Meningitis in Adults Due to Campylobacter fetus Subspecies fetus

Campylobacteriosis is a zoonosis that occurs worldwide. Although the most common clinical manifestation is cryptogenic bacteremia, sites of localized infections have been described [1, 2]. Meningitis in adults due to Campylobacter fetus subspecies fetus is a rare entity and, to our knowledge, only seven cases have been reported in the French-, Spanish-, and English-language literature since 1983 [3–7]. We describe an additional case of meningitis due to C. fetus subspecies fetus in a patient with chronic alcoholism.

A previously healthy, 47-year-old man with chronic alcoholism (250 g alcohol per day) presented to the emergency department for evaluation of fever and pretilial cellulitis of 1 week’s duration. Blood was drawn for two cultures. The patient was discharged on amoxicillin/clavulanate for 10 days, and his condition partially improved. Two weeks later (on 21 April 1997) the patient developed a high-grade fever (temperature, 39°C to 39.5°C), malaise, nausea, vomiting, photophobia, and a severe frontal headache. Findings on physical examination were notable for a temperature of 38°C, normal mentation, neck stiffness, and mild hepatomegaly. The patient indicated that he had two dogs and one cat, but he denied exposure to raw or undercooked meat or to unpasteurized milk.

The patient’s WBC count was 9,700/mm³ with a normal differential. Serologies for antibodies to HIV and hepatitis C virus were negative; however, there was evidence of previous infection with hepatitis B, given that serologies for antibodies to hepatitis B surface antigen (HBsAg) and hepatitis B core antigen (HBeAg) were positive. A contrast-enhanced CT of the head was normal. Specimens for two additional blood cultures were obtained. The patient underwent a lumbar puncture, and evaluation of CSF revealed the following values: glucose, 3.2 mmol/L (7.2 mmol/L in blood); protein, 0.85 g/L; WBCs, 300/µL (80% neutrophils); and no RBCs. Evaluation of the CSF was negative for microorganisms. Empirical antibiotic therapy with a combination of cefotaxime, for 14 days, and vancomycin, for 3 days, was instituted. Cultures of blood (four specimens, the first and last of which were drawn 13 days apart) yielded C. fetus subspecies fetus. A culture of CSF remained negative. The patient’s condition gradually improved, and he remained afebrile and was discharged.

Subsequently, the patient developed malaise, low-grade fever, and a mild frontal headache. A fourth lumbar puncture was performed, and a CSF specimen inoculated in two blood culture bottles (in a microaerobic environment at 25°C and 35°C) yielded pure growth of C. fetus subspecies fetus identified by use of API-Campy (bioMérieux, Cedex, France; API code no. 2400714) and PCR assay (Centers for Disease Control and Prevention [CDC], Atlanta). The MICs of the following antibiotics for the isolate were: penicillin, 94 µg/mL; cefotaxime, >32 µg/mL; ceftazidime, 128 µg/mL; nalidixic acid, >256 µg/mL; erythromycin, 0.75 µg/mL; ofloxacin, 1 µg/mL; gentamicin, 1 µg/mL; amoxicillin/clavulanate, 1 µg/mL; and imipenem, 0.064 µg/mL. Therapy with ofloxacin (400 mg t.i.d. for 4 weeks) and gentamicin (240 mg q.d. for 3 weeks) was instituted. On day 21 of therapy, the following levels of antibiotics were measured in blood/CSF 2 hours after administration: ofloxacin, 3.9/2.3 µg/mL; gentamicin, 5.68/0.36 µg/mL. Endocarditis was ruled out. The patient’s condition gradually improved; there were no neurological sequelae, and results of all laboratory evaluations were normal. Nine months after treatment the patient continues to be healthy and asymptomatic.

A MEDLINE search (from 1983 to July 1997) for reports of meningitis in adults due to C. fetus subspecies fetus identified only seven cases (table 1) [3–7]. All patients had underlying predisposing conditions, chronic alcoholism and alcoholic cirrhosis being the two most common (six cases). Six patients had positive CSF cultures and five of eight patients had associated bacteremia. A history of ingestion of raw food or exposure to domestic or farm animals may help determine the diagnosis. One Moroccan patient had a cat, although Campylobacter species were not recovered from the animal’s feces [4]. Another patient had traveled to Mexico to receive nutritional therapy, and this travel history might have contributed to the clinical illness [5]. The patient we described had two dogs and one cat, and they were not examined for carriage of fecal microorganisms, but they were the most likely origin of infection. This information was not available for the remaining five cases.

Community-acquired bacterial meningitis due to gram-negative bacilli is rare. C. fetus subspecies fetus is an uncommon human pathogen, particularly in association with meningitis. Some investigators have pointed out the paucity of C. fetus isolates recovered from humans; only 22 of 394 Campylobacter species isolates were identified in blood cultures during an 11-year period [2]. None of the isolates were identified in CSF. Classically, C. fetus has been differentiated from Campylobacter jejuni and other species on the basis of its sensitivity to cephalothin, resistance to nalidixic acid, and inability to grow at 42°C; however, it is currently accepted that a few strains may grow at 42°C and may be resistant to cephalexin [8, 9]. Kwon et al. [9], in a study of the antimicrobial susceptibility of 25 isolates of C. fetus subspecies fetus recovered from blood and synovial fluid samples, reported that a significant proportion of isolates were interpreted as intermediate or resistant.

