Case report

Cellulitis with persistent bacteremia caused by *Campylobacter lari* in a patient with mantle-cell lymphoma

Yayoi Miyamatsu[a], Ryutaro Tanizaki[a,*], Satoko Yamada[b], Isuzu Tsujimura[b], Hideki Wakabayashi[c]

[a] Department of Internal Medicine, Ise Municipal General Hospital, 3038, Kusubecho, Ise, Mie, Japan
[b] Department of Clinical Laboratory, Ise Municipal General Hospital, 3038, Kusubecho, Ise, Mie, Japan
[c] Department of Community Medicine, Kameyama, Mie University School of Medicine, 2-174, Edobashi, Tsu, Mie, Japan

ABSTRACT

Campylobacter lari is an organism occasionally isolated in humans but rarely causes bacteremia. We report the first case of cellulitis with bacteremia due to *C. lari* in a patient undergoing mantle-cell lymphoma. A 51-year-old man presented with a two-month history of fever and bilateral leg pain and redness. Despite oral ciprofloxacin administration, his symptoms had not improved. The blood culture sample in the anaerobic bottle yielded positive results and *C. lari* was identified by mass spectrometry. The bacteremia did not initially respond to oral azithromycin but responded to intravenous meropenem and amikacin for five days followed by oral minocycline. This report indicates that *C. lari* bacteremia may be treated with oral minocycline following short-term intravenous antimicrobial therapy even among patients undergoing hematological malignancies.

© 2021 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Campylobacter lari (formerly known as *Campylobacter laridis*) [1,2] is an organism isolated mainly in poultry and some animals [3]. It is occasionally isolated in humans but rarely causes bacteremia, and appropriate antimicrobial regimens for its treatment have not been established. Although several cases of *C. lari* bacteremia have been described [1,2,4–11], to our knowledge, no cases of cellulitis with bacteremia have been reported. We herein describe a case of cellulitis with bacteremia due to *C. lari* in an immunocompromised patient.

Case report

In October 2019, a 51-year-old man was referred to our hospital from a private clinic on account of a two-month history of fever and bilateral leg pain and redness. Despite oral ciprofloxacin administration, his symptoms had not improved. He had been diagnosed with mantle cell lymphoma and had undergone peripheral blood stem cell transplantation last year followed by long-term rituximab, administered every two months. He worked as a cook and did not report eating raw foods.

On physical examination, he was afebrile and his vital signs were unremarkable. He had tenderness and redness of both lower legs without any wound. His laboratory test results showed no abnormalities except for an elevated serum C-reactive protein (CRP) concentration (8.25 mg/dL). Based on these findings, a diagnosis of cellulitis was made and treatment was initiated with oral cephalexin (750 mg per day) after obtaining two blood culture samples (day 1). On day 3, a blood culture sample which had been incubated in the BACTEC FX system (Becton, Dickinson and Company, Franklin Lakes, New Jersey, USA) yielded positive results in the anaerobic bottle (BD BACTEC Plus Anaerobic/F Culture Vial). However, a Gram stained smear revealed no bacteria. The positive blood culture fluid was centrifuged and the sediment was cultured on Trypticase Soy Agar with 5% Sheep Blood (Nippon Becton Dickinson, Tokyo, Japan) at 37 °C in an environment with 5% CO_2. A microcolony was observed on day 5 which revealed spiral-shaped gram-negative rods on Gram stain (Fig. 1) and was identified as *C. lari* by mass spectrometry (MALDI Biotyper, Bruker Daltonics, Bremen, Germany). We recommended to the patient that he be admitted to hospital, but he refused. The disk-diffusion antimicrobial susceptibility test, performed in accordance with the criteria for *Campylobacter jejuni* and *Campylobacter coli* in Clinical and Laboratory Standards Institute document M45-A2 [12], showed that the bacteria were susceptible to macrolides but resistant to
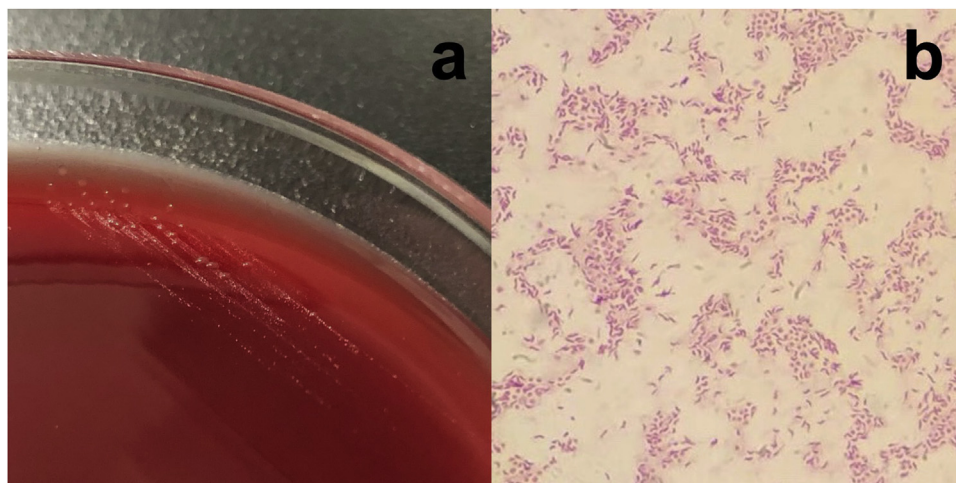
Fig. 1. A small colony (a) and Gram stain examination (b) of *Campylobacter lari* cultured on Trypticase Soy Agar with 5% Sheep Blood (Nippon Becton Dickinson, Tokyo, Japan).

