Streptococcus bovis Infection of the Central Nervous System: Report of Two Cases and Review

Lisa F. Cohen, Sherry A. Dunbar, D. M. Sirbasku, and Jill E. Clarridge III

Streptococcus bovis is an uncommon cause of meningitis and subdural empyema. We report one case each of meningitis and subdural empyema in which S. bovis biotype II was isolated from both the spinal fluid and blood. In one case, the organisms were seen on a gram-stained preparation of cerebrospinal fluid. The first patient presented with gastrointestinal symptoms of unknown etiology, was immunosuppressed, and recovered. The second patient presented with syncope, developed a subdural empyema, and died; at autopsy, a colonic adenoma was found. A review of the English-language literature revealed only 14 previously reported cases of meningitis due to S. bovis and no cases of subdural empyema due to S. bovis. These cases indicate the importance of complete laboratory identification of specific organisms and confirm the need for a thorough neurological examination and search for underlying gastrointestinal disease in cases of S. bovis infection.

Streptococcus bovis can be isolated from the lower gastrointestinal tract and, less frequently, from the mouths of healthy subjects [1, 2]. It is an important cause of both bacterial endocarditis and septicemia. There is a well-established association between S. bovis septicemia and colonic neoplasms [3–5]. However, isolation of S. bovis from the spinal fluid of patients is very rare. We report one case of S. bovis meningitis and one case of S. bovis subdural empyema occurring in a 2-month period at the Veterans Affairs Medical Center in Houston and review the previously reported cases.

Case Reports

Case 1

A 53-year-old HIV-positive man was admitted to the hospital on 24 July 1996 for evaluation of fever (temperature to 103°F), headaches, nausea, vomiting, and diarrhea of 5 days’ duration. He had a CD4 cell count of 490/mm³ and a history of chronic prostatitis and idiopathic thrombocytopenic purpura requiring splenectomy 5 months before admission.

Physical examination showed a well-nourished man in mild distress secondary to pain. His temperature was 103.6°F; blood pressure, 120/80 mm Hg; pulse rate, 30; and respiration rate, 23. His conjunctivae were injected, and he was photosensitive. He had decreased range of motion of his neck and tenderness to palpation over his lower lumbar spine. Cardiovascular, respiratory, and abdominal examinations were unremarkable. Neurological examination did not reveal any focal signs.

Laboratory studies of blood revealed the following values: WBCs, 16.3/mm³ (53% neutrophils, 5% band forms, 26% lymphocytes, 10% monocytes, 3% metamyelocytes, 3% myelocytes), and hematocrit, 40%. Laboratory studies of CSF disclosed the following values: WBCs, 140/mm³ (39% neutrophils, 57% lymphocytes, 4% monocytes); glucose, 6 mg/dL; and protein, 297 mg/dL. Gram staining of CSF showed few to moderate gram-positive cocci in pairs with moderate inflammatory cells. Therapy with cefotaxime and vancomycin for meningitis and ciprofloxacin for gastrointestinal disease was started. Blood and CSF cultures yielded S. bovis biotype II susceptible to penicillin G (MIC, ≤0.094 µg/mL); therapy with vancomycin and cefotaxime was discontinued, and penicillin G treatment was started. An echocardiogram revealed no evidence of endocarditis, and colonoscopy was negative; an MRI of the spine revealed degenerative joint disease of L-3–S-1, which was the likely cause of his lumbar pain. He was discharged after he received a total of 2 weeks of antibiotic iv therapy.

Case 2

A 70-year-old man was admitted to the Veterans Affairs Medical Center on 20 August 1996 because of a syncopal episode. He had a history of diabetes treated with glyipizide, chronic renal insufficiency, alcohol abuse, hypertension, and a seizure disorder. One month before admission, he had been evaluated for diarrhea and malabsorption. It was believed that the diarrhea was due to pancreatic insufficiency, and he was treated with pancreatic lipase.

