Meningitis and Endocarditis Caused by Group B Streptococcus in a Human Immunodeficiency Virus (HIV) Infected Patient

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We present a case of meningitis and endocarditis caused by Streptococcus agalactiae (group B streptococcus) in an adult patient with human immunodeficiency virus (HIV) infection. To our knowledge, only four other cases of meningitis, none of which had concomitant endocarditis, have been reported so far. A 45-year-old homosexual patient presented with fever, confusion, and signs of meningeal irritation. Streptococcus agalactiae was cultured from the blood, urine, and cerebrospinal fluid (CSF). Diagnosis of meningitis caused by streptococcus agalactiae was made. On day 35, a heart murmur was noticed, and patient developed cardiac decompensation. Echocardiography revealed vegetations on the mitral and aortic valve. After nine weeks of antibiotic treatment, the patient was discharged from the hospital in good general condition, with improved CSF and echocardiographic findings.

Key words: AIDS seropositivity; endocarditis; HIV infection; HIV seropositivity; meningitis, bacterial; streptococcal infections; Streptococcus agalactiae

Streptococcus agalactiae (group B streptococcus) is a major cause of neonatal sepsis and meningitis (1,2) but it is being increasingly recognized as a common cause of invasive disease in adults (3-6). Pregnant women, elderly patients, and individuals with serious underlying diseases, such as liver disease, history of alcohol abuse, cardiovascular disease, and human immunodeficiency virus (HIV) infection are at special risk of group B streptococcus infection (1,3,5-8). HIV-infected patients have 30 times higher risk of invasive group B streptococcus infection than age-matched adults without HIV infection (5). Clinical manifestations of group B streptococcus infection in adults (pregnant women not included) include urogenital infections, pneumonia, endocarditis, meningitis, and sepsis (1,3,5-7). The case fatality rate of invasive group B streptococcus infections in adults (pregnant women not included) lies between 21% and 35% (5,8); it is slightly higher for group B streptococcus meningitis (about 30%) (9,10) and group B streptococcus endocarditis (50%) (1,11). In the population-based study by Schwartz et al (6), the mean time-interval between a positive culture and death for immunosuppressed patients was 4 days (compared with 14 days for nonimmunosuppressed individuals), and a fatal outcome was more likely in patients with bacteremia than in non-bacteremic patients (40% vs 12.5%).

We report a case of invasive infection due to Streptococcus agalactiae in an adult patient with HIV infection.

Case Report

A 45-year-old homosexual male was admitted to the University Hospital for Infectious Diseases, Zagreb, Croatia, in April 1998, with a three-day history of fever, weakness, malaise, chills and shivers, headache, and vomiting. The patient had been diagnosed with HIV infection in 1990. He had been treated for tuberculosis in May 1996, when antiretroviral treatment with zidovudine and didanosine had also been started, but the patient did not take the medications. The CD4+ T cell count in February 1998 had been 248/µL and the plasma HIV-1 RNA level 168,704 copies/mL (Amplicor HIV-1 Monitor, Roche, Basel, Switzerland). Although the patient consumed alcohol, signs of liver cirrhosis were not present. During 1997, mild to moderate arterial hypertension was recorded, but no antihypertensives were prescribed. In January 1998, the patient had an episode of cardiac decompensation that responded well to treatment with digitalis and diuretics. The patient was instructed to take 40 mg of furosemide every other day.

On admission in April 1998, the patient was febrile (40°C), confused, and disoriented. The Glasgow coma scale score (12) was 11. He had a petechial rash on lower extremities and signs of herpes virus infection on lips and nostrils. Oral candidiasis was also present. His blood pressure was 130/90 mm Hg, pulse rate 90 beats/min, and respiration rate 24/min. Neurological examination revealed signs of meningeal irritation (stiff neck, Kernig and Brudzinski signs).
No heart murmur or other clinical signs of endocarditis were noted on initial examination.

Erythrocyte sedimentation rate was 120 mm/h, white blood cell count 7,800/mm³ with 73% of polymorphonuclears, blood urea nitrogen 11 mmol/L, and creatinine 135 µmol/L. He had proteinuria (3+) and 6-8 white blood cells and 10-15 red blood cells per high power field. A lumbar puncture revealed cloudy cerebrospinal fluid (CSF) with white blood cell count of 1,800 cells/µL (88% neutrophils), raised protein level (1,315 mg/L), and glucose concentration of 0.2 mmol/L (serum glucose concentration obtained at the time was 4.8 mmol/L). The electroencephalogram showed diffuse disinhibitory activity and diffuse slow waves.