Table 1
Campylobacter lari drug susceptibility pattern of the isolate from the culture sample collected of day 1 according to the Clinical and Laboratory Standards Institute criteria.

Antimicrobials	MIC (μg/mL) (present case)	Breakpoint for susceptible strain for *Campylobacter jejuni* and *Campylobacter coli* (μg/mL)
Ampicillin	≤0.5	32
Imipenem	≤0.5	4
Gentamicin	≤1	16
Erythromycin	≤2	32[a]
Minocycline	≤1	16[a]
Ciprofloxacin	>2	4[a]

Abbreviation: MIC, minimum inhibitory concentration.
[a] The breakpoint of minocycline was calculated in reference to that of tetracycline in the Clinical and Laboratory Standards Institute M45-A2 document [12]. The breakpoints of ampicillin, imipenem, and gentamicin were calculated in reference to those for Enterobacterales in the CLSI M100-S30 document [14].

ciprofloxacin (Table 1). The antimicrobials were changed to oral azithromycin 2 g that lasts for 1 week with a single dose of 2 g [13] and two additional sets of blood culture samples were obtained on day 5 to further investigate for persistent bacteremia. The blood culture samples obtained on day 5 yielded negative results using an automated blood culture system.

By day 10, the patient's cellulitis had resolved, and his serum CRP concentration had decreased to 6.04 mg/dL. We obtained additional blood culture samples on day 10 to confirm the negative results. However, the culture yielded positive results on day 12. Based on these unexpected results, a centrifuged sediment of the day 5 blood culture, which was obtained on day 5 and once judged

negative on day 10, was sub-cultured on Trypticase Soy Agar with 5% Sheep Blood (Nippon Becton Dickinson, Tokyo, Japan) at 37 °C in an environment with 5% CO_2. *C. lari* was subsequently grown on subculture. The patient agreed to intravenous antimicrobial therapy and was admitted to our hospital. His chest and abdominal computed tomography scans showed no deep abscess. Transthoracic echocardiography revealed no evidence of infective endocarditis. On day 18, treatment with intravenous meropenem (1 g every 8 h) and amikacin (1200 mg [15 mg/kg] every 24 h) was initiated. On day 22, the patient was discharged from hospital and the antimicrobial therapy was changed to oral minocycline (100 mg twice daily). The results of blood cultures obtained on days 19, 24,
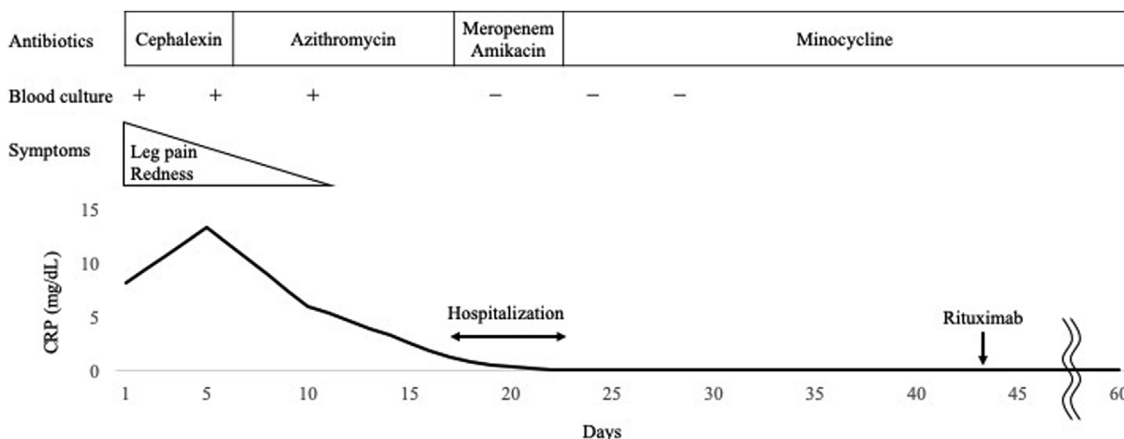

Fig. 2. Clinical course of our patient.

