Increased Incidence of *Staphylococcus aureus* Bacteremia in Hospitalized Patients with Acquired Immunodeficiency Syndrome

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*Staphylococcus aureus* is a common cause of bacterial infections in patients infected with human immunodeficiency virus (HIV). We studied 53 male patients who had 57 episodes of *S. aureus* bacteremia (SAB). The incidence of SAB per 1000 hospitalized patients was 13.2 among HIV-positive male patients and 0.8 among HIV-negative male patients, yielding a 16.5-fold increase in the odds ratio for SAB among HIV-positive male patients. Almost all episodes of SAB were community acquired. Long-term indwelling catheters were the most common predisposing factor. Prior antibiotic use was more frequently associated with SAB in HIV-positive patients than in HIV-negative patients. A trend was seen among HIV-positive patients toward more numerous infections with β-lactam antibiotic-resistant (i.e., methicillin-resistant) *S. aureus*, but such patients had similar outcomes, even though they often did not receive vancomycin during the initial 48 hours of treatment. A better understanding of the epidemiology and clinical manifestations of SAB in HIV-positive patients will offer important opportunities for prevention of this frequent complication.

HIV-positive patients, especially those whose condition has progressed to AIDS, are at increased risk for both opportunistic and common bacterial infections [1]. *Staphylococcus aureus* has resurged as one of the most common nosocomial pathogens in all hospitalized patients [2, 3] and ranks among the most common causes of bacterial infections in HIV-positive patients [1]. No previous studies have compared the incidence, clinical characteristics, and outcomes of episodes of *S. aureus* bacteremia (SAB) in hospitalized HIV-positive patients versus a comparable group of HIV-negative patients. Therefore, we compared the characteristics of SAB in these 2 groups during two 1-year study periods: from 1 July 1994 through 30 June 1995 and from 1 July 1996 through 30 June 1997. The study was carried out at the Illinois Masonic Medical Center (IMMC; Chicago), a community-based tertiary-care teaching institution that has a very active inpatient HIV/AIDS care unit. The original intention was to compare the incidence of SAB in HIV-positive patients with that in HIV-negative patients and to compare SAB incidence among HIV-positive patients not yet receiving protease inhibitors with that among HIV-positive patients receiving protease inhibitors, which were generally in use during the 1996–1997 study period. This comparison could not be made, however, because only patients not receiving protease inhibitors acquired SAB during both time periods.

**METHODS**

We obtained a comprehensive list of patients at the IMMC whose blood cultures yielded *S. aureus*, using a computer-based search of diagnostic codes. Charts were then reviewed to determine whether the patients fit the
diagnostic criteria for true bacteremia (described below). For qualified patients, we retrospectively collected and analyzed a variety of data. Hospital statistics for numbers of acute medical/surgical beds and diagnoses for patients admitted were also obtained and analyzed.

A diagnosis was considered to be “true bacteremia” if the clinical situation was appropriate and ≥2 blood cultures were positive for *S. aureus*. Bacteremia was considered to be “community acquired” if the first positive blood culture result was obtained before or during the first 3 days of hospitalization and “nosocomial” if the episode of SAB occurred after 3 days in the hospital [4]. Days of fever were counted as the number of days for which the patient had a temperature >100°F at any time. Antibiotic therapy was deemed to be “appropriate” when the strain of *S. aureus* isolated from the blood was susceptible to any of the antibiotics given to the patient at the initiation of therapy. Patients with HIV were classified as simply HIV-seropositive or as having AIDS, on the basis of standard AIDS-defining criteria [5]. Bacteriological outcome was evaluated as “cure” if both clinical and laboratory parameters improved. “Failure” (of treatment) was noted when persistence of bacteremia, a complication directly related to the episode of SAB, or death attributable to the infection occurred.

Clinical and laboratory variables were recorded only from the day of admission. The maximum and minimum temperature data were obtained for the entire hospital stay. Opportunistic infections and clinical conditions were recorded for HIV-positive patients, as listed in the surveillance case definition for AIDS established by the Centers for Disease Control and Prevention [5]. For all patients, other active medical diseases (i.e., other diagnosed clinical diseases for which the patient was under active clinical surveillance and receiving treatment) were recorded.

Factors known to predispose patients to episodes of SAB were sought [6] and included the following: iv drug use, skin conditions (including a variety of dermatoses, skin ulcers, and surgical wounds), insulin-dependent diabetes mellitus, dialysis-dependent renal failure, prior episodes of SAB, and presence of an indwelling intravascular catheter.

Statistical analyses were carried out as follows: Two-tailed unpaired t tests were used, with an α of .05 for continuous, normally distributed variables with 2 groups with unequal variances. The Pearson χ² test with appropriate degrees of freedom was used for discrete variables to compare 2 unpaired groups, and differences were analyzed for statistical significance.

