JCM Journals.ASM.org

CASE REPORT

First Case Report of Fatal Sepsis Due to *Campylobacter upsaliensis*

Itaru Nakamura,[a] Nami Omori,[b] Ayaka Umeda,[b] Kiyofumi Ohkusu,[c] Tetsuya Matsumoto[c]

Department of Infection Control and Prevention, Tokyo Medical University Hospital, Tokyo, Japan[a]; Department of Microbiology, Tokyo Medical University Hospital, Tokyo, Japan[b]; Department of Microbiology, Tokyo Medical University, Tokyo, Japan[c]

We encountered a rare case of severe fatal infection in a 70-year-old woman due to *Campylobacter upsaliensis*, identified by PCR amplification and sequencing analysis of the 16S rRNA gene using DNA extracted from the isolates. To our knowledge, fatal sepsis due to this organism has never been described to date.

CASE REPORT

A 70-year-old woman was admitted to the emergency department complaining of loss of consciousness. On admission, her vital signs showed lethargy, hypothermia (35.1°C), hypotension (systolic blood pressure of 80 mm Hg), and tachycardia (pulse rate of 160 per minute). She did not have any recent episodes of diarrhea or enterocolitis, as assessed at her periodic visits to our hospital. Prolonged hypoglycemia with treatment resistance was also observed, and glucose was administered more than once. She had a history of left ureteral cancer, thyroid cancer, ectopic Cushing's syndrome, hypertension, and atrial fibrillation. Laboratory examination showed a normal white blood cell count, thrombocytopenia, a high serum transaminase level, and acute kidney injury (estimated glomerular filtration rate of 15.4 ml/min/liter). Severe metabolic acidosis and lactic acidosis were also observed. Enhanced computed tomography imaging led to a diagnosis of Stanford type A dissecting aortic aneurysm with cardiac tamponade. Enteritis and abscesses were not observed. Although pericardiocentesis was performed for the cardiac tamponade caused by the dissecting aortic aneurysm, the patient chose not to have artificial blood vessel replacement performed. Large amounts of vasopressors (noradrenaline and dopamine) and glucose were administered while the patient was in the intensive care unit. Cefazolin (2 g per day) was administered to prevent surgical site infection following pericardiocentesis rather than as a treatment for the original infection. However, severe hypotension, hypoglycemia, and liver failure worsened without improvement. The patient died due to multiorgan failure 2 days after admission.

Bacterial isolates from the blood of the patient, which was taken at admission for the evaluation of hypertension, were positive in Bactec aerobic bottles alone (BD, Franklin Lakes, NJ, USA). Subculture of the positive blood culture bottle yielded growth after 72 h of microaerobic incubation at 37°C (2 days after the patient's death). Bacterial identification using API Campy (Sysmex-bioMérieux, Tokyo, Japan) did not yield a definitive identification. Therefore, PCR amplification and sequencing were performed to analyze the 16S rRNA gene using DNA extracted from the isolates. Genomic DNA from all strains grown were extracted by physical extraction using zirconia beads (Mora extraction kit; AMR Co., Gifu, Japan), according to the manufacturer's instructions. The universal primers 8UA (5′-AGAGTTTGATCMTGGCTCAG-3′) and 1485B (5′-ACGGGCGGTGTGTRC-3′) were used as described previously (1). We performed sequencing analysis using a GenBank BLAST search and EzTaxon (http://www.ezbiocloud.net/eztaxon/). The sequence of the 16S rRNA gene (GenBank accession no. AB980278) was 99.1% identical (1,437 bp over the entire 1,450 bp fragment) with that of *Campylobacter upsaliensis* strain DSM5365 (accession number L14628). Based on the sequencing results, we identified the isolate as *C. upsaliensis*. Antimicrobial susceptibility testing was performed according to the Clinical and Laboratory Standards Institute (CLSI) standards for *Campylobacter jejuni* and *Campylobacter coli* (2). The MICs of the antibiotic agents were determined by the broth microdilution method using MicroScan (Siemens, Tokyo, Japan), except for azithromycin (AZM), for which Etest (bioMérieux, France) was used. The MICs of antibiotics against the *C. upsaliensis* strain are shown in Table 1. Antibiotic agents like penicillins, cephalosporins, and macrolides, including AZM, showed low MICs, consistent with previous reports (3–5). On the other hand, the MIC of fluoroquinolone (levofloxacin) was >8 μg/ml, indicating resistance to fluoroquinolone, as seen in a previous report (4).

