Campylobacter fetus subspecies venerealis meningitis associated with a companion dog in a young adult: a case report

Yeol Jung Seong1, Seung Hun Lee2, Eun Jin Kim1, Young Hwa Choi1, Tae-Joon Kim3, Wee Gyo Lee4*† and Jung Yeon Heo1*†

Abstract

Background: Campylobacter spp., common commensals in the gastrointestinal tract of animals, especially poultry, can cause acute gastrointestinal illness in humans through animal-to-human transmission. Although Campylobacter fetus, especially subspecies fetus, rarely leads to systemic infections such as bacteremia in immunocompromised patients, it is unclear whether Campylobacter fetus subspecies venerealis (Cfv) causes infectious diseases in humans.

Case presentation: A 28-year-old man with a history of chronic alcoholism visited the emergency department with weakness of the left extremities. The patient was clinically diagnosed with community-acquired bacterial meningitis. The organism from the blood culture was subsequently identified as Campylobacter fetus. On phylogenetic analysis, the 16S rRNA sequence showed 99.93% similarity with other Cfv 16S rRNA sequences. The patient had no exposure to identifiable sources except for close contact with a companion dog, which could have been a possible source of transmission.

Conclusions: This case suggests that Cfv could lead to human systemic infections such as meningitis and that companion animals, in addition to well-known animal hosts, could be sources of transmission.

Keywords: Bacterial meningitis, Campylobacter fetus subsp. venerealis, Companion animal, Zoonotic infectious diseases

Background

Campylobacter spp., a zoonotic pathogen found in a wide range of animals whose primary reservoirs are the intestinal tracts, usually cause diarrheal illness in humans [1]. Although the vast majority of cases of Campylobacter infection in humans are caused by Campylobacter jejuni or Campylobacter coli, Campylobacter fetus occasionally causes extraintestinal infections, such as bloodstream infection, rather than enteric disease [2]. Invasive C. fetus infection has a broad spectrum of clinical presentation from bloodstream infection without apparent localized infection to various types of localized infections, including infection of central nervous system (CNS), osteomyelitis, lung abscess, arthritis, and perinatal infection. Human C. fetus infection is uncommon and usually occurs in patients with immunosuppressed conditions or underlying diseases such as cardiovascular disease with valve abnormalities, liver disease, and diabetes mellitus. Two major subspecies of C. fetus have been described: C. fetus subsp. fetus (Cff) and C. fetus subsp. venerealis.
(Cfv) [3]. Human infections with a new subspecies of C. fetus, which has a reptilian origin [4]. Almost nearly all cases of C. fetus infection in humans are known to be caused by Cff, and little is known about human infections caused by Cfv. We recently encountered a case of bacterial meningitis caused by Cfv in a young adult. The patient strongly denied having been in close contact with domestic animals or ingesting raw animal products. The route of transmission was suspected to be the frequent close contact with a companion dog, such as while kissing. We also performed a systematic review to enhance our understanding of human C. fetus infections of the central nervous system (CNS).

**Case presentation**

A 28-year-old man with a history of chronic alcoholism visited the emergency department owing to weakness in the left extremities. He was under treatment with an antiepileptic drug for the past 6 months since a traumatic subdural hemorrhage occurred during a fall down the stairs. At that time, he underwent facial nerve decompression for left-sided facial palsy due to ear bleeding and a temporal bone fracture. He complained of a 5-day history of myalgia and upper respiratory infection symptoms, such as coughing and sore throat. Initially, his vital signs were stable except for a body temperature of 38.6 °C. He was responsive to the medical staff’s questions, but his answers lacked fluency. Findings of a physical examination performed on arrival to the emergency room were unremarkable, and mild neck stiffness was observed during a neurological examination.

Baseline laboratory data of complete blood count showed leukocytosis (white blood cell [WBC] count, 15,090/μL; neutrophils, 87.5%; lymphocytes, 4.9%) with mild C-reactive protein elevation (2.08 mg/dL). Since the patient’s neck stiffness worsened and stupor was noted, a cerebrospinal fluid (CSF) analysis was performed. The CSF analysis showed pleocytosis (WBC count of 390/μL; polymorphonuclear leukocyte count, 60%), high protein level (161.3 mg/dL; reference range, 15–40 mg/dL), and low glucose level (30 mg/dL; reference range, 40–70 mg/dL) with a negative Gram stain. No focal lesions were observed on brain magnetic resonance imaging (Additional file 1: Fig. S1). Intravenous ceftriaxone (2 g every 12 h) and vancomycin (1 g every 12 h) as empirical antibiotic therapy were administered with intravenous dexamethasone, as the findings were suggestive of bacterial meningitis caused by Streptococcus pneumoniae or Neisseria meningitidis.

