Nontyphoidal Salmonella Intracranial Infections in HIV-Infected Patients

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Salmonella focal intracranial infections are unusual in human immunodeficiency virus (HIV)-infected patients. Six such infections have been reported in the world literature. We report a case of salmonella subdural and epidural cerebral empyema with concomitant osteomyelitis of the frontal bone. Such a complication in the course of salmonellosis is reported for the first time. In previously published case reports, four patients had brain abscess and two had subdural empyema. Salmonella typhimurium was isolated from two patients, and different serotypes were recovered from the others. All patients had advanced HIV disease, and all but two had had opportunistic infections before the diagnosis of salmonella intracranial infection. Surgical drainage combined with systemic antibiotic therapy resulted in the recovery of four of five patients. No regression of the lesions occurred in one patient treated only with antibiotics for multiple cerebral abscesses.

Nontyphoidal salmonella infection is a common occurrence among HIV-infected patients, and salmonella bacteremia is a frequent finding. The estimated incidence of salmonellosis among patients with AIDS has been 20- to 100-fold more than that among the general population, and 45%–78% of reported patients have presented with bacteremia [1, 2]. However, localized salmonella infections have rarely been noted in these patients. We report a case of Salmonella enteritidis infection presenting as subdural and epidural cerebral empyema, with concomitant osteomyelitis of the frontal bone. To our knowledge, this is the first time that such a complication of salmonella infection in an individual with AIDS has been reported.

Case Report

A 37-year-old bisexual man was admitted to the hospital because of constant right-frontal headache, rigors, and fever for 7 days. He had remained asymptomatic until 2 months before admission, when he developed varicella with pneumonitis. He was found to have HIV infection but refused any further treatment. Since then, he had had diarrhea with 2–3 watery bowel movements a day. At presentation his temperature was 39°C, his blood pressure was 120/60 mm Hg, and his pulse was 90/min. Physical examination revealed a 2 × 3–cm tender subcutaneous swelling over the right frontal region of the cranium; the overlying skin was slightly erythematous. He was obtunded and had right-sided facial weakness and hepatosplenomegaly. There were no other clinical examination findings.

The hemoglobin level was 11 g/dL, and the mean corpuscular volume was 95 fl. The WBC count was 2,300/mm³ (80% neutrophils, 10% lymphocytes, 7% monocytes, 1% basophils, and 2% eosinophils). The CD4 cell count was 18/mm³ (2%). The platelet count was 166,000/mm³ and the erythrocyte sedimentation rate was 102 mm/h. The prothrombin and partial thromboplastin times were normal, as were the values for glucose, creatinine, electrolytes, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase. Findings of chest radiography and urinalysis were also normal. A CT scan of the head revealed a subcutaneous fluid collection in the right frontal region, associated with osteolytic lesions in the frontal bone (figure 1). Subdural and epidural fluid was also demonstrated.

Needle aspiration of the subcutaneous collection yielded purulent fluid. The isolate on the culture plates was identified by standard biochemical and serological tests as S. enteritidis. The same microorganism also grew in stool culture and all three blood culture sets. A craniotomy was performed, producing purulent fluid that was drained. Bacterial culture of purulent material from the abscess cavity yielded S. enteritidis. Susceptibility studies with use of a commercial broth microdilution method (PASCO MIC/ID gram-negative panel; Difco Laboratories, Detroit) demonstrated that the organism was susceptible to chloramphenicol, trimethoprim-sulfamethoxazole (TMP-SMZ), ampicillin, ciprofloxacin, and ceftriaxone.

Therapy with iv ciprofloxacin (800 mg/d) was begun, resulting in rapid improvement in the patient’s condition. After 4 weeks of therapy, the patient was discharged in good health and began treatment with TMP-SMZ (1 double-strength tablet per day) and zidovudine. No relapse occurred in 9 months of follow-up.

Discussion

The incidence of nontyphoidal salmonella infection among patients with AIDS exceeds that among the general population.
Undoubtedly, the defects in both cellular and humoral immunity caused by HIV infection make these patients especially prone to salmonellosis [1, 2]. Salmonellosis in this patient population is frequently complicated by bacteremia. Reviews of cases of bacteremia in patients with AIDS revealed that salmonellae, after staphylococci, were the second most common cause of episodes of bacteremia [3, 4]. Although the rate of salmonella bacteremia appears to be high in this population, suppurative complications have been rarely reported [1, 5], particularly those affecting the CNS.

Using the MEDLINE database back to 1984, we found that six cases of localized intracranial salmonella infection in patients with AIDS were reported in the world medical literature [6–12]. Before this date, no patients with salmonella intracranial infection were reported to be HIV-infected [13].

The clinical features of the six patients and the one described herein are summarized in table 1. Four patients had brain abscess, one of whom also had bilateral cerebellar abscess; two had subdural empyema; and our patient had subdural and epidural abscess. There was no characteristic location of either brain abscess or subdural/epidural empyema. Salmonella typhi-

Table 1. Data from the seven reported cases of salmonella focal intracranial infections in HIV-infected patients.