Physical examination revealed a cachectic man. His temperature was 98°F; blood pressure, 225/119 mm Hg; pulse rate, 81; and respiration rate, 20. His cardiovascular, respiratory, and abdominal examinations were unremarkable. Neurological examination revealed an alert man who was oriented times three. The results of his mental status examination and motor and sensory examination were normal. His deep tendon reflexes

Received 9 December 1996; revised 18 March 1997.

Clinical Infectious Diseases 1997;25:819–23

This article is in the public domain.
in all extremities were appropriate, and the cerebellar function was intact.

Laboratory studies of blood disclosed the following values: glucose, 30 mg/dL; WBCs, 12.8×10^3/mm^3 (79% neutrophils, 16% lymphocytes, 5% monocytes, eosinophils, and basophils); hematocrit, 31.3%; and creatinine, 1.7 mg/dL. A chest roentgenogram revealed no changes in the past year; an electrocardiogram showed a new T wave inversion, but myocardial enzyme levels were normal. It was believed that he had syncope secondary to hypoglycemia, and his glypicide dose was adjusted. He remained in the hospital to evaluate his anemia and stabilize his hypertension.

Fifteen days after admission, he developed a headache, and a CT scan revealed a small right subdural hematoma without mass effect. Two days later, he had a seizure and developed right facial weakness, a positive Romber’s sign, a wide-based gait, and a temperature of 103°F. A lumbar puncture yielded fluid with the following values: WBCs, 12,750/mm^3 (97% neutrophils, 2% lymphocytes, 1% monocytes); RBCs, 20,950/mm^3; protein, 613 mg/dL; and glucose, 78 mg/dL. No organisms were seen on gram staining of CSF, and therapy with cefotaxime and ampicillin/subactam was started. Both blood and CSF cultures yielded *S. bovis* biotype II that was susceptible to penicillin G.

A repeated CT scan showed a collection of fluid consistent with a subdural empyema rather than a hematoma. Therapy was switched to intravenous penicillin G, and the subdural empyema was surgically drained. Culture of the empyema fluid also yielded *S. bovis*. After surgery, he continued to have frequent seizures that were not controlled with carbamazepine and phenobarbital treatment, and he became uremic. The family requested a do not resuscitate status for the patient, and he died on 26 September 1996.

At autopsy, there remained a large subdural empyema with purulent exudate covering the meninges over the right frontal pial lobe. There was a tubular adenoma in the transverse colon, and the cardiac valves were normal.

**Microbiology**

In case 1, *S. bovis* biotype II was identified by using a commercial biochemical identification system (API 20 Strep System, bioMérieux, Marcy l’Etoile, France) and an automated identification system (Vitek 120, bioMérieux, Hazelwood, MO). The API biotype number for this isolate was 5650450, and the Vitek biotype number was 75616660500. Similarly, the organism isolated in case 2 was identified as *S. bovis* biotype II by the same Vitek biotype number and the API biotype number 7250450. These numbers identify the bacterium as *S. bovis* by 35 biochemical tests, including the ability to hydrolyze esculin and ferment lactose and the inability to grow in the presence of 6.5% NaCl. Biotype II is indicated by the inability of the bacterium to utilize mannitol and glycogen.

**Discussion**

The features of our cases of *S. bovis* menigitis and subdural empyema as well as the 14 previously reported cases of menigitis due to *S. bovis* are summarized in table 1. Prior gastrointestinal disease or exposure occurred in 10 patients (62%); concomitant endocarditis, in 3 (19%); and possible oral flora exposure, in 3 (19%) (cases 14–16).

The gastrointestinal tract was probably the source of *S. bovis* in both of our patients because both had prior gastroenteritis. In case 1, the patient had nausea, vomiting, and diarrhea 5 days before admission, and in case 2, the patient had diarrhea requiring hospitalization 1 month before admission. Many studies have confirmed the increased incidence of both benign and malignant gastrointestinal lesions in patients with *S. bovis* bacteremia [3–5]. A review of 119 cases of *S. bovis* endocarditis or bacteremia that were investigated for gastrointestinal lesions found neoplasms in 48 patients (40.3%), nearly one-half (22) of which were adenocarcinoma [7].