On day 6 of hospitalization, blood culture revealed Gram-negative bacilli growth in the aerobic and anaerobic bottles. On day 11 of hospitalization, the organism was identified as C. fetus. However, these organisms were not identified in the CSF culture. The CSF specimen was collected 6 h after prompt empirical antibiotic treatment. Doripenem (500 mg every 8 h) was administered for 10 days until the meningitis symptoms completely resolved without neurological sequelae. The automated susceptibility test (VITEK2 system, bioMérieux, France) showed that the isolate was susceptible to erythromycin and ciprofloxacin. The patient regularly visited the outpatient clinic for 2 years, without recurrence of the meningitis. He stated that he had been raising a companion dog and denied contact with livestock animals such as cattle and sheep or ingestion of raw or undercooked meat.

To confirm the species and identify the subspecies of the isolated C. fetus sample, a sequence analysis of the 16s rRNA gene was conducted using the polymerase chain reaction primers 27F 5′-AGA GTT TGA TCM TGG CTC-3′ and 1492R 5′-TAC GGY TAC CTT GG TAC ACT-3′. The sequencing primers 785F 5′-GGG TGA GAT ACC CTG GTA-3′ and 907R 5′-CCG TCA ATT CMT TTR AGT TT-3′ were used. The C. fetus 16S rRNA sequence was compared to the published sequences from GenBank. Phylogenetic analysis (Jukes-Cantor/Neighbor Joining) revealed that the 16S rRNA sequence in this case showed high similarity (99.93%) with other Cfv 16S rRNA sequences (Fig. 1). These sequences were also distinct from those of Cff and other Campylobacter spp. compared with previously reported 16S rRNA nucleotides of other Campylobacter species (C. coli, C. jejuni, Cff) (Fig. 2).

**Discussion and conclusions**

Here we described a case of C. fetus meningitis in a young adult with a history of heavy alcoholism who was being treated with an antiepileptic drug for a traumatic cerebral hemorrhage. A culture isolate of C. fetus was identified as Cfv by sequence analysis of the 16s rRNA gene. C. fetus is divided into two major subspecies: Cff and Cfv [3]. These subspecies are genetically closely related but have different habitats and clinical importance. The primary reservoir of Cff is the intestinal tract of cattle and sheep [5]. Cff is a clinically significant pathogenic organism in animals and an opportunistic pathogen in humans. It has been identified in human cases of bloodstream infection, vascular infection, and cellulitis in addition to meningitis [6, 7]. In contrast, Cfv is a commensal organism of the bovine genital tract that causes an infectious disease known as bovine genital campylobacteriosis, which leads to infertility and enzootic abortion in cattle, resulting in considerable economic losses [8]. Cfv has been isolated from human specimens in only a few cases [9], and its clinical significance remains uncertain. Thus, this is a rare case of systemic human infection caused by Cfv.
To perform a systematic review for *Campylobacter fetus* meningitis, the MEDLINE database was searched using keywords *Campylobacter fetus* AND meningitis, *Vibrio fetus* AND meningitis, and *Spirillum serpens* AND meningitis. Literature written in English, French, German, Spanish, Japanese, and Korean were included. Case descriptions of animals or children were excluded. We identified 38 cases of CNS infections in 34 related articles published since 1960 (Table 1). Among these patients, 30 were men (78.9%). The median age was 49.5 years (interquartile range, 39.8–57.0 years). Immunocompromised conditions were observed in 24 cases (63.2%), and the prevalent underlying conditions were alcoholism (14 cases [36.8%]) and diabetes (6 cases [15.8%]). Although *C. fetus* is a zootoxic pathogen, the potential source of infection, such as animal or animal product contact, was
Table 1  A case summary of *Campylobacter fetus* meningitis based on a systematic literature review

