestinal carriage and reservoir of recurring infection. The addition of oral kanamycin with intravenous antibiotics was successful in eradicating *C. coli* from the blood and intestine.

Key words: *Campylobacter coli*, X-linked agammaglobulinemia, oral kanamycin

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Introduction

*Campylobacter jejuni* and *Campylobacter coli* (*C. coli*) frequently cause enteritis, but rarely cause bacteremia or extraintestinal infections in immunologically normal hosts (1, 2). However, in immunocompromised hosts, especially in patients with humoral immunodeficiency, these organisms occasionally develop prolonged, severe extraintestinal infection such as bacteremia, osteomyelitis, and arthritis (1, 3-5). We report a case of bacteremia, endocarditis, and osteomyelitis with *C. coli* in a patient with X-linked agammaglobulinemia. Bacteremia relapsed repeatedly in spite of treatment with combined intravenous antibiotics. *Campylobacter* was never isolated from stool cultures, but observed in the biopsy specimens from intestinal mucosa, suggesting the intestinal carriage. The addition of oral kanamycin with intravenous antibiotics was successful in eradicating *C. coli* from the blood, the bone and the intestine.

Case Report

A 33-year-old man with X-linked agammaglobulinemia was admitted to our hospital because of sustained fever and cellulitis of the left leg. The patient had history of recurrent diarrhea, upper respiratory infection and otitis media, and had been receiving immunoglobulin replacement therapy every two weeks. He had no history of overseas travel. He did not remember having raw meat such as chicken or coming into contact with animals in the past year. At the outpatient visits, oral cefcapene pivoxil and then intravenous ceftriaxone were administered, but the fever and cellulitis did not improve.

On admission, his temperature was 39.5°C, and his left leg was swollen. A grade 1/6 holosystolic cardiac murmur was heard. The abdomen was normal. The white blood cell count was 2,700/mm³, the C reactive protein level was 1.09 mg/dL. The serum IgG was 893 mg/dL, but neither IgA nor IgM was detectable. Meropenem and then intravenous ciprofloxacin were administered for ten days. Seven days after discontinuation of the intravenous antibiotics, cel-
Iritis of his left leg worsened again. Blood culture was positive for *Campylobacter* species, which was determined as *C. coli* by a polymerase chain reaction assay. Stool cultures obtained repeatedly during the hospitalization did not yield *C. coli* (Fig. 1).

Intravenous administration of ciprofloxacin and gentamicin was started. Blood cultures continued to be positive for *C. coli*. A transesophageal echocardiography showed vegetation on the mitral valve, which suggested infective endocarditis. A colon fiberscope revealed mild inflammation. Antibiotics were switched to imipenem/cilastatin, and one week after the switch, blood culture turned negative. But four days after discontinuation of the 8-week antibiotic therapy, he became febrile again, and blood culture turned positive for *C. coli*. Intravenous imipenem/cilastatin and gentamicin were restarted. A magnetic resonance imaging study of the lower extremities revealed osteomyelitis of the left leg. Fosfomycin, which was susceptible in MIC test, was added to imipenem/cilastatin and gentamicin (Table 1). Gentamicin was discontinued because of renal tubular injury. Failing to eradicate *C. coli* from the blood, imipenem/cilastatin was switched to meropenem, ciprofloxacin and minocycline according to the susceptibility tests, and oral azithromycin, were sequentially added. In spite of disappearance of vegetation on the mitral valve in a transesophageal echocardiography and resolution of osteomyelitis of the left leg, bacteremia with *C. coli* continued (Fig. 1). During the combined antibiotic therapy, diarrhea and abdominal fullness became more prominent, although toxin A of *Clostridium difficile* was not detected from the stool. A colon fiberscope was performed again. The ascending colon was edematous, and the terminal ileum and the hepatic flexure were erosive. Although bacteria could not be detected histologically, all cultures of biopsy specimens sampled from the mucosa of the colon and the ileum yielded *Campylobacter* spp., suggesting intestinal carriage and reservoir of recurring infection.

