Case report

*Campylobacter fetus* meningitis associated with eating habits of raw meat and raw liver in a healthy patient: A case report and literature review

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**ABSTRACT**

Meningitis caused by the zoonotic pathogen *Campylobacter fetus* in immunocompetent adults is rare. We report a 48-year-old Japanese woman with no underlying disease who was found to have meningitis caused by *C. fetus*. Both *C. fetus* subsp. *fetus* and *C. fetus* subsp. *venerealis* were isolated from the cerebrospinal fluid culture. The mode of infection in our patient was considered to be associated with the consumption of raw beef and raw cattle liver on a regular basis. Public awareness and education to avoid the consumption of raw or undercooked meat might help prevent *C. fetus* meningitis.

**Introduction**

*Campylobacter fetus* (formerly called as *Spirillum serpens* or *Vibrio fetus*) is a zoonotic pathogen with major reservoirs of cattle and sheep. *C. fetus* is a rare cause of bacterial meningitis. Thus far, *C. fetus* meningitis has been reported to occur in those who frequently chew khat (an alkaloid containing plant) in an animal sanctuary, come in contact with domestic animals, or consume the raw meat or raw liver of cattle and sheep [1].

*C. fetus* infections frequently occur among patients with impaired immunity including conditions such as chronic alcoholism, liver disease, old age, diabetes mellitus, and malignancies [2]. There are only a few case reports of *C. fetus* bacteremia and meningitis in healthy adults [3–6]. However, immunosuppression may not be the sole risk factor [7]. In this study, we report a case of *C. fetus* meningitis in a healthy adult and conducted a literature review.

**Case**

While in the emergency department of our hospital, she was alert and oriented, and not in acute distress. Her blood pressure was 132/60 mmHg, her heart rate was 64/min, her respiratory rate was 30/min, and her body temperature was 38.4 °C. The physical examination revealed nuchal rigidity without focal neurological abnormalities. Her laboratory tests revealed a white blood cell count of 14,200/μL; she tested negative for human immunodeficiency virus (HIV) antigens and antibodies and her electrolyte and aminotransferase levels were within normal limits. Cerebrospinal fluid (CSF) testing revealed leukocytosis with high protein and low glucose levels (Table 1). Her CSF showed increased white blood cells with neutrophil dominance with no organisms seen on Gram stain. Dexamethasone, ceftriaxone, ampicillin, vancomycin, and acyclovir were administered to treat both bacterial and viral meningitis. In addition, minocycline was administered to treat rickettsiosis. The serum cryptococcal antigen and serum nontreponemal and treponemal tests were negative. The acid-fast bacilli smear test and tuberculosis polymerase chain reaction (PCR) of the CSF were both negative.

On day three of admission, the patient’s headaches began to recede. Vancomycin and dexamethasone were discontinued as meningitis due to *Streptococcus pneumoniae* was thought to be less likely as the CSF cultures were negative. On day five of admission, Gram-negative spiral