C. upsaliensis is known as a catalase-negative or weakly positive thermotolerant *Campylobacter* species (3). This organism's characteristics include the absence of H_2S production on triple sugar iron agar and susceptibility to nalidixic acid and cephalosporin. Therefore, *C. upsaliensis* was reported as being intolerant to the culture conditions optimized for *C. jejuni* and *C. coli* (6). Because routine laboratory procedures also overlooked this organism in our case, cases of *C. upsaliensis* infection might still be underdiagnosed.

C. upsaliensis has been reported mainly as an organism causing diarrhea not only in dogs (7) but in humans (8). The presumed transmission of this organism from dogs and cats to humans has been reported (7, 9). Water or food contaminated with the feces of

Received 19 August 2014 **Returned for modification** 23 September 2014
Accepted 7 November 2014

Accepted manuscript posted online 19 November 2014

Citation Nakamura I, Omori N, Umeda A, Ohkusu K, Matsumoto T. 2015. First case report of fatal sepsis due to *Campylobacter upsaliensis*. J Clin Microbiol 53:713–715. doi:10.1128/JCM.02349-14.

Editor: P. Bourbeau

Address correspondence to Kiyofumi Ohkusu, ohkusu@tokyo-med.ac.jp.

doi:10.1128/JCM.02349-14

TABLE 1 MICs of antibiotics against *C. upsaliensis* isolated from the patient's blood culture

Antimicrobial agent	MIC (μg/ml)[a]
Penicillin G	0.5
Ampicillin	≤0.06
Ampicillin-sulbactam	≤0.25/0.125
Cefotiam	1.0
Ceftriaxone	1.0
Meropenem	≤0.12
Erythromycin	≤0.12
Azithromycin	1.25
Levofloxacin	>8
Sulfamethoxazole-trimethoprim	≤0.5/9.5

[a] The MIC of each antibiotic was determined by broth microdilution performed according to the CLSI standards, except for azithromycin, whose MIC was determined using Etest.

TABLE 2 Thirty-four cases of *C. upsaliensis* infection from previous reports[a]

Age (yrs or as indicated)	Sex	Underlying disease	Clinical presentation	Reference
—	—	—	Hemolytic uremic syndrome	16
4	—	—	Guillain-Barré syndrome	17
64	M	—	Guillain-Barré syndrome	18
83	M	CHF, CRF, COPD	Bacteremia	14
10 (mo)	M	None	Bacteremia	14
20	M	None	Enteritis	14
72	M	CRF	Peritonitis	14
35	F	AML	Enteritis	14
6 (mo)	M	None	URI, erythematous tympanic membranes	14
38	M	AIDS	Bacteremia	14
1	M	URI	Enteritis	14
80	F	Glioblastoma	Bacteremia	14
25	F	REP	Bacteremia	14
64	M	LC	Bacteremia	14
11	F	None	Enteritis	12
36	M	Alcohol syndrome	Pneumonia	12
30	F	None	Burn	12
4	F	None	Enteritis	12
6	M	Anorexia	Enteritis	12
9	M	Kwashiorkor	Bacteremia	12
13	F	None	Enteritis	12
9	M	Anemia	Pneumonia	12
7	F	Myocarditis	Bacteremia	12
6	M	None	Enteritis	12
18	M	Kwashiorkor	Bacteremia	12
27	M	Kwashiorkor	Enteritis	12
10	F	Underweight for age	Enteritis	12
12	M	None	Enteritis	12
2	F	Kwashiorkor	Enteritis	12
18	F	Kwashiorkor	Bacteremia	12
46	F	None	Breast abscess	19
26	F	None	Abortion	9
24	M	Knee arthroplasty	Prosthetic knee infection	15
83	M	IBS	Persistent bloody diarrhea	5
70	M	UC, TC, CS	Severe sepsis	This report