Table 2
Characteristics of reported cases of *Campylobacter lari* bacteremia.

Case (Reference)	Age, years	Sex	Immunosuppressive status	Source	Antimicrobial therapy	Treatment duration	Outcome
1 [1]	71	M	Multiple myeloma, renal cell carcinoma	Bacteremia	Vancomycin, gentamicin, moxalactam, penicillin G	3 days	Death
2 [2]	42	M	Not described	Gastroenteritis	Erythromycin	3 days	Recovered
3 [4]	25 days	M	None	Gastroenteritis	Netilmicin IV, erythromycin	2 weeks	Recovered
4 [5]	80	M	None	Bacteremia	Amoxicillin and clavulanic acid, ofloxacin	18 days	Death
5 [6]	83	F	None	Pacemaker infection	Imipenem, gentamicin	4 weeks	Recovered
6 [7]	10	F	Large cell anaplastic lymphoma	Bacteremia	Amoxicillin and clavulanic acid, amikacin	Not described	Recovered
7 [8]	75	M	None	Bacteremia	Imipenem, amoxicillin and clavulanic acid, doxycycline	4 weeks	Recovered
8 [9]	81	M	None	Prosthetic joint infection	Penicillin G, flucloxacillin, gentamicin	2 days	Death
9 [10]	15	M	X-linked agammaglobulinemia	Bacteremia	Gentamicin, ceftazidime, cefotaxime, amikacin, amoxicillin and clavulanic acid	2 weeks	Recovered
10 [11]	58	M	Myelodysplastic syndromes	Lumbar pyogenic spondylitis	Tazobactam/piperacillin, erythromycin, sulfamethoxazole/ trimethoprim	25 days	Recovered
This report	51	M	Mantle-cell lymphoma	Cellulitis	Meropenem, amikacin, minocycline	6 weeks	Recovered

IV: intravenously.

and 28 all yielded negative results. Rituximab therapy was resumed on day 43, and antimicrobial therapy was discontinued 6 weeks after confirming the first negative blood culture result (Fig. 2).

Discussion

We report the first case of cellulitis with bacteremia due to *C. lari* in an immunocompromised patient. To date, only ten cases of bacteremia caused by *C. lari* have been reported (Table 2). The source of infection varied as follows: gastroenteritis [2,4], permanent pacemaker infection [6], prosthetic joint infection [9], lumbar pyogenic spondylitis [11], and unknown [1,5,7,8,10] (Table 2). Our patient was immunosuppressed. There have been four cases of *C. lari* bacteremia in immunosuppressed patients reported previously associated with multiple myeloma and renal cell carcinoma [1], large cell anaplastic lymphoma [7], X-linked agammaglobulinemia [10], and myelodysplastic syndrome [11].

The accurate identification of *Campylobacter* species is still challenging due to the lack of reliable identification methods with routine biochemical tests. In general, most *Campylobacter* species grow in aerobic cultures, but *C. lari* grows only in anaerobic bottles [11]. This may be helpful for distinguishing *C. lari* from other *Campylobacter* species. Recently, 16 s rRNA [11] and mass spectrometry have readily enabled the identification of *Campylobacter* species, including *C. lari*, and we identified *C. lari* using mass spectrometry. In the patient, *C. lari* was not detected on Gram stain, even using positive blood culture fluid. A similar case was described by Morishita et al. [11], who attributed the negative Gram stain result to a low concentration of bacteria in the positive blood culture bottles. Furthermore, when the culture solution from the blood culture bottle with a negative result was subcultured, the subculture was positive for *C. lari*. This suggests that subculture may be necessary to confirm negative conversion of *C. lari* bacteremia, even if an automated system yields negative results.

