Case Report

Campylobacter jejuni Bacteremia in a Patient With Acute Lymphocytic Leukemia

Mojtaba Anvarinejad,[1] Maneli Amin Shahidi,[1] Gholam Reza Pouladfar,[1] Mohammad Ali Dehyadegari,[1] and Jalal Mardaneh[2,*]

[1]Professor Alborzi Clinical Microbiology Research Center, Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz, IR Iran
[2]Department of Microbiology, School of Medicine, Gonabad University of Medical Sciences, Gonabad, IR Iran

[*]*Corresponding author*: Jalal Mardaneh, Department of Microbiology, School of Medicine, Gonabad University of Medical Sciences, Gonabad, IR Iran. Tel/Fax: +98-5157220578, E-mail: Jalalmardaneh@yahoo.com

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, cephalexin, 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 immunocompromised 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-*

juni 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_2, 5% O_2, and 85% N_2 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, ceftizoxime, gentamicin, imipenem, meropenem, tetracycline, and doxycycline. Isolated *C. jejuni* strains exhibited resistance to ciprofloxacin, cefotaxime, cephalexin, 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.

References

1. Janssen R, Krogfelt KA, Cawthraw SA, van Pelt W, Wagenaar JA, Owen RJ. Host-pathogen interactions in Campylobacter infections: the host perspective. *Clin Microbiol Rev.* 2008;**21**(3):505–18. doi: 10.1128/CMR.00055-07. [PubMed: 18625685].

2. Allos BM. Campylobacter jejuni Infections: update on emerging issues and trends. *Clin Infect Dis.* 2001;**32**(8):1201–6. doi: 10.1086/319760. [PubMed: 11283810].

3. Schielke A, Rosner BM, Stark K. Epidemiology of campylobacteriosis in Germany - insights from 10 years of surveillance. *BMC Infect Dis.* 2014;**14**:30. doi: 10.1186/1471-2334-14-30. [PubMed: 24422983].

4. Islam D, Lewis MD, Srijan A, Bodhidatta L, Aksomboon A, Gettayacamin M, et al. Establishment of a non-human primate Campylobacter disease model for the pre-clinical evaluation of Campylobacter vaccine formulations. *Vaccine.* 2006;**24**(18):3762–71. doi: 10.1016/j.vaccine.2005.07.023. [PubMed: 16098634].

5. Pradhan AK, Van Kessel JS, Karns JS, Wolfgang DR, Hovingh E, Nelen KA, et al. Dynamics of endemic infectious diseases of animal and human importance on three dairy herds in the northeastern United States. *J Dairy Sci.* 2009;**92**(4):1811–25. doi: 10.3168/jds.2008-1486. [PubMed: 19307664].

6. Tee W, Mijch A. Campylobacter jejuni bacteremia in human immunodeficiency virus (HIV)-infected and non-HIV-infected patients: comparison of clinical features and review. *Clin Infect Dis.* 1998;**26**(1):91–6. [PubMed: 9455515].

7. Adedayo O, Kirkpatrick BD. Campylobacter jejuni Infections: Update on presentation, diagnosis, and management. *Hospital Physician.* 2008:9–15.

8. Ibrahim NG, Zafar A, Hasan R. Evaluation of frequency of isolation and trends in antibiotic resistance among Campylobacter isolates over 11 year period. *J Pak Med Assoc.* 2004;**54**(6):291–4. [PubMed: 15366792].

9. Ngotho M, Ngure RM, Kamau DM, Kagira JM, Gichuki C, Farah IO, et al. A fatal outbreak of Campylobacter jejuni enteritis in a colony of Vervet Monkeys in Kenya. *Scand J Lab Anim Sci.* 2006;**33**(4):205–10.

10. Tribble DR, Sanders JW, Pang LW, Mason C, Pitarangsi C, Baqar S, et al. Traveler's diarrhea in Thailand: randomized, double-blind trial comparing single-dose and 3-day azithromycin-based regimens with a 3-day levofloxacin regimen. *Clin Infect Dis.* 2007;**44**(3):338–46. doi: 10.1086/510589. [PubMed: 17205438].

11. Ge B, Wang F, Sjolund-Karlsson M, McDermott PF. Antimicrobial resistance in campylobacter: susceptibility testing methods and resistance trends. *J Microbiol Methods.* 2013;**95**(1):57–67. doi: 10.1016/j.mimet.2013.06.021. [PubMed: 23827324].

12. Gouveia R, Costa FT, Ramos A. Campylobacter fetus bacteremia in a peritoneal dialysis patient. *Port J Nephrol Hypert.* 2014;**28**(2):160–3.

13. Ariganello P, Angelino G, Scarselli A, Salfa I, Della Corte M, De Matteis A, et al. Relapsing Campylobacter jejuni Systemic Infections in a Child with X-Linked Agammaglobulinemia. *Case Reports in Pediatrics.* 2013;**2013**:1–3. doi: 10.1155/2013/735108.

14. O'Hara JR, Feener TD, Fischer CD, Buret AG. Campylobacter jejuni disrupts protective Toll-like receptor 9 signaling in colonic epithelial cells and increases the severity of dextran sulfate sodium-induced colitis in mice. *Infect Immun.* 2012;**80**(4):1563–71. doi: 10.1128/IAI.06066-11. [PubMed: 22311925].

15. Backert S, Boehm M, Wessler S, Tegtmeyer N. Transmigration route of Campylobacter jejuni across polarized intestinal epithelial cells: paracellular, transcellular or both?. *Cell Commun Signal.* 2013;**11**:72. doi: 10.1186/1478-811X-11-72. [PubMed: 24079544].

16. Pigrau C, Bartolome R, Almirante B, Planes AM, Gavalda J, Pahissa A. Bacteremia due to Campylobacter species: clinical findings and antimicrobial susceptibility patterns. *Clin Infect Dis.* 1997;**25**(6):1414–20. [PubMed: 9431389].

17. Brauner A, Brandt L, Frisan T, Thelestam M, Ekbom A. Is there a risk of cancer development after Campylobacter infection?. *Scand J Gastroenterol.* 2010;**45**(7-8):893–7. doi: 10.3109/00365521003734133. [PubMed: 20334473].

18. Mardaneh J, Dallal MM. Isolation, identification and antimicrobial susceptibility of Pantoea (Enterobacter) agglomerans isolated from consumed powdered infant formula milk (PIF) in NICU ward: First report from Iran. *Iran J Microbiol.* 2013;**5**(3):263–7. [PubMed: 24475334].

19. Mardaneh J, Soltan-Dallal MM. Isolation and Identification of E. cowanii from powdered infant formula in NICU and determination of antimicrobial susceptibility of isolates. *Iran J Pediatr.* 2014;**24**(3):261–6. [PubMed: 25562018].