Although the mechanism of infection is not completely understood, it is believed that gastrointestinal ulceration with the breakdown of the mucosal barrier that occurs in gastrointestinal lesions allows the organisms to enter the bloodstream. In addition, Klein et al. [18] showed that whereas *S. bovis* can be cultured from the stool of 10%–16% of healthy subjects, the fecal carriage rate among patients with colon cancer is 56%. This finding suggests that the neoplasm had a promoting effect or that there was a disruption of the normal flora upon treatment of the neoplasm. Our patient in case 1 had no gastrointestinal lesions during colonoscopy; however, the patient in case 2 was found to have a tubular adenoma in the transverse colon.

All of the previously reported cases of CNS infection with *S. bovis* share a few important features. Results of gram staining of CSF were reported in 11 of the 14 cases and were negative in all cases. Gram staining in case 2 was negative; however, gram staining of CSF in case 1 revealed gram-positive cocci in pairs. Case 1 is the only case of *S. bovis* meningitis in which positive results of gram staining have been reported. Results of blood cultures were reported in 12 cases (including our two cases); all blood cultures yielded *S. bovis*.

In many patients with CNS infection due to *S. bovis*, the presenting neurological changes were subtle, as occurred in case 2. It was not until days after admission that our patient developed focal neurological signs.

In 12 of the 14 previous cases, the patients were cured of their meningitis and were alive and well at the time that their case was reported. One 90-year-old woman (case 4) died of a cardiac arrest on the 12th hospital day but had no evidence of meningeal infection at autopsy. An HIV-positive man (case 10) also died during his hospitalization for meningitis. He had an unrelated nosocomial infection, and autopsy results were not reported. In case 1, our patient recovered well from his meningitis and was discharged after 2 weeks of therapy. In case 2, our patient died in the hospital, and evidence of residual...
Table 1. Characteristics of 16 patients with CNS infection caused by *Streptococcus bovis*.