**RESULTS**

**Demographic characteristics of patients.** Our study concentrated on 2 groups of patients: HIV-positive and HIV-negative male patients. The HIV-negative male patients served roughly as control subjects to determine ORs and to compare and contrast clinical manifestations and outcomes of episodes of SAB; however, this was not a case-control study.

Overall, 77 patients developed true bacteremia caused by *S. aureus* during the two 1-year study periods. These 77 patients had 84 episodes of SAB. All of the HIV-positive patients with SAB (28 patients) were men. Of the 49 HIV-negative patients, 24 were women. We opted, however, to include only the 25 male patients in the analysis of the HIV-negative group, because all members of the HIV-positive group were men. This approach yielded 57 SAB episodes in 53 men, with 32 episodes in 28 HIV-positive patients and 25 episodes in 25 HIV-negative patients. The incidence of SAB per 1000 hospitalized patients was 13.2 among HIV-positive male patients and 0.8 among HIV-negative male patients. Thus, there was a 16.5-fold increase in OR for SAB in HIV-positive male patients. When age was divided into deciles, 26 of the 28 HIV-positive patients were clustered in the age group of 30–49 years; the ages of HIV-negative patients had a much wider range (20–99 years). The mean age for the HIV-positive patients was 39 years (95% CI, 37–41 years), whereas for HIV-negative patients it was 56 years (95% CI, 49–63 years).

**Clinical data.** Clinical factors that predisposed patients in the 2 groups to SAB are shown in table 1, and the number of such factors leading to the development of each episode of SAB is shown in table 2. No patient had >3 predisposing factors.

A high percentage of patients in both groups had long-term indwelling intravascular catheters (tables 1 and 3). In the HIV-positive group, 25 (78%) of the 32 SAB episodes were associated with such catheters; in the HIV-negative group, catheters were present in 14 (56%) of 25 episodes. Table 3 summarizes the numbers and types of catheters used. HIV-positive patients predominantly had long-term indwelling catheters (Groshong [Bard

### Table 1. Clinical factors predisposing to episodes of *Staphylococcus aureus* bacteremia (SAB) in HIV-positive and HIV-negative male patients.

<table>
<thead>
<tr>
<th>Clinical factor</th>
<th>No. (%) of SAB episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In HIV-positive patients</td>
</tr>
<tr>
<td></td>
<td>(n = 32)</td>
</tr>
<tr>
<td>Intravenous drug use</td>
<td>8 (25)</td>
</tr>
<tr>
<td>Skin condition(s)</td>
<td>14 (44)</td>
</tr>
<tr>
<td>Insulin-dependent diabetes mellitus</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Dialysis-dependent renal failure</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Prior SAB episode</td>
<td>12 (36)</td>
</tr>
<tr>
<td>Intravascular catheter</td>
<td>25 (78)</td>
</tr>
</tbody>
</table>

**NOTE.** Some patients had >1 predisposing clinical factor.
Access] and peripherally inserted central venous catheters), whereas HIV-negative patients predominantly had short-term catheters (Quinton, Swan-Ganz, and triple-lumen catheters).

We were able to identify the most likely source of each episode of SAB in 31 (97%) of the 32 SAB episodes in the HIV-positive group and in 22 (88%) of the 25 episodes in the HIV-negative group. The most likely source was skin condition in 10 (31%) of 32 episodes and 7 (28%) of 25 episodes and a catheter in 17 (54%) of 32 and 9 (36%) of 25 episodes in the HIV-positive and HIV-negative groups, respectively. Skin conditions and catheters together contributed to 3 (9%) of 32 and 4 (16%) of 25 episodes in these groups. Use of iv drugs and endocarditis were responsible for 1 (3%) of 32 and 1 (4%) of 25 SAB episodes in the 2 groups.

With regard to the status of the HIV infection, the mean CD4 cell count was 52 cells/mm³ in the HIV-positive group. The conditions of almost all of the HIV-positive patients (30 [94%] of 32 patients) who developed SAB had progressed to AIDS. Measurement of virus load (still an emerging technology, even in 1997) was done for only 2 of the patients, with results an emerging technology.

Among the HIV-positive patients, on the other hand, the incidence of S. aureus bacteremia (SAB) was higher, (20 [80%] of 25). Among the HIV-positive patients, on the other hand, the incidence of β-lactam antibiotic–resistant S. aureus was higher, which accounted for almost one-half (15 [47%] of 32) of the SAB episodes. These differences, however, were not statistically significant.

Clinical responses to infection were similar in both patient groups with respect to maximum and minimum temperatures during hospitalization. The mean (±SD) duration of fever was also similar in the HIV-positive and HIV-negative groups.

Table 2. Summary of clinical factors predisposing to episodes of Staphylococcus aureus bacteremia (SAB) in HIV-positive and HIV