

## *Campylobacter jejuni* Bacteremia in a Patient With Acute Lymphocytic Leukemia

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### Abstract

**Introduction:** *Campylobacter jejuni* is a slender, motile, non-spore-forming, helical-shaped, gram-negative bacterium. It is one of the most common causes of human gastroenteritis in the world. The aim of this study was to present a patient with acute lymphocytic leukemia (ALL), who was infected with *Campylobacter jejuni*.

**Case Presentation:** We describe the medical records of a pediatric ALL patient with bacteremia caused by *C. jejuni*, who was diagnosed at Amir hospital, Shiraz, Iran. This 14-year-old male visited the emergency department of Amir hospital with night sweats, severe polar high-grade fever, reduced appetite, and nausea in August 2013. Given the suspected presence of an anaerobic or microaerophilic microorganism, aerobic and anaerobic blood cultures were performed using an automated blood cultivator, the BACTEC 9240 system. In order to characterize the isolate, diagnostic biochemical tests were used. Antibiotic susceptibility testing was done with the disk diffusion method. The primary culture was found to be positive for *Campylobacter*, and the subculture of the solid plate yielded a confluent growth of colonies typical for *Campylobacter*, which was identified as *C. jejuni* by morphological and biochemical tests. The isolate was resistant to ciprofloxacin, cefotaxime, cephalixin, piperacillin/tazobactam, nalidixic acid, aztreonam, cefuroxime, cefixime, ceftazidime, and tobramycin.

**Conclusions:** *C. jejuni* should be considered in the differential diagnosis as a potential cause of bacteremia in immunosuppressed patients. In cases where the BACTEC result is positive in aerobic conditions but the organism cannot be isolated, an anaerobic culture medium is suggested, especially in immunocompromised patients.

**Keywords:** Acute Lymphocytic Leukemia (ALL), Bacteremia, *Campylobacter jejuni*

### 1. Introduction

*Campylobacter* species are gram-negative, microaerophilic, non-fermenting, motile rods (spiral-shaped, S-shaped, or curved) with a single polar flagellum. They are oxidase-positive and grow optimally at 37° or 42°C (1-3). The organism grows quite slowly; 72 - 96 hours is required for primary isolation, and its isolation from the blood can take even longer (1, 2). *Campylobacter* is the main cause of bacterial gastrointestinal infections occurring at any age, but it peaks in children and young adults. *C. jejuni* and *C. fetus* are the main agents for Campylobacteriosis in humans (3).

Clinically, a *Campylobacter* infection is indistinguishable from acute gastrointestinal infections produced by other bacterial pathogens (4). Compared to *Salmonella*, *Shigella*, and other species of *Campylobacter*, such as *C. fetus*, *C. jejuni* bacteremia is relatively rare and only a small number of cases are reported (5). Bacteremia has been reported in human immunodeficiency virus patients and other im-

munocompromised individuals (6).

In some patients, diarrhea occurs at the peak of the illness, while in others, diarrhea is minimal; fever is reported in more than 90% of patients (2, 7). The fatality rate from *Campylobacter* is 0.05 per 1,000 infections (2). An alarming recent trend is the rapid emergence of antimicrobial agent-resistant *Campylobacter* strains all over the world (8). The epidemiology of *Campylobacter* infections is quite different in developing countries than in the industrialized world (2).

Asymptomatic infections occur commonly in both children and adults in developing nations, whereas in developed countries, such infections are unusual. *C. jejuni* infections respond to a variety of antibiotics (9), the most commonly used including azithromycin, levofloxacin, and ciprofloxacin (10).

The aim of this study was to present a patient with acute lymphocytic leukemia (ALL) who was infected with *C. jejuni*. To our knowledge, this is the first report of *C. je-*

*jejunii* isolation from the blood of an ALL patient in Iran.

This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

## 2. Case Presentation

We describe the medical records of a pediatric patient (case report) who had bacteremia caused by *C. jejuni*, and who also had a diagnosis of ALL, at Amir hospital in Shiraz, Iran. This 14-year-old male visited the emergency department of Amir Hospital with night sweats, severe polar high-grade fever, reduced appetite, and nausea in August 2013. Previously diagnosed with ALL, the patient had received chemotherapy. On admission, his temperature was 39°C, heart rate was 110 beats/minutes, and respiratory rate was 23 breaths/minutes.

The complete blood count included hemoglobin of 5.8, white blood cell count of 600, and platelet count of 125,000. Chemistry results showed an ESR of 12, CRP of 6, LDH of 468, AST of 33, and ALT of 28. Other laboratory studies, including liver function tests, electrolytes, and hematocrit levels, were normal. As the patient had a high-grade fever, intravenous injection of 600 units of imipenem was initiated. Simultaneously, an aerobic blood culture was performed using an automated blood cultivator, the BACTEC 9240 system (Becton Dickinson, NJ, USA), and this culture was positive after 59 hours (time of detection). Gram staining of the BACTEC tube showed curved gram-negative rods that were motile. Subcultures were performed on common bacteriological culture media, including blood agar and MacConkey agar (Merck Co., Germany), but no microorganism growth on the plate culture was seen after 48 hours of incubation at 35°C.