Two separately taken blood cultures grew *Streptococcus agalactiae* and the same organism was isolated from the CSF and urine. The microorganism was identified by latex agglutination (Slidex Strep-To-Kit, bioMerieux, Marcy-l’Etoile, France), production of cyclic adenosine monophosphate, and hippurate hydrolysis test (13). The disc diffusion method (14) revealed that the isolate was susceptible to penicillin, chloramphenicol, cefuroxime, ceftriaxone, vancomycin, and clindamycin. Minimal inhibitory concentrations of antimicrobial agents were not determined.

The patient was initially treated with ceftriaxone (4 g/day) for two weeks. Fluconazole (300 mg/day) and acyclovir (1 g/day) were also given because of fungal infection. Penicillin (4 g/day) was started in addition to penicillin G and continued for 9 weeks. After two weeks of treatment, the course of illness was complicated by a nosocomial pneumonia. Ceftriaxone was stopped and intravenous ciprofloxacin (800 mg/day) was given for the next two weeks. On the 35th day of illness, a cardiac decompensation developed and, for the first time, a II/VI diastolic murmur at the left sternal border was heard. On transthoracic echocardiography performed the next day, vegetations of the mitral and aortic valves were found. The vegetation seemed to be small and flat, and a small perforation of the left coronary cusp of the aortic valve was noted. Mitral and aortic regurgitation with a left ventricular ejection fraction of 45% were also recorded, as well as a small pericardial effusion. At that point, therapy with gentamicin (3 mg/kg/day) was started in addition to penicillin G and continued for 2 weeks. On day 50, the patient had recrudescence of fever; a furuncle in the abdominal region was noted. Culture of the furuncle swab yielded *Pseudomonas aeruginosa* resistant to ceftazidime, cefopazone, and ciprofloxacin, so imipenem/cilastatin (2 g/day) was added to penicillin G for the next two weeks. Blood cultures were sterile at that point.

The patient was treated with antibiotics for a total of 9 weeks. He recovered and was discharged from the hospital in good general condition. Control echocardiography performed 50 days after the first one showed morphological and functional improvement, decreased regurgitation, and no pericardial effusion. During the two-year follow-up, the patient had neither recurrence of endocarditis, nor any invasive group B streptococcal infection.

**Discussion**

To our knowledge, a case of sepsis with meningitis and endocarditis due to group B streptococcus has not yet been described in an adult HIV-infected patient. There are reports of individual cases (15-19) and small series of patients with endocarditis (11,20-23) or meningitis (9,10,24), but patients with both endocarditis and meningitis caused by group B streptococcus have been rarely described. In addition, they all

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**Table 1.** Reports published on adult patients with both meningitis and endocarditis caused by *Streptococcus agalactiae*<sup>a</sup>

<table>
<thead>
<tr>
<th>Patient</th>
<th>Findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author, year (ref. No.) age/sex underlying diseases</td>
<td>valve involved other manifestations complications/contents</td>
<td>positive GBS cultures antimicrobial duration surgical outcome</td>
</tr>
<tr>
<td>Wolstani, 1973 (25)</td>
<td>73/F DM, gomphus foot MV NA</td>
<td>heart murmur on 30th day after presentation of BM; BE at autopsy</td>
</tr>
<tr>
<td>Lemer, 1975 (26)</td>
<td>71/F no</td>
<td>AV NA</td>
</tr>
<tr>
<td>Bazer et al, 1976 (27)</td>
<td>61/M DM</td>
<td>AV cellulitis (leg ulcer)</td>
</tr>
<tr>
<td>John et al, 1977 (28)</td>
<td>76/M no</td>
<td>AV NA</td>
</tr>
<tr>
<td>Lemer et al, 1977 (29)</td>
<td>32/M NA</td>
<td>MV NA</td>
</tr>
<tr>
<td>Wilkinson, 1978 (30)</td>
<td>59/M NA</td>
<td>NA NA</td>
</tr>
<tr>
<td>Brockman et al, 1979 (31)</td>
<td>45/F RA, AA, HC</td>
<td>NA cellulitis on autopsy: PN, PM, MA, PP, RF</td>
</tr>
<tr>
<td>Dunne et al, 1993 (9)</td>
<td>82/F CAD, SRD, DM, MDS</td>
<td>AV cellulitis A-v fistula thrombosis</td>
</tr>
<tr>
<td>Cillone et al, 1995 (32)</td>
<td>89/F CoIa, CerCa</td>
<td>NA NA</td>
</tr>
<tr>
<td>Domingo et al, 1997 (10)</td>
<td>63/F DM</td>
<td>NA NA</td>
</tr>
<tr>
<td>Case from this report</td>
<td>45/M HIV, AA, prior CD AV + MV no</td>
<td>HSF, Fl, CD, nosocomial PN and furuncle</td>
</tr>
</tbody>
</table>