**Table 1**

| Cerebrospinal fluid test. |  |
|--------------------------|----------------|
| Leukocytes               | 1219/μL       |
| Polynuclear cells        | 799/μL (65%)  |
| Mononuclear cells        | 418/μL (34%)  |
| Protein                  | 80 mg/dL      |
| Glucose                  | 51 mg/dL      |
| (Blood glucose)          | 134 mg/dL     |
| Case no. | Year  | Author             | Country     | Age  | Sex | Underlying conditions                                      | Cause                      | Bacteriology | Method to identify the organism | Outcome | Blood culture | CSF culture | Outcome |
|---------|-------|--------------------|-------------|------|-----|-----------------------------------------------------------|----------------------------|--------------|--------------------------------|---------|---------------|-------------|---------|
| 1       | 1960  | Edwards CE         | United States | 50   | F   | Hypertension                                              | Spirillum serpens          | Blood culture | +                                | Cured   |               |             |         |
| 2       | 1964  | Collins S          | United States | 40   | F   | Handling fecal discharges of rats                        | Vibrio fetus               | Blood culture | +                                | Relapsed → Cured |               |             |         |
| 3       | 1966  | Killam H           | United States | 46   | M   | Handling fecal discharges of rats                        | Vibrio fetus               | Blood culture | +                                | Deeply comatose | Cured   |             |         |
| 4       | 1969  | Reyman TA          | United States | 59   | M   | Handling fecal discharges of rats                        | Vibrio fetus               | Blood culture | +                                | Died    |               |             |         |
| 5       | 1971  | Gubina M           | Yugoslavia   | 46   | M   | Unknown                                                   | C. fetus subsp.intestinalis | Blood culture | +                                | Relapsed → Cured | Cured   |             |         |
| 6       | 1976  | Gubina M           | Yugoslavia   | 40   | M   | Unknown                                                   | C. fetus subsp.intestinalis | Blood culture | +                                | Cured   |               |             |         |
| 7       | 1976  | Gubina M           | Yugoslavia   | 50   | M   | Unknown                                                   | C. fetus subsp.intestinalis | Blood culture | +                                | Cured   |               |             |         |
| 8       | 1976  | Gubina M           | Yugoslavia   | 40   | M   | Unknown                                                   | C. fetus subsp.intestinalis | Blood culture | +                                | Cured   |               |             |         |
| 9       | 1978  | Iida Y             | Japan        | 50   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 10      | 1979  | Inoue Y            | Japan        | 40   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 11      | 1983  | Dronda F           | United States | 47   | M   | Drug abuse                                                | C. fetus subsp. fetus      | Blood culture | +                                | Relapsed → Cured | Cured   |             |         |
| 12      | 1985  | Ozeki T            | United States | 49   | M   | Unknown                                                   | C. fetus subsp. fetus      | Blood culture | +                                | Relapsed → Cured | Cured   |             |         |
| 13      | 1986  | Iida H             | United States | 46   | M   | Unknown                                                   | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 14      | 1986  | Yamazaki E         | Japan        | 46   | M   | Unknown                                                   | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 15      | 1987  | Shioyama M         | Japan        | 45   | M   | Unknown                                                   | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 16      | 1990  | Kato H             | Japan        | 55   | M   | Chronic alcoholism, Diabetes mellitus                   | A. Ishihara et al.         | Biochemical, PCR | +                                | Cured   |               |             |         |
| 17      | 1993  | Inoue Y            | Japan        | 40   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 18      | 1994  | Suy F              | France       | 75   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 19      | 2002  | Herve J            | France       | 71   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 20      | 2004  | Inoue Y            | Japan        | 53   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 21      | 2006  | Inoue Y            | Japan        | 47   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 22      | 2007  | Inoue Y            | Japan        | 40   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 23      | 2010  | Inoue Y            | Japan        | 46   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 24      | 2012  | Inoue Y            | Japan        | 46   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 25      | 2013  | Inoue Y            | Japan        | 46   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 26      | 2013  | Inoue Y            | Japan        | 46   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 27      | 2014  | Inoue Y            | Japan        | 46   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 28      | 2015  | Inoue Y            | Japan        | 46   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 29      | 2016  | Inoue Y            | Japan        | 46   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |
| 30      | 2017  | Inoue Y            | Japan        | 46   | M   | Ingesting raw beef                                       | C. fetus subsp. fetus      | Blood culture | +                                | Cured   |               |             |         |

*C. fetus subsp. fetus is formerly described as C. fetus subsp. intestinalis [10].*
bacilli were isolated from the CSF culture. Acyclovir, ampicillin, and minocycline were discontinued, and only ceftriaxone was continued. On day 12 of admission, matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF-MS) identified the organisms isolated from the CSF specimen as *C. fetus* subsp. *venerealis* (score 2.378) and *C. fetus* subsp. *fetus* (score 2.334). At this point, repeated history taking revealed that she had been consuming raw beef and raw cattle liver every weekend. Thus, the diagnosis of *C. fetus* as a cause of meningitis was made.

Ceftriaxone was changed to meropenem as she developed generalized skin rash most likely as a side-effect of ceftriaxone. She was discharged home after she received four weeks of intravenous antimicrobial treatment, and she did not show any signs of recurrence. 16S rRNA gene sequencing was performed to confirm the identification of the organisms. Gene sequencing revealed 100% coincidence with *C. fetus* subsp. *venerealis* and 99% coincidence with *C. fetus* subsp. *fetus*.

