Infectious Endocarditis Due to Non-typhi Salmonella in Patients Infected with Human Immunodeficiency Virus: Report of Two Cases and Review

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Endocarditis is not usually considered a complication of AIDS. Because salmonellal bacteremia is common in HIV-infected patients and because salmonellae have a propensity to adhere to endothelial cells, these patients are at risk of endocarditis and endarteritis. We report two cases of endocarditis due to Salmonella enteritidis and review three previously reported cases. All five patients had underlying heart valve disease and developed fever, breakthrough or relapsing bacteremia, heart murmurs, and cardiac failure; four of five patients were older than 45 years. One patient died, but the other four were successfully treated with β-lactam agents alone or in combination with aminoglycosides or with ofloxacin (valve replacement was not required). As AIDS patients get older, the number of cases of endocarditis or endarteritis due to Salmonella species may increase, particularly in geographic areas where Salmonella species are prevalent.

Salmonellal bacteremia is 100 times more prevalent in HIV-infected patients than in immunocompetent persons [1]. Because salmonellae have a peculiar predilection for the vascular endothelium [2], the number of HIV-infected patients with endocarditis and endarteritis may increase in the coming years, particularly as these patients get older.

Case Reports

Case 1. A 59-year-old man who had received a prosthetic mitral valve in 1982 was admitted to the hospital in April 1991 because of fever. In January 1991 he had developed a low-grade fever and lymphadenopathy. Tests for antibodies to HIV were positive. He denied risk factors other than blood transfusions. On admission, a physical examination showed a systolic murmur and enlargement of the liver. A transthoracic echocardiogram (TTE) did not show vegetations or signs of valve dysfunction. Blood samples were taken for culture, and therapy with ampicillin (12 g/d iv) plus gentamicin (4.5 mg/[kg·d] iv) was started.

Cultures of three blood samples taken on admission and two others taken after 3 days of treatment yielded Salmonella enteritidis. The patient’s fever subsided, and therapy with ampicillin was continued for another 3 weeks. Four days after discontinuation of treatment, fever recurred and three new sets of blood cultures again yielded S. enteritidis. Therapy with ampicillin was reinitiated, but the patient remained febrile and a new systolic murmur was found in the apex cordis. He developed cardiac failure, and bacteremia was detected after 10 days of treatment with ampicillin. A new TTE showed mitral regurgitation. His physicians decided not to replace his valve, and he died of pulmonary edema.

Case 2. A 64-year-old homosexual man with a 1-week history of shortness of breath and fever was admitted to the hospital. Physical examination showed a high-pitched systolic murmur in the apex cords, hepatomegaly, extensive edema in the legs, and plaques of Kaposi’s sarcoma on his soles. Culture of six blood samples taken over 72 hours yielded S. enteritidis that was resistant to ampicillin but susceptible to ofloxacin (MIC, 0.12 μg/mL). A TTE showed a mitral valve prolapse with a 15 × 8-mm vegetation in the posterior cusp and severe mitral regurgitation.

Therapy with iv ofloxacin (400 mg every 12 hours) was started, and the patient’s fever subsided within the first 48 hours of treatment. Tests for HIV-1 antibody were positive, and the CD4 cell count was 242/μL. The patient’s clinical course was uneventful. Parenteral therapy with ofloxacin was administered for 4 weeks; at the end of therapy, blood cultures remained negative and the patient’s fever did not relapse. He was discharged from the hospital with a prescription for oral ofloxacin (200 mg every other day). He died 4 months later of acute gastrointestinal bleeding. Blood cultures were negative.