<table>
<thead>
<tr>
<th>Case no., patient’s factor</th>
<th>No. of CD4 cells/mm³</th>
<th>Symptom(s) and sign(s)</th>
<th>Brain CT scan findings</th>
<th>Type of infection</th>
<th>Culture isolates (sources)</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 [7, 8]</td>
<td>34/F IVDU Thrush, PCP</td>
<td>NR</td>
<td>Blurred vision, headache, dizziness, lethargy</td>
<td>Left parietal contrast-enhancing mass</td>
<td>Brain abscess</td>
<td><em>Nocardia asteroides</em>, <em>Salmonella group B</em> (brain biopsy specimen)</td>
<td>Drainage; nafcillin, chloramphenicol</td>
</tr>
<tr>
<td>3 [9]</td>
<td>47/M IVDU Thrush, <em>Salmonella enteritidis</em> meningitis and bacteremia</td>
<td>NR</td>
<td>NR</td>
<td>Right frontal contrast-enhancing mass</td>
<td>Brain abscess</td>
<td><em>Salmonella enteritidis</em> (abscess fluid)</td>
<td>Drainage; ampicillin, TMP-SMZ</td>
</tr>
<tr>
<td>4 [10]</td>
<td>63/F Nigerian None</td>
<td>62</td>
<td>Weakness, diarrhea, right facial weakness, dysphasia, thrush</td>
<td>Left frontoparietal subdural collection</td>
<td>Subdural empyema</td>
<td><em>Salmonella dublin</em> (blood)</td>
<td>Drainage; cefotaxime, ciprofloxacin</td>
</tr>
<tr>
<td>5 [11]</td>
<td>29/M IVDU Cerebral toxoplasmosis</td>
<td>18</td>
<td>Fever, headache, left hemianopsia</td>
<td>Right parietal subdural collection</td>
<td>Subdural empyema</td>
<td><em>Salmonella copenhagen</em> (abscess fluid)</td>
<td>Drainage; cefotaxime, chloramphenicol</td>
</tr>
<tr>
<td>6 [12]</td>
<td>34/M NR None</td>
<td>20</td>
<td>Fever, seizures*</td>
<td>Parieto-occipital and cerebellar collections</td>
<td>Brain abscesses</td>
<td><em>Salmonella typhimurium</em> (brain biopsy specimen)</td>
<td>Amoxicillin, TMP-SMZ, thiamphenicol</td>
</tr>
<tr>
<td>7 [PR]</td>
<td>37/M Bisexual Varicella pneumonia</td>
<td>18</td>
<td>Fever, rigors, headache, diarrhea, right subcutaneous swelling, right facial weakness</td>
<td>Right frontal epidural and right frontoparietal collections</td>
<td>Subdural and epidural empyema</td>
<td><em>Salmonella enteritidis</em> (abscess fluid, blood, stool)</td>
<td>Drainage; ciprofloxacin</td>
</tr>
</tbody>
</table>

NOTE. IVDU = intravenous drug user; NR = not reported; PCP = Pneumocystis carinii pneumonia; PR = present report; TMP-SMZ = trimethoprim-sulfamethoxazole.

* The patient had occipital and parietal focal neurological findings (unspecified).
murium and S. enteritidis were isolated from two patients, respectively, and other serotypes of Salmonella from three. *Salmonella dublin* was recovered from the blood of patient 4 but could not be recovered from pus obtained by intracranial surgical drainage. The procedure was performed while the patient was being treated with ciprofloxacin. The culture of one abscess yielded both *Salmonella* group B organisms and *Nocardi a asteroides*.

Four of these patients had salmonella bacteremia. Concomitant meningitis was found in one patient, who developed frontal abscess formation in the course of relapsing salmonella meningitis. Our patient had skull osteomyelitis as the precipitating factor of the intracranial infection. Skull infection has been noted in two patients with salmonella brain abscess before the era of AIDS [14, 15], and Mastroianni et al. reported a case of frontal salmonella osteomyelitis in an AIDS patient without intracranial complications [16].

All patients had a low CD4 cell count and/or previous opportunistic infections, suggesting advanced HIV disease. Only two had not had complicating opportunistic infections before the diagnosis of salmonella intracranial infection. The most frequent symptoms included headache and fever (in four patients each). Diarrhea occurred in two patients. Focal neurological deficits were observed in four patients, one of whom also had seizures.

The treatment received by one patient is not known. Surgical drainage combined with systemic antibiotic therapy resulted in the recovery of four of five patients. In contrast, one patient was treated only with antibiotics for multiple cerebral abscesses, and no regression of the abscesses was noted. These results are in agreement with prior reviews of salmonella brain infections in patients without AIDS [13, 17]. In these studies, most patients have done well with surgical drainage and prolonged antibiotic therapy (of at least 4 weeks’ duration).

Of the six patients for whom details about treatment are reported, two received treatment with regimens including chloramphenicol. The proper antibiotic regimen for CNS salmonella infection is still undetermined. Early studies recommended chloramphenicol as the drug of choice [13]. However, resistance of nontyphoidal *Salmonella* to chloramphenicol is growing [18], and failures of treatment to eradicate *Salmonella* from CNS have been reported [9, 19, 20].

Therefore, some authors suggest it is preferable to use a bactericidal antibiotic in therapy [5]; the most reliable choices appear to be third-generation cephalosporins and new quinolones [5, 18]. We prefer ciprofloxacin because its utility in treating CNS salmonella infection—for which other treatments have failed—has been reported [20]. In addition, ciprofloxacin may prevent recurrent salmonella bacteremia in patients with AIDS [5].

Salmonella focal intracranial infections are rare manifestations of salmonellosis. Clinicians should consider this diagnosis as a cause of acute CNS disorder in patients with advanced HIV disease, since prompt diagnosis and prolonged antibiotic therapy, along with surgical drainage, will result in recovery from infection in most cases.

**References**