| Year | Ref  | Age/Sex | Underlying condition | Source of infection | Specimens | (Sub)species | Clinical manifestations | Treatment | Outcome         |
|------|------|---------|----------------------|---------------------|-----------|--------------|------------------------|-----------|-----------------|
| 2021 | 33/F | ALL     | Undercooked beef ingestion | Blood and CSF       | Cf        | Meningitis   | MER                    | Recovery  |
| 2019 | 56/M | Chronic alcoholism | Unknown | CSF        | Cf        | Meningoencephalitis | AMP       | Recovery     |
| 2019 | 35/F | No      | Unknown             | Blood              | Cf        | Meningitis and spondyloclisis | MEP, AMP    | Recovery     |
| 2018 | 48/F | No      | Raw beef and cattle liver ingestion | CSF               | Cff/Cfv   | Meningitis   | CRO                   | Recovery  |
| 2017 | 64/M | Alcoholic liver cirrhosis and diabetes | Unknown  | Blood   | Cff       | Meningitis   | DOR                   | Recovery  |
| 2016 | 23/F | No      | Domestic animals worked on a farm | CSF              | Cf        | Meningitis   | CRO, MER              | Cured after relapse, cognitive defect |
| 2016 | 52/M | No      | Farmer              | Blood and CSF      | Cff       | Meningitis   | CRO, MER, IPM, GEN    | Recovery  |
| 2013 | 75/M | Diabetes | Unknown             | Blood and CSF      | Cff       | Meningitis and endocarditis | CRO, MER, IPM, GEN | Recovery  |
| 2013 | 28/M | Seizure disorder  | Khat chewing | Blood, CSF, and stool | Cff       | Meningitis   | CRO                   | Recovery  |
| 2009 | 40/M | No      | Unknown             | Blood and CSF      | Cff       | Subdural empyema | NA                   | Recovery  |
| 2008 | 51/M | No      | Unknown             | Blood and CSF      | Cff       | Meningitis   | MER                   | Recovery  |
| 2004 | 71/M | Diabetes | Unknown             | CSF                | Cf        | Meningitis   | IPM                   | Recovery  |
| 2002 | 49/M | Chronic alcoholism | Unknown  | Blood and CSF | Cff       | Meningoencephalitis and spondyloclisis | NA       | Recovery     |
| 1998 | 47/M | Chronic alcoholism | Dog and cat | Blood   | Cff       | Meningitis   | CTX, OFX, GEN         | Recovery  |
| 1997 | 70/M | Chronic alcoholism | Unknown  | CSF      | Cf        | Infected subdural hematoma | IPM       | Recovery     |
| 1996 | 84/M | Alcoholic liver cirrhosis | Unknown  | Blood and CSF | Cff       | Meningitis   | CRO, CIP              | Died      |
| 1993 | 40/M | No      | Raw beef            | Blood and CSF      | Cff       | Meningitis   | IPM                   | Recovery  |
| 1990 | 55/M | Chronic alcoholism and diabetes | Unknown  | CSF      | Cff       | Meningitis   | AMP                   | Recovery  |
| 1989 | 39/F | Chronic alcoholism, epilepsy | Unknown  | Blood and CSF | Cff       | Meningitis   | AMS                   | Recovery  |
| 1989 | 36/M | Chronic alcoholism | Unknown  | Blood   | Cff       | Meningitis   | AMP                   | Recovery  |
| 1987 | 47/M | Kidney transplantation recipient | Raw cattle liver ingestion | Blood and CSF | Cfi      | Meningitis   | ERY, CHL              | Recovery  |
| 1986 | 30/M | No      | Raw cattle liver ingestion | CSF              | Cff       | Meningitis   | AMP                   | Recovery  |
| 1986 | 42/M | No      | Unknown             | CSF                | Cff       | Meningitis   | MIN                   | Recovery  |
| 1985 | 68/M | Rectal cancer with hepatic metastasis | Unknown  | Blood and CSF | Cff       | Meningitis   | CFZ, TOB, ERY, AMP, GEN | Died      |
| 1985 | 65/M | Alcoholic liver cirrhosis | Unknown  | Blood      | Cff       | Meningitis   | ERY                   | Cured after relapse  |
| 1985 | 38/M | Chronic alcoholism | Cat      | CSF      | Cff       | Meningitis   | AMP, GEN              | Recovery  |
| 1984 | 53/M | No      | Unknown             | Blood and CSF      | Cff       | Meningitis   | CHL                   | Recovery  |
| 1980 | 34/M | No      | Unknown             | CSF                | Cff       | Meningitis   | CHL                   | Recovery  |
identified in only 15 cases (39.5%). Among the identified cases, the likely source of infection and the major risk factors for exposure to *C. fetus* were the ingestion of raw or undercooked meat (6 cases [40.0%]) and frequent contact with animals (5 cases [33.3%]).

This case shared common features of chronic alcoholism and frequent animal contact with the findings of the systematic review. In addition, the previous subdural hemorrhage in this case may have been a predisposing factor for meningitis. Potential disruption of the blood–brain barrier could be a pathway for microbes to invade the central nervous system. However, other potential sources of infection were not identified, except for contact with the companion dog. We were unable to demonstrate that the dog was the source of transmission; however, given that *C. jejuni* transmission from a companion dog was genetically proven previously [10], the same is certainly plausible in this case. This case suggests that companion dogs could be a reservoir for zoonotic pathogens and their owners should be educated on zoonotic disease risk and prevention.