Oral kanamycin was added to the intravenous antibiotics (Fig. 1). The following day his fever was resolved, and the abdominal symptoms improved. Blood cultures remained negative and intravenous antibiotics were discontinued six weeks after blood culture turned negative. A colon fiberscope was performed again, and oral kanamycin was discontinued after negativity of cultures of biopsy specimens from intestinal mucosa was confirmed. The total duration of oral kanamycin was ten weeks. The patient has been well for about eight months without relapse of bacteremia and diarrhea.

**Discussion**

*Campylobacter coli* is one of the most common *Campylobacter* species associated with diarrhea illness other than *C. coli*.
Among them six cases had stool cultures positive for Campylobacter bacteremia has been noted (10, 11). Paired antibody response to infected with human immunodeficiency virus (HIV), an impaired antibody response to C. jejuni/coli infection including bacteremia has been noted (10, 11).

There have been eleven case reports of X-linked agammaglobulinemia with Campylobacter bacteremia (12-19). Among them six cases had stool cultures positive for Campylobacter species and the other five cases had no description about stool cultures. Furthermore, among the six postive stool culture cases, five cases had no gastrointestinal symptoms such as abdominal pain or diarrhea. We speculated that intestinal carriage of Campylobacter with or without gastrointestinal symptoms might be a risk factor of recurrent bacteremia in immunocompromised patients. Stool cultures had sensitivity of 40% for Campylobacter bacteremia (1). In the present patient, stool cultures were consistently negative for C. coli, but cultures of biopsy specimens from intestinal mucosa were positive for C. coli. Furthermore in our case, infective endocarditis and osteomyelitis were clinically resolved in spite of persistent bacteremia. We speculated that the intestinal tract would be a reservoir for C. coli. The mechanism of intestinal carriage of Campylobacter in immunocompromised patients remained unclarified, but it has been supposed that failure of humoral immune response in these patients might permit colonization of Campylobacter in the epithelium and lamina propria and induction of tissue damage (20, 21). A study on Campylobacter infections in 38 HIV-infected patients reported that in two patients with diarrhea, the cultures were positive only in the blood, and in one patient a culture of biopsy specimen from intestinal mucosa yielded C. jejuni after disappearance in stool culture (22). We consider that in compromised patients, who are suspected to be infected with Campylobacter but have negative stool cultures for bacteria, culture of intestinal mucosa might be useful for diagnosing the intestinal carriage.

Macrolides and fluoroquinolones are antibiotic agents frequently used to treat Campylobacter infection (2). However, in C. coli bacteremia in compromised patients, treatment with these drugs might fail, and combined therapy of intravenous antibiotics such as carbapenems and aminoglycosides has been used (18). There have been three reports in which administration of oral antibiotics in addition to intravenous antibiotics were effective in eradicating C. coli from the intestine (12, 15, 18). In the present case, oral antibiotics other than azithromycin had not been tried until isolation of C. coli from the culture of intestinal mucosa, because the intestinal carriage had not been considered from mild nonspecific inflammatory findings in the first colonoscopy and repeated negative stool culture. Intestinal biopsy was not performed in the previous reports, and this is the first case in which culture of intestinal mucosa was used for diagnosing the intestinal carriage with C.coli and confirming the eradication by the treatment with oral antibiotics. Oral kanamycin was selected in our case because the isolated Campylobacter strain was susceptible to gentamicin. Since aminoglycosides including kanamycin have poor bioavailability, we considered that oral administration of kanamycin could not reach a sufficiently high serum concentration to treat endocarditis or osteomyelitis, but the administration could reach a sufficient concentration in the intestinal mucosa for eradicating Campylobacter spp. from the intestine. We suggested that in a case of bacteremia and intestinal carriage with Campylobacter which was refractory to intravenous antibiotics, oral aminoglycoside therapy combined with intravenous antibiotics could be effective.

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