<table>
<thead>
<tr>
<th>Case no. [reference]</th>
<th>Age/sex</th>
<th>Organisms seen on CSF gram staining</th>
<th>CSF WBC count (/mm³)</th>
<th>Treatment</th>
<th>GI disease or exposure</th>
<th>Concomitant endocarditis</th>
<th>Additional clinical information</th>
<th>Outcome</th>
<th>Positive cultures</th>
<th>MIC and/or MBC of Pen G</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 [PR]</td>
<td>53 y/M</td>
<td>Gram-positive cocci in pairs</td>
<td>140</td>
<td>Vm, 2 g/d for 7 d; Ctax, 8 g/d for 7 d; Pen G, 12 million U/d for 10 d</td>
<td>Gastroenteritis</td>
<td>HIV-positive</td>
<td>Recovered</td>
<td>CSF and blood</td>
<td>MIC, 0.094 µg/mL</td>
<td></td>
</tr>
<tr>
<td>2 [PR]</td>
<td>70 y/M</td>
<td>None</td>
<td>12,750</td>
<td>Amp/Sulb, 6 g/d for 4 d; Ctax, 8 g/d for 5 d; Pen G, 6–24 million U/d for 14 d</td>
<td>Gastroenteritis, tubular adenoma</td>
<td>Diabetes, alcoholic</td>
<td>Died of subdural empyema</td>
<td>CSF and blood</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>3 [6]</td>
<td>3 d/M</td>
<td>None</td>
<td>3,580</td>
<td>Amp, 100 mg/ (mg·d) for 14 d; Km, 20 mg/ (kg·d) for 2 d; Gm, for 8 d</td>
<td>Mother’s GI and vaginal flora</td>
<td>Recovered</td>
<td>CSF and blood</td>
<td>Not given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 [17]</td>
<td>90 y/F</td>
<td>None</td>
<td>5,600</td>
<td>Pen G, 24 million U/d for 13 d</td>
<td>Adeno-carcinoma of colon</td>
<td>Recovered from meningitis; died of cardiac arrest on hospital day 12</td>
<td>CSF and blood</td>
<td>Not given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 [8]</td>
<td>56 y/F</td>
<td>None</td>
<td>1,000</td>
<td>Mox, 12 g/d for 14 d; Tic, 15 g/d</td>
<td>Radiation enterocolitis</td>
<td>Lymphoma</td>
<td>Recovered</td>
<td>CSF and blood</td>
<td>Not given</td>
<td></td>
</tr>
<tr>
<td>6 [9]</td>
<td>7 w/F</td>
<td>None</td>
<td>756</td>
<td>Amp, for 14 d; Chl, Gm</td>
<td>Gastroenteritis</td>
<td>Recovered</td>
<td>CSF</td>
<td>Not given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 [10]</td>
<td>79 y/M</td>
<td>NA</td>
<td>3,493</td>
<td>Pen G, 24 million U/d for 14 d</td>
<td>Fresh manure enterocolitis</td>
<td>Pneumonia, polymygalgia rheumatica</td>
<td>Recovered</td>
<td>CSF and blood</td>
<td>Not given</td>
<td></td>
</tr>
<tr>
<td>8 [11]</td>
<td>61 y/M</td>
<td>None</td>
<td>9,800</td>
<td>Ctax, 2 g q6h</td>
<td>Hyperplastic polyp, diverticula</td>
<td>Chronic bronchitis, polycythemia</td>
<td>Recovered</td>
<td>CSF and blood</td>
<td>MIC, 0.06 µg/mL</td>
<td></td>
</tr>
<tr>
<td>9 [12]</td>
<td>41 y/M</td>
<td>None</td>
<td>8,650</td>
<td>Pen G, 24 million U/d for 14 d</td>
<td>Tubular adenoma</td>
<td>Recovered</td>
<td>CSF</td>
<td>Not given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 [13]</td>
<td>37 y/M</td>
<td>None</td>
<td>1,251</td>
<td>Pen G, 24 million U/d</td>
<td>Pseudomembranous colitis due to <em>Strongyloides</em></td>
<td>HIV-positive</td>
<td>Died of nosocomial infection</td>
<td>CSF and blood</td>
<td>Not given</td>
<td></td>
</tr>
<tr>
<td>11 [14]</td>
<td>66 y/M</td>
<td>None</td>
<td>250</td>
<td>Pen G, 24 million U/d for 28 d</td>
<td>Possible bacterial endocarditis</td>
<td>Psoriasis</td>
<td>Recovered</td>
<td>CSF and blood</td>
<td>MIC, 0.038 µg/mL</td>
<td></td>
</tr>
<tr>
<td>13 [15]</td>
<td>49 y/F</td>
<td>None</td>
<td>6,068</td>
<td>Pen G, 12–24 million U/d for 28 d, Stm</td>
<td>Acute endocarditis</td>
<td>Recovered</td>
<td>CSF and blood</td>
<td>Not given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 [16]</td>
<td>55 y/M</td>
<td>None</td>
<td>1,600</td>
<td>Pen G, 30 million U/d for 15 d</td>
<td>Mandibular nerve block for dental procedure</td>
<td>Recovered</td>
<td>CSF</td>
<td>MIC, 0.06 µg/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 [17]</td>
<td>59 y/M</td>
<td>None</td>
<td>8,600</td>
<td>Pen G, 18 million U/d for 14 d, Stm, 1 g/d for 11 d</td>
<td>Periodontal disease, diabetes, alcoholic cirrhosis</td>
<td>Recovered</td>
<td>CSF and blood</td>
<td>Both MIC and MBC, &lt;0.06 µg/mL</td>
<td>Not given</td>
<td></td>
</tr>
<tr>
<td>16 [10]</td>
<td>32 y/F</td>
<td>NA</td>
<td>494</td>
<td>Pen G, 24 million U/d for 14 d</td>
<td>Possible retrograde spread from mouth to CSF due to defect in petrous bone</td>
<td>Recovered</td>
<td>CSF</td>
<td>Not given</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** Amp = ampicillin; Chl = chloramphenicol; Ctax = cefotaxime; GI = gastrointestinal; Gm = gentamicin; Km = kanamycin; Mox = moxalactam; NA = not available; ND = not done; Pen G = penicillin G; PR = present report; Stm = streptomycin; Sulb = sulfactam; Tic = ticarcillin; Vm = vancomycin.
subdural empyema was found at autopsy. Case 2 is the only reported case of residual CNS disease after penicillin G therapy for *S. bovis* infection. In addition, it is the only report of *S. bovis* infection associated with a subdural empyema. It is possible that the large accumulation of organisms in the exudate could not be effectively treated with penicillin G.