Systemic *C. fetus* infections, such as sepsis or meningitis, should be treated with parenteral antibiotics. Through a systematic review, we identified that most of the recently reported cases of *C. fetus* meningitis were treated with carbapenem antibiotics, similar to the present case. However, *C. fetus* is generally susceptible to ampicillin, cefotaxime, ciprofloxacin, aminoglycoside, and imipenem but not erythromycin [11]. Despite these patterns of antimicrobial susceptibility, *C. fetus* infection in the central nervous system should be treated with prolonged antibiotic treatment for at least 2–3 weeks [1]. The surface-layer proteins of *C. fetus*, critical factors in its virulence that form a capsule-like structure, can undergo antigenic variation that enables evasion of the host’s immune system [12]. Therefore, an invasive *C. fetus* infection could relapse or persist even several years after the initial episode.

To the best of our knowledge, human *Cfv* infection has rarely been reported: We found only one case of an adult with meningitis and five cases of patients with bacteremia [9, 13]. These human cases with *Cfv* infection were mainly identified by 16S rRNA sequencing analysis. However, it could be difficult to differentiate between subspecies *fetus* and *venerealis* because of the modest subspecies-specific variation at the genome level [14]. A case of meningitis revealed that *Cff* and *Cfv* were identified through matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF-MD) and 16S rRNA sequencing. Although five cases of bacteremia were identified as *Cfv* on the 16S rRNA sequencing analysis, three cases were identified as *Cff* and the other two cases were identified as *Cfv* by the multiplex PCR method using the cadF, hipO, and asp genes. Other
bacteremia or meningitis cases attributed to *C. fetus* subspecies were mostly caused by *Cff*. The present case demonstrated that CFv isolated from the blood has sequences distinct from *Cff* based on the 16S rRNA sequence and phylogenetic analysis.

Our case suggests that CFv could cause human systemic infections, such as meningitis, and may be associated with companion animals in addition to well-known animal hosts.

**Abbreviations**
- ALL: Acute lymphoblastic leukemia
- AMP: Ampicillin
- AMS: Ampicillin/sulbactam
- C. *coli*: *Campylobacter* *coli*
- C. *fetus*: *Campylobacter* *fetus*
- C. *jejuni*: *Campylobacter* *jejuni*
- Cfv: *Campylobacter fetus*
- CF: *Campylobacter fetus* Subspecies *fetus*
- Cff: *Campylobacter fetus* Subspecies *intestinale*
- CFz: *Campylobacter fetus* Subspecies *jejunii*
- Campylobacter fetus Subspecies *jejuni*
- C. *jejuni* Subspecies *jejuni*
- C. *jejuni* Subspecies *venerealis*
- CFz: Cefazolin
- CHL: Chloramphenicol
- CIP: Ciprofloxacin
- CLL: Chronic lymphocytic leukemia
- CNS: Central nervous system
- CRO: Ceftriaxone
- CSF: Cerebrospinal fluid
- CTX: Cefotaxime
- DOR: Doripenem
- ERY: Erythromycin
- GEN: Gentamicin
- IPM: Imipenem
- ITET: Tetracycline
- KAN: Kanamycin
- MEP: Meropenem
- MIN: Minocycline
- NA: Not available
- OFX: Oflloxacin
- PEN: Penicillin
- PIP: Piperacillin
- SFZ: Sulfadiazine
- WBC: White blood cell

**Supplementary Information**
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**Authors’ contributions**
JYS and JYH contributed to the study conception and design. YJS, WGL, and JYH analyzed the data and take responsibility for its integrity and prepared the manuscript. All authors contributed to acquiring the clinical and laboratory data. YJS, SHL, EJK, YWC, TJK, WGL, and JYS contributed to the data analysis and interpretation. All authors critically revised the manuscript for intellectual content and approved the final draft for submission. All authors read and approved the final manuscript.

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**Availability of data and materials**
The 16S rRNA sequences of *Campylobacter fetus* subsp *venerealis* are available in the GenBank database (Accession Number: MZ810518).

**Declarations**

**Ethics approval and consent to participate**
The study was conducted in accordance with institutional ethical guidelines. The patient provided written informed consent to participate in the research.

**Consent for publication**
Written informed consent was obtained from the patient for the publication of this case report. A copy of the written consent is available for review by the editor of this journal.

**Competing interests**
The authors declare no competing interests.

**Author details**

1. Department of Infectious Diseases, Ajou University School of Medicine, 164 Worldcup-ro, Youngtong-gu, Suwon, Gyeonggi-do 16499, Republic of Korea.
2. Division of Infectious Disease Diagnosis Control, Honam Regional Center for Disease Control and Prevention, Korea Disease Control and Prevention Agency, Gwangju, Republic of Korea.
3. Department of Laboratory Medicine, Ajou University School of Medicine, 164 Worldcup-ro, Youngtong-gu, Suwon, Gyeonggi-do 16499, Republic of Korea.

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