**Discussion**

A literature search in Pubmed was performed, and all clinical cases of *C. fetus* meningitis in adults published in English and Japanese were reviewed. The following keywords were used: “meningitis AND *Campylobacter fetus*,” “meningitis AND *Vibrio fetus*,” and “*Spirillum serpens* AND meningitis.” The major findings are summarized in Table 2.

Two subspecies of *C. fetus* were identified: *C. fetus* subsp. *fetus* and *C. fetus* subsp. *venerealis*. *C. fetus* subsp. *fetus* is associated with abortion in cattle and sheep and also causes infections in humans [2]. Conversely, *C. fetus* subsp. *venerealis* is associated with abortion in cattle [8], but its role in humans is uncertain. *C. fetus* subsp. *venerealis* has only been isolated from the stools of two homosexual men in Australia and from two women with bacterial vaginosis [2].

Our literature review revealed that all cases of meningitis were caused by *C. fetus* subsp. *fetus*. Our patient was unique as her CSF culture showed two subspecies: *C. fetus* subsp. *fetus* and *C. fetus* subsp. *venerealis*. MALDI-TOF-MS and 16S rRNA gene sequencing identified both subspecies. We considered two hypotheses. One was that our patient was infected by both the subspecies *C. fetus* subsp. *fetus* and *venerealis*. The other was that MALDI-TOF-MS and 16S rRNA gene sequencing failed to distinguish the two subspecies. Differentiation between the two subspecies has traditionally been determined by the 1% glycin tolerance test, and PCR assays have also been reported as a valuable adjunctive technique [9]. We did not perform these tests; however, *C. fetus* subsp. *venerealis* reported a higher score on performing MALDI-TOF-MS and a higher coincidence on performing 16S rRNA gene sequencing. *C. fetus* subsp. *venerealis*, an extremely rare organism to cause infections in humans, could be the pathogen that caused meningitis in our patient.

Another remarkable point in our literature review is that five patients were infected by consuming raw meat or raw liver and that three of them were Japanese with no past medical history, including our patient. It is not a rare occasion for people in Japan and other Asian countries to consume raw beef and raw cattle liver. Therefore, eating habits can be a major risk factor for these people even if they are immunocompetent.

In 2012, the Japanese Ministry of Health, Labour and Welfare prohibited serving raw cattle liver at restaurants. However, self-barbecue restaurants still provide raw meat and raw liver, and there are no legal restrictions regarding how restaurant customers cook raw meat and raw liver that was provided. Public awareness and education to prevent *C. fetus* meningitis should be warranted not only in Japan but also in other Asian countries where these eating habits exist.

**Conflict of interest**

All authors do not have any conflict of interest.