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Table 1. Clinical characteristics of cases of meningitis in adults due to *Campylobacter fetus* subspecies *fetus* since 1983.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (y)</th>
<th>Underlying disease</th>
<th>WBC ('/mm³) in CSF</th>
<th>CSF protein level</th>
<th>CSF glucose level (blood*)</th>
<th>Blood cultures</th>
<th>CSF cultures</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 [4]</td>
<td>38/M</td>
<td>Chronic alcoholism</td>
<td>2,040 (84% neutrophils)</td>
<td>1 g/L</td>
<td>2.7 mmol/L (6.2 mmol/L)</td>
<td>–</td>
<td>–</td>
<td>Amp 12 g/d; Gm 180 mg/d, 2 w</td>
<td>Cured</td>
</tr>
<tr>
<td>2 [3]</td>
<td>68/M</td>
<td>Metastatic adenocarcinoma of the rectum</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>–</td>
<td>+</td>
<td>Em 2 g/d, 1 d</td>
<td>Died 1 d after onset</td>
</tr>
<tr>
<td>3 [3]</td>
<td>65/M</td>
<td>Alcoholic cirrhosis</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>+</td>
<td>–</td>
<td>Cfx 4 g/d; Tm 240 mg/d, 8 d; Em 17 d</td>
<td>Improved, then relapsed</td>
</tr>
<tr>
<td>4 [5]</td>
<td>47/M</td>
<td>Diabetes mellitus, KTR</td>
<td>48 (70% neutrophils)</td>
<td>0.81 g/L</td>
<td>5.8 mmol/L (NA)</td>
<td>+</td>
<td>+</td>
<td>Chl 6 g/d, 2 d (4 g/d, 13 d); Em 1 g/d, 4 w</td>
<td>Cured</td>
</tr>
<tr>
<td>5 [6]</td>
<td>39/F</td>
<td>Chronic alcoholism, epilepsy</td>
<td>NA (1,800 neutrophils)</td>
<td>1.31 g/L</td>
<td>0.30 mmol/L (NA)</td>
<td>–</td>
<td>–</td>
<td>Amp/Clv 12 g/d, 18 d</td>
<td>Cured</td>
</tr>
<tr>
<td>6 [6]</td>
<td>36/M</td>
<td>Chronic alcoholism</td>
<td>NA (154 neutrophils)</td>
<td>0.95 g/L</td>
<td>1.22 mmol/L (NA)</td>
<td>+</td>
<td>–</td>
<td>Amp 12 g/d; then Thp (3 g/d)</td>
<td>Cured</td>
</tr>
<tr>
<td>7 [7]</td>
<td>83/M</td>
<td>Alcoholic cirrhosis</td>
<td>577 (96% neutrophils)</td>
<td>0.6 g/L</td>
<td>5.1 mmol/L (NA)</td>
<td>+</td>
<td>–</td>
<td>Cpx and Ctri</td>
<td>Died 13 d after onset</td>
</tr>
<tr>
<td>8 [PR]</td>
<td>47/M</td>
<td>Chronic alcoholism</td>
<td>300 (80% neutrophils)</td>
<td>0.85 g/L</td>
<td>3.2 mmol/L (7.2 mmol/L)</td>
<td>+</td>
<td>+</td>
<td>Ofx 1.2 g/d, 4 w; Gm 240 mg/d, 3 w</td>
<td>Cured</td>
</tr>
</tbody>
</table>

NOTE. Six cases published in Japanese journals are not included in this review. Amp = ampicillin; Amp/Clv = ampicillin/clavulanic acid; Cfx = cefazolin; Chl = chloramphenicol; Cfx = ciprofloxacin; Ctri = ceftriaxone; Em = erythromycin; Gm = gentamicin; KTR = kidney transplant recipient; NA = not available; Ofx = ofloxacin; PR = present report; Thp = thiophenicol; Tm = tobramycin; – = negative; + = positive.

to ampicillin, cephalotin, and cefotaxime. Morooka et al. [10] studied eight strains of *C. fetus* subspecies *fetus* isolated from CSF in five cases, and concluded that imipenem and gentamicin had the strongest bacteriostatic and bactericidal effects on all *C. fetus* subspecies *fetus* clinical isolates (MICs ≤ 0.2 μg/mL).

It is difficult to draw conclusions concerning appropriate antimicrobial therapy for serious infections due to *C. fetus* subspecies *fetus*, although a minimum of 3–4 weeks of therapy is recommended. It appears that erythromycin therapy is not adequate for treatment of serious infections such as bacteremia or meningitis. Morooka et al. [10] studied eight strains of *C. fetus* subspecies *fetus* [3]. The patient we described was definitively cured with combination therapy consisting of ofloxacin and gentamicin. Cephalosporins should be avoided for treatment of serious infections due to *C. fetus* although a minimum of 3–4 weeks of therapy is recommended. It appears that erythromycin therapy is not adequate for treatment of serious infections such as bacteremia or meningitis.

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References