There is no established antimicrobial regimen for the treatment of *C. lari* bacteremia. In previous reports, most patients were treated with intravenous antimicrobials, including beta lactams with or without aminoglycosides [1,4–11]. Our patient was initially treated with oral azithromycin, to which the organism appeared susceptible on sensitivity testing using disk diffusion. However, the results of blood culture were persistently positive. Jirapongsananuruk et al.

[10] reported that prophylactic administration of oral azithromycin did not prevent recurrence. Thus, oral azithromycin may not be effective for *C. lari* bacteremia. Although the optimal treatment duration of *C. lari* bacteremia is uncertain, patients who recovered in previous reports were treated for approximately 2–4 weeks [4,6,8,10,11]. We decided to administer a longer course of to prevent relapse of bacteremia because our patient was immunocompromised due to being on rituximab treatment for his lymphoma, and we continued oral minocycline for 6 weeks after the first confirmed negative blood culture result. The patient received rituximab 24 days after obtaining negative blood culture results while taking minocycline, and did not experience a recurrence of bacteremia.

Although the treatment strategy for *C. lari* bacteremia has not been determined, this report indicates that *C. lari* bacteremia may be treated with oral minocycline following short-term intravenous antimicrobial therapy even among patients with hematological malignancies undergoing immunosuppressive treatment.

Ethical approval

Not applicable.

Consent

The patient's consent was obtained.

Author contribution'

Yayoi Miyamatsu and Ryutaro Tanizaki wrote the manuscript. Satoko Yamada and Isuzu Tsujimura partly wrote the manuscript regarding the microbiological technique. Hideki Wakabayashi supervised the manuscript.

Funding

Declaration of Competing Interest

The authors report no declarations of interest.

Acknowledgments

References

[1] Nachamkin I, Stowell C, Skalina D, Jones AM, Hoop RM, Smibert M. *Campylobacter laridis* causing bacteremia in an immunosuppressed patient. Ann Intern Med 1984;101:55–7.

[2] Söderström C, Schalén C, Walder M. Septicemia caused by an unusual *Campylobacter* species (*C. Laridis* and *C. mucosalis*). Scand J Infect Dis 1991;23:369–71.

[3] Skirrow MB, Benjamin J. 1001 Campylobacters: cultural characteristics of intestinal Campylobacters from man and animals. J Hyg (Lond) 1980;185:427–42.

[4] Chiu CH, Kuo CY, Ou JT. Chronic diarrhea and bacteremia caused by *Campylobacter lari* in a neonate. Clin Infect Dis 1995;21:700–1.

[5] Bruneau B, Burc L, Bizet C, Lambert-Zechovsky N, Branger C. Purulent pleurisy caused by *Campylobacter lari*. Eur J Clin Microbiol Infect Dis 1998;17:185–8.

[6] Morris CN, Scully B, Garvey GJ. *Campylobacter lari* associated with permanent pacemaker infection and bacteremia. Clin Infect Dis 1998;27:220–1.

[7] Martinot M, Jaulhac B, Moog R, De Martino S, Kehrli P, Monteil H, et al. *Campylobacter lari* bacteremia. Clin Microbiol Infect 2001;7:96–7.

[8] Krause R, Ramschak-Schwarzer S, Gorkiewicz G, Schnedl WJ, Feierl G, Wenisch C, et al. Recurrent septicemia due to *Campylobacter fetus* and *Campylobacter lari* in an immunocompetent patient. Infection 2002;30:171–4.

[9] Werno AM, Klena JD, Shaw GM, Murdoch DR. Fatal case of *Campylobacter lari* prosthetic joint infection and bacteremia in an immunocompetent patient. J Clin Microbiol 2002;40:1053–5.

[10] Jirapongsananuruk O, Wanotayan K, Phongsamart W, et al. Recurrent *Campylobacter lari* bacteremia in X-linked agammaglobulinemia: a case report and review. Asian Pac J Allergy Immunol 2006;24:171–4.

[11] Morishita S, Fujiwara H, Murota H, Maeda Y, Hara A, Horii T. Bloodstream infection caused by *Campylobacter lari*. J Infect Chemother 2013;19:333–7.

[12] CLSI. Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria; approved guideline–Second edition. CLSI document M45-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.

[13] Liu P, Allaudeen H, Chandra R, et al. Comparative pharmacokinetics of azithromycin in serum and white blood cells of healthy subjects receiving a single-dose extended-release regimen versus a 3-day immediate-release regimen. Antimicrob Agents Chemother 2007;51:103–9.

[14] CLSI. Performance standards for antimicrobial susceptibility testing. CLSI supplement m 100. 30th ed Wayne, PA: Clinical and Laboratory Standards Institute; 2020.