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### Appendix A

**References**

1. Edwards CE. *Spirillum serpens* meningitis. Report of a case. N Engl J Med. 1960;262:458-60.
2. Collins S. Protected bacteremia and meningitis due to *Vibrio fetus*. Arch Intern Med. 1964;113:361-4.
3. Killam H. Pericarditis due to *Vibrio fetus*. Am J Cardiol. 1966;17(5):723-4.
4. Reymann TA. *Vibrio fetus* septicaemia. Am J Clin Pathol. 1969;51(5):578-83.
5. Gunderson CH. Neurology of *Vibrio fetus* infection. Neurology. 1971;21(3):307-9.
6. Gubna M. Septicaemia and meningitis with *campylobacter fetus* subspecies *intestinalis*. Infection. 1976;4(2):115-8.
7. Zelingser KS. Central nervous system infection by *Vibrio fetus*. Neurology. 1978;28:906-71.
8. Hanai N. *Campylobacter fetus* meningitis in an adult male. Kansenshogakukai Zasshi. 1984;58(5):441-6.
9. 10. Fracielo P. *Campylobacter fetus* subspecies *fetus* bacteremia. Arch Intern Med. 1985;145(2):289-92.
10. 12. Iida Y. Two cases of *Campylobacter fetus* subsp. *meningitis*. Kansenshogakukai Zasshi. 1986;60(3):271-6.
11. 14,15. Yamazaki E. Four cases of infection by *Campylobacter fetus* subsp. *fetus*. Rinsho Byori. 1986;34(6):716-22.
12. 16. Rao K.V. Meningitis due to *Campylobacter fetus* intestinalis in a kidney transplant recipient. A case report. Am J Nephrol. 1987;7(5):402-3.
13. 17. Kato H. *Campylobacter fetus* subspecies *fetus* meningitis with chronic alcoholism and diabetes mellitus. Jpn J Med. 1990;29(5):542-4.
14. 18. Inoue A. A case of *Campylobacter fetus* subsp. *venerealis* meningitis. Kansenshogakukai Zasshi. 1993;67(1):66-70.
15. 19. Dronda F. Meningitis in adults due to *Campylobacter fetus* subsp. *fetus*. Clin Infect Dis. 1998;27(4):906-7.
16. 20. Ozeki T. A case of meningococcal meningitis and spondylodiscitis caused by *Campylobacter fetus* subsp. *fetus* infection. Rinsho Shinkeigaku. 2002;42(1):38-41.
17. 21. Herve J. *Campylobacter fetus* meningitis in a diabetic adult cured by imipenem. Eur J Clin Microbiol Infect Dis. 2004;23(9):722-4.
18. 22. Shioyama M. Bacterial meningitis with *Campylobacter fetus* manifesting chronic clinical course. Rinsho Shinkeigaku. 2006;46(10):699-701.
19. 23. Kanayama S. Case of bilateral subdural empyema complicating *Campylobacter fetus* subspecies *fetus* meningitis. Brain Nerve. 2008;60(6):659-62.
20. 24. Umehara Y. *Campylobacter fetus* meningitis in a patient with Crohn disease. Inflamm Bowel Dis. 2009;15(5):645-6.
21. 25. Martinez-Balzano C. *Campylobacter fetus* bacteremia in a young healthy adult transmitted by khat chewing. J infect. 2013;66(2):184-6.
22. 26. Soy F. Meningitis and endocarditis caused by *Campylobacter fetus* after raw-liver ingestion. J Clin Microbiol. 2013;51(9):3147-50.
23. 27,28. van Samkar A. *Campylobacter fetus* meningitis in adults. Report of 2 cases and review of the literature. Medicine. 2016;95(8):e2858.

References cited in Table 2.
References

[1] van Samkar Anusha. Campylobacter fetus meningitis in adults: report of 2 cases and review of the literature. Medicine (Baltimore) 2016;95(8):e2858.
[2] Mandell, Douglas, and Bennett’s principles and practice of infections diseases. 8th ed. Saunders: Elsevier; 2015.
[3] Chavez AC. Campylobacter fetus bacteremia in a healthy patient returning from a trip to the Ecuadorian Amazonia. Zoonoses Public Health 2017;64(5):391-3.
[4] Mikals K. Campylobacter fetus bacteremia in an immunocompetent traveler. Am J Trop Med Hyg. 2014;91(4):766.
[5] Nagy MT. Campylobacter fetus sepsis in an immunocompetent patient with hematological complication. BMJ Case Rep 2013. http://dx.doi.org/10.1136/bcr-2013-008610.
[6] Zonios DI. Campylobacter fetus bacteremia in a healthy individual: clinical and therapeutical implications. J Infect 2005;51(4):329-32.
[7] Martinez-Balzano C. Campylobacter fetus bacteremia in a young healthy adult transmitted by khat chewing. J Infect 2013;66(2):184-6.
[8] Salama SM. Differentiation of the subspecies of Campylobacter fetus by genomic sizing. Int J Syst Bacteriol 1992;42(3):446-50.
[9] Schulze F. Identification of Campylobacter fetus subspecies by phenotypic differentiation and PCR. J Clin Microbiol 2006;44(6):2019-24.
[10] Veron M, Chatelain R. Taxonomic study of genus Campylobacter Sebald and Veron and designation of the neotype strain for the type species, Campylobacter fetus(Smith and Taylor) Sebald and Veron. Int J Syst Bacteriol 1973;23(2):122–34.