Discussion

The rarity of endocarditis in patients with AIDS (in the absence of drug abuse) is probably due to a lack of predisposing heart conditions in patients aged 25–35 years as well as a low prevalence of infection due to endocardial pathogens. However, the risk of endocarditis may be greater in HIV-infected patients who are older than 50 years. At present, 10% of AIDS cases have been diagnosed in patients 50 years of age or older, and
Table 1. Summary of clinical and microbiological features of patients with HIV infection and endocarditis due to non-typhi Salmonella.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (y)/sex</th>
<th>Risk factor for HIV infection</th>
<th>Predisposing condition or heart disease</th>
<th>Heart valve involved</th>
<th>Findings of blood cultures</th>
<th>Findings of other manifestations of AIDS</th>
<th>Clinical findings</th>
<th>Other manifestations of AIDS</th>
<th>Treatment (duration)</th>
<th>Outcome, duration of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>[5]</td>
<td>46/M</td>
<td>Drug abuse</td>
<td>None</td>
<td>Tricuspid</td>
<td>Salmonella choleraesuis</td>
<td>Fever, chest pain, heart murmur, heart valve vegetations</td>
<td>Oral candidiasis, CD4 cell count of 142/mm³</td>
<td>Ceftriaxone (6 w, iv)</td>
<td>Cured, 20 mo</td>
<td></td>
</tr>
<tr>
<td>[6]</td>
<td>19/M</td>
<td>Drug abuse</td>
<td>None</td>
<td>Tricuspid</td>
<td>Salmonella species</td>
<td>Fever, heart murmurs, heart valve vegetations</td>
<td>Generalized lymphadenopathy</td>
<td>β-Lactam agents (4 w, iv) plus gentamicin (3 w, iv)</td>
<td>Cured, unknown</td>
<td></td>
</tr>
<tr>
<td>[PR, case 1]</td>
<td>59/M</td>
<td>Blood transfusion</td>
<td>Prosthetic valve</td>
<td>Mitral</td>
<td>Salmonella enteritidis</td>
<td>Fever, breakthrough, relapsing bacteremia, new heart murmur, cardiac failure</td>
<td>Generalized lymphadenopathy, CD4 cell count of 312/mm³</td>
<td>Ampicillin (2 w, iv) plus gentamicin (2 w, iv)</td>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>[PR, case 2]</td>
<td>64/M</td>
<td>Homosexuality</td>
<td>Mitral valve prolapse</td>
<td>Mitral</td>
<td>S. enteritidis</td>
<td>Fever, heart murmurs, anemia, cardiac failure</td>
<td>Kapostí’s sarcoma</td>
<td>Ofloxacin (4 w, iv) plus ofloxacin (4 mo, oral)</td>
<td>Cured (died 5 mo later of unrelated condition)</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. OI = opportunistic infection; PR = present report.

persons over 60 years account for 25% of these cases [3]. The prevalence of cardiac diseases is expected to be higher in this subset of patients.

In addition, of the microorganisms associated with spontaneous bacteremia in patients with AIDS, salmonellae have the unique propensity to adhere to damaged endothelium, which may explain why Salmonella species are the gram-negative bacteria most likely to produce valvular infection and endarteritis in patients with preexisting atherosclerotic aneurysms [2, 4].

Four cases of endocarditis due to Salmonella species in patients infected with HIV have been reported [5–8], but only three contained enough information for review purposes [5–7] (table 1). With only one exception [6], all the patients were older than 45 years and salmonellal bacteremia was a manifestation of an advanced immunosuppressive state [5, 7]. However, as illustrated by case 1, salmonellal endocarditis may be the first serious complication of HIV infection.

The optimal antimicrobial therapy for endocarditis due to Salmonella species is not known. Ampicillin has been suggested as the treatment of choice for infections caused by ampicillin-susceptible strains [2], and third-generation cephalosporins and fluoroquinolones have been successfully used for treating extraintestinal infections (e.g., endocarditis) caused by ampicillin-resistant Salmonella species [4, 9].

In an experimental model of S. enteritidis aortic endocarditis in rabbits, Torres et al. found that, for one ampicillin-susceptible strain, ampicillin, cefotaxime, and ofloxacin showed equivalent efficacy in reducing the number of salmonellae in cardiac vegetations. On the other hand, neither ampicillin nor gentamicin reduced the number of ampicillin-resistant S. enteritidis organisms in vegetations. Both cefotaxime and ofloxacin exhibited the highest bactericidal activity in vivo against this resistant S. enteritidis strain [10].

Results of ofloxacin therapy in cases of endocarditis in humans have not been published. The fact that patient 2 was successfully treated with ofloxacin validates our own experimental studies and suggests that ofloxacin may be a reasonable treatment alternative for endocarditis due to Salmonella species.

References