[a] —: unknown; M, male; F, female; CHF, congestive heart failure; CRF, chronic renal insufficiency; COPD, chronic obstructive pulmonary disease; AML, acute myeloid leukemia; URI, upper respiratory illness; REP, ruptured ectopic pregnancy; LC, liver cirrhosis; IBS, irritable bowel syndrome; UC, ureteral cancer; TC, thyroid cancer; CS, Cushing's syndrome.

pets, such as dogs or cats, might be routes of transmission. On the other hand, the majority of human-infecting strains are genetically separate from the canine-infecting strains, indicating that dogs may not be the main source of human infection (10). In addition, there is only 1 report to date on human-to-human transmission (11). Although *C. upsaliensis* is an emerging diarrhea-causing pathogen that is thought to be transmitted from household pets (7, 9), the patient had no history of owning pets. She also did not have contact with any other person with diarrhea or colitis; therefore, her infection route is unclear.

C. upsaliensis has most frequently been reported as the causative organism in cases of enteritis and bacteremia (Table 2). In addition, *C. upsaliensis* was also isolated from patients with extraintestinal infections. These previous reports are summarized in Table 2. However, to our knowledge, a severe fatal case due to this organism has never been described to date, and the clinical spectrum of this organism in humans is not fully understood.

We concluded that the patient's severe hypotension, severe acute liver failure, acute kidney injury, lactic acidosis, and hypoglycemia were all caused by the sepsis, because no other cause of these symptoms could be identified. In addition, enteritis was not observed in the patient. Infections due to *C. upsaliensis* have been reported to be associated with an underlying disease or immunocompromised state, including human immunodeficiency virus infection (12–14). This patient also had a history of cancer and endocrine disease.

To our knowledge, a severe fatal case of *C. upsaliensis* infection resulting in multiorgan failure, such as this case, has never been reported to date. Dissecting aortic aneurysms are usually induced by aortic sclerosis. The causal association between *C. upsaliensis* bacteremia and the aneurysm in this case is unclear, because an infected aneurysm is usually of the saccular type, and *C. upsaliensis* was detected only in the blood culture (the patient's aortic tissue was not obtained).

In previous reports, erythromycin resistance of *C. upsaliensis* infections ranged from 10% to 15% (6, 14), and ciprofloxacin resistance was approximately 5% (4). *C. upsaliensis* isolated from our patient showed a high MIC only for fluoroquinolone, in addition to macrolides, similar to a previous report (15). For the selection of antibiotic treatments, further data on the antibiograms of *C. upsaliensis* strains from different countries are required. In addition, there was a significant time lag until the identification of this organism in our case. Because *C. upsaliensis* infection is rare in clinical settings, if a patient has underlying disease, as in our case, treatment assuming *C. upsaliensis* infection is unlikely to be performed.

This case report is thought to be valuable since it highlights a severe and rare case due to *C. upsaliensis*, an emerging pathogen. It is important to clarify the conditions and medium required to culture this organism. The clinical spectrum of *C. upsaliensis* infection remains unclear, and further studies are required to establish appropriate treatments.

ACKNOWLEDGMENTS

We are indebted to the medical editors of the Department of International Medical Communications of Tokyo Medical University for the editorial review of the English manuscript.

We declare no conflicts of interest associated with this study.