*S. bovis* reacts with antibodies to the Lancefield group D streptococci, as does *Enterococcus* species. It is important to differentiate *S. bovis* from enterococcus because it is usually susceptible to penicillin alone, and both endocarditis and meningitis due to *S. bovis* have a better prognosis. The mortality rate associated with *S. bovis* endocarditis is 14%, while that associated with enterococcal endocarditis is 46% [19]. Similarly, the mortality rate associated with meningitis due to non-*S. bovis* group D streptococci is 33% [20]. In our series of CNS infection due to *S. bovis*, three (19%) of 16 patients died; however, the death of only one patient (6%) can be attributed to the CNS disease. Although most cases of *S. bovis* infection can be treated with penicillin alone, it is important to report a MIC because Savitch et al. [21] found that two isolates from adults with *S. bovis* endocarditis were resistant to penicillin G.

Two distinct biotypes of *S. bovis* (I and II) have been identified. Although in our laboratory the two biotypes are equally frequent, *S. bovis* biotype II has been reported as more commonly associated with endocarditis [22–24]. Ruoff et al. [22] reported that the association with colonic neoplasms is stronger for *S. bovis* biotype I than for *S. bovis* biotype II. In five of our 14 previously reported cases, the authors disclosed how the organism was identified, but only one case gave sufficient data to determine biotype. In these cases (cases 3, 4, 6, 8, and 14), the organism was defined as a group D streptococcus by its ability to hydrolyze esculin in the presence of bile, as nonenterococci by its inability to grow in the presence of 6.5% NaCl, and as distinct from *Streptococcus equinus* (the other group D nonenterococcus) by its ability to ferment lactose. One case (case 14) also showed that *S. bovis* hydrolyzed starch, thus suggesting that the strain was *S. bovis* biotype I.

More recently, the API 20 Strept System and Vitek 120 were used to help identify the organism (cases 1, 2, and 8). Our review could not definitively answer whether *S. bovis* biotype II more commonly causes meningitis or disseminated infections because most descriptions of organisms were incomplete. However, all organisms that were fully identified were biotype II (cases 1, 2, and 8).

In six of the cases, patients had some type of immunosuppression, thus indicating a possible opportunistic nature of this organism. Three patients (cases 7, 8, and 11) had received corticosteroid therapy for polymyalgia rheumatica, hyperreactive bronchitis, and psoriasis, respectively. One woman (case 5) underwent both radiotherapy and chemotherapy for lymphoma. Two men (cases 1 and 10) were HIV-positive. The immunosuppression could have contributed to the meningeal spread of the bacteria.

In summary, *S. bovis* is an uncommon cause of CNS infection. Predisposing factors include gastrointestinal disease, endocarditis, and oral lesions. Gram staining of CSF is usually negative, but in cases with numerous organisms, gram-positive cocci can be seen. The presenting neurological signs are often subtle, and most patients recover well with treatment with penicillin G alone. In this review, when biotyping was attempted, three of four strains were identified as *S. bovis* biotype II. These 16 cases of CNS infection with *S. bovis* illustrate that uncommon organisms such as *S. bovis* do occasionally cause CNS disease. These cases can be correctly diagnosed with complete laboratory identification in addition to a thorough physical examination.

References