Due to the suspected presence of an anaerobic or microaerophilic microorganism, we performed an anaerobic and microaerophilic blood culture, which was positive after 72 hours of incubation within 35°C to 37°C. Gram staining and the microscopic findings of *Campylobacter* isolated from the blood culture revealed slightly curved gram-negative bacilli. The gram stain results showed spiral-shaped gram-negative bacilli. Then, the blood sample was cultured on Columbia agar (Merck Co., Germany), and enriched with yeast extract, fetal calf serum, and horse blood under anaerobic and microaerophilic conditions for 72 hours at 36°C.

Interestingly, the primary culture was positive for *Campylobacter*, and the subculture from the solid plate yielded a confluent growth of colonies typical for *Campylobacter*, which were motile and oxidase- and catalase-positive, with a characteristic microscopic appearance featuring S-shaped and curved rods. The curved bacteria were suspicious for *Campylobacter*, and biochemical tests were

done to identify a special strain. In order to characterize the isolate, the following biochemical tests (Merck Co., Germany) were used: nitrate reduction (+), urease (-), indoxyl acetate hydrolysis (+), growth at 42°C (+), growth in the presence of 1% glycine (+), hippurate hydrolysis (+), growth in the presence of 1.5% NaCl (-), susceptibility to nalidixic acid (resistant), and cephalothin (resistant). According to the results, the isolate was finally identified as *C. jejuni*.

After the presence of *C. jejuni* was confirmed, antibiotic susceptibility testing was done with the disk diffusion method, according to the clinical and laboratory standards institute (CLSI) guidelines. Antibiotic susceptibility was determined using Mueller-Hinton agar supplemented with 5% defibrinated horse blood, and the culture suspension with turbidity adjusted to be equivalent to a McFarland opacity standard of 2.0 to 3.0 was used to inoculate onto the plates. The growth conditions included an atmosphere of 10% CO<sub>2</sub>, 5% O<sub>2</sub>, and 85% N<sub>2</sub> at 36°C for 48 hours followed by 42°C for 24 hours (11). The effects of different antibiotics (MAST Co., UK) on the isolate were investigated. The isolate was susceptible to azithromycin, nitrofurantoin, clindamycin, erythromycin, ampicillin/sulbactam, ofloxacin, Augmentin, amikacin, ampicillin, chloramphenicol, ceftriaxone, cefprozime, gentamicin, imipenem, meropenem, tetracycline, and doxycycline. Isolated *C. jejuni* strains exhibited resistance to ciprofloxacin, cefotaxime, cephalixin, piperacillin/tazobactam, nalidixic acid, aztreonam, cefuroxime, cefixime, ceftazidime, and tobramycin.

## 3. Discussion

Two major *Campylobacter* spp. that cause disease in humans are *C. jejuni* and *C. fetus*. Unlike the closely related organism *C. fetus*, *C. jejuni* is not frequently associated with bacteremia and is responsible for self-limiting gastrointestinal infections in immunocompetent subjects. *C. jejuni* is usually associated with enteritis or extraintestinal localization (12, 13). Nevertheless, a decreased immune system response, which may occur in elderly people or immunocompromised patients (i.e., those with immunodeficiency, HIV, diabetes, cirrhosis, or cancer, and those undergoing chemotherapy), increases the risk of developing a severe infection from this pathogen (13-15).

Several cases of bacteremia have been reported in HIV-infected patients and immunosuppressed drug-users following transplantation (6). In the present case, the patient had ALL and underwent chemotherapy. A misdiagnosis of *Campylobacter* may occur in some patients without diarrhea but with the presence of the organism.

Pacanwsk reported that 63% of patients with *Campylobacter* bacteremia had underlying medical conditions

(16, 17). There are a few reports from developing countries of the presence of *C. jejuni* in the blood. This is the first report from Iran, and a number of cases might have been undetected due to inappropriate detection methods and ignorance of the conditions of growth for this organism. Also, blood cultures are not routinely performed for patients with acute gastrointestinal illnesses.

Neonates and high risk groups (e.g. immunosuppressed and HIV positive individuals, senile persons) are particularly assailable for opportunistic foodborne pathogens (18, 19). The diagnosis and treatment of *C. jejuni* bacteremia is usually delayed because of very slow growth and the special (selective) culture media that are required for these bacteria. This is dangerous in immunocompromised patients because of the increased risk of mortality. Failure to initiate timely and targeted antibiotic therapy is associated with higher mortality rates of up to 88% in immunosuppressed patients.

No controlled clinical trial has been published on the optimal antibiotic regime, and the duration of treatment of *Campylobacter* infections varies among different isolates and regions, given the different antibiotic-resistance patterns. Fluoroquinolone, macrolide, and carbapenem seem to be appropriate choices for the empirical therapy of *Campylobacter* infections. In cases in which the BACTEC results are positive under aerobic conditions but the organism cannot be isolated, an anaerobic culture medium is suggested, especially for immunocompromised patients.

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## Footnotes

**Authors' Contribution:** All of the authors made sufficient contributions to the project to be included as authors, and all who qualified as authors are listed in the author byline.

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