REFERENCES

1. **Funato M, Kaneko H, Ohkusu K, Sasai H, Kubota K, Ohnishi H, Kato Z, Fukao T, Kondo N.** 2011. Refractory chronic pleurisy caused by Helicobacter equorum-like bacterium in a patient with X-linked agammaglobulinemia. J Clin Microbiol **49:**3432–3435. http://dx.doi.org/10.1128/JCM.00478-11.
2. **CLSI.** 2010. Methods for antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria; approved guideline, 2nd ed. CLSI document M45-A2. CLSI, Wayne, PA.
3. **Bourke B, Chan VL, Sherman P.** 1998. Campylobacter upsaliensis: waiting in the wings. Clin Microbiol Rev **11:**440–449.
4. **Vandenberg O, Houf K, Douat N, Vlaes L, Retore P, Butzler JP, Dediste A.** 2006. Antimicrobial susceptibility of clinical isolates of non-jejuni/coli campylobacters and arcobacters from Belgium. J Antimicrob Chemother **57:**908–913. http://dx.doi.org/10.1093/jac/dkl080.
5. **Couturier BA, Hale DC, Couturier MR.** 2012. Association of Campylobacter upsaliensis with persistent bloody diarrhea. J Clin Microbiol **50:**3792–3794. http://dx.doi.org/10.1128/JCM.01807-12.
6. **Goossens H, Pot B, Vlaes L, Van den Borre C, Van den Abbeele R, Van Naelten C, Levy J, Cogniau H, Marbehant P, Verhoef J.** 1990. Characterization and description of "Campylobacter upsaliensis" isolated from human feces. J Clin Microbiol **28:**1039–1046.
7. **Goossens H, Vlaes L, Butzler JP, Adnet A, Hanicq P, N'Jufom S, Massart D, de Schrijver G, Blomme W.** 1991. Campylobacter upsaliensis enteritis associated with canine infections. Lancet **337:**1486–1487. http://dx.doi.org/10.1016/0140-6736(91)93182-9.
8. **Man SM.** 2011. The clinical importance of emerging Campylobacter species. Nat Rev Gastroenterol Hepatol **8:**669–685. http://dx.doi.org/10.1038/nrgastro.2011.191.
9. **Gurgan T, Diker KS.** 1994. Abortion associated with Campylobacter upsaliensis. J Clin Microbiol **32:**3093–3094.
10. **Damborg P, Guardabassi L, Pedersen K, Kokotovic B.** 2008. Comparative analysis of human and canine Campylobacter upsaliensis isolates by amplified fragment length polymorphism. J Clin Microbiol **46:**1504–1506. http://dx.doi.org/10.1128/JCM.00079-08.
11. **Goossens H, Giesendorf BA, Vandamme P, Vlaes L, Van den Borre C, Koeken A, Quint WG, Blomme W, Hanicq P, Koster DS, Hofstra H, Butzler J-P, Van der Plas J.** 1995. Investigation of an outbreak of Campylobacter upsaliensis in day care centers in Brussels: analysis of relationships among isolates by phenotypic and genotypic typing methods. J Infect Dis **172:**1298–1305. http://dx.doi.org/10.1093/infdis/172.5.1298.
12. **Lastovica AJ, Le Roux E, Penner JL.** 1989. "Campylobacter upsaliensis" isolated from blood cultures of pediatric patients. J Clin Microbiol **27:**657–659.
13. **Jenkin GA, Tee W.** 1998. Campylobacter upsaliensis-associated diarrhea in human immunodeficiency virus-infected patients. Clin Infect Dis **27:**816–821. http://dx.doi.org/10.1086/514957.
14. **Patton CM, Shaffer N, Edmonds P, Barrett TJ, Lambert MA, Baker C, Perlman DM, Brenner DJ.** 1989. Human disease associated with "Campylobacter upsaliensis" (catalase-negative or weakly positive Campylobacter species) in the United States. J Clin Microbiol **27:**66–73.
15. **Issartel B, Pariset C, Roure C, Boibieux A, Peyramond D.** 2002. Successful treatment of prosthetic knee infection due to Campylobacter upsaliensis. Eur J Clin Microbiol Infect Dis **21:**234–235. http://dx.doi.org/10.1007/s10096-001-0693-x.
16. **Carter JE, Cimolai N.** 1996. Hemolytic-uremic syndrome associated with acute Campylobacter upsaliensis gastroenteritis. Nephron **74:**489. http://dx.doi.org/10.1159/000189403.
17. **Goddard EA, Lastovica AJ, Argent AC.** 1997. Campylobacter 0:41 isolation in Guillain-Barre syndrome. Arch Dis Child **76:**526–528. http://dx.doi.org/10.1136/adc.76.6.526.
18. **Ho TW, Hsieh ST, Nachamkin I, Willison HJ, Sheikh K, Kiehlbauch J, Flanigan K, McArthur JC, Cornblath DR, McKhann GM, Griffin JW.** 1997. Motor nerve terminal degeneration provides a potential mechanism for rapid recovery in acute motor axonal neuropathy after Campylobacter infection. Neurology **48:**717–724. http://dx.doi.org/10.1212/WNL.48.3.717.
19. **Gaudreau C, Lamothe F.** 1992. Campylobacter upsaliensis isolated from a breast abscess. J Clin Microbiol **30:**1354–1356.