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<sup>3</sup>Gentamicin was added for two weeks, and other antimicrobial agents were administered for nosocomial infections (see the report).
had underlying diseases other than HIV infection (Table 1). Our patient had several predisposing conditions for invasive group B streptococcal infection: HIV infection, alcohol abuse, and prior cardiac failure.

There are only four published cases of meningitis caused by group B streptococcus in HIV infected patients, but they were all current or former intravenous drug users (7,16,24,33). In most reported cases the CD4 cell count was low at the time of diagnosis of group B streptococcal meningitis, e.g., 150/µL (24) or 173/µL (33), and in the present case it was 248/µL; CD4 T cell count was normal in only one case described (1,100/µL) (16). None of the patients, including ours, died of group B streptococcal meningitis.

The patient described in our report presented with typical signs of meningitis. From a clinical perspective, meningitis caused by group B streptococcus is indistinguishable from meningitis caused by other pyogenic bacteria. Scattered petechial lesions seen in our patient have also been described in patients with group B streptococcal meningitis, rather then the widespread petechial rash of meningococcal disease. A distant focus of infection has been present in almost 40% of the patients with meningitis caused by group B streptococcus. The most frequent distant foci were the endometrium, respiratory tract, and the endocardium (10). Our patient had two distant foci, the urinary tract and endocardium. Thus, when group B streptococcal meningitis is diagnosed, a careful search for remote foci of infection should be undertaken because they may give rise to meningitis. This is the most likely explanation for the findings in our patient, although it is not clear whether the urinary tract infection preceded or followed the endocarditis.

Meningitis associated with endocarditis occurs as either an embolic meningeal septic process or a sterile inflammation within the brain (34). Group B streptococcal endocarditis is often associated with large vegetations and large vessel embolization early in the course of the disease (11). Our belief that our patient had already had group B streptococcal endocarditis on admission was supported by the echocardiographic findings suggesting a subacute stage of endocarditis on day 36. The small perforation of the left coronary cusp of the aortic valve contributed, in addition to predisposing heart conditions, to the development of cardiac failure. Almost any type of structural heart disease may predispose to bacterial endocarditis (1). Possible causes of the first episode of cardiac decompensation (January 1998) in our patient include hypertension, alcoholism, and HIV-related left ventricular dysfunction (35). However, since echocardiography was not performed, the structural abnormality and the type of possible valvular heart disease were not precisely defined at that time.

Although group B streptococci are 4- to 10-fold less susceptible to penicillin than the group A streptococci (1), high-dose penicillin G is nevertheless the treatment of choice for all forms of invasive group B streptococcal infections. It is recommended that antimicrobial therapy for meningitis should last a minimum of 2-3 weeks, and for endocarditis 4-6 weeks (1). There is no relevant information in the published work whether the choice of antimicrobial agent and duration of therapy should be different in treatment of such invasive infections in immunocompromised patients. This is important because the optimal management of a first episode of group B streptococcal infection minimizes the likelihood of recurrent disease (36). The antibiotic treatment in our patient was prolonged due to both severity of illness and nosocomially acquired infections, and lasted for 9 weeks. It is questionable whether our patient has survived because of the prompt diagnosis of meningitis or a prolonged treatment. However, there were no clinical signs of relapse of invasive group B streptococcal infection in the 2-year follow-up. This raises hope that even severe and life-threatening invasive group B streptococcal infections in HIV-infected patients can be successfully treated.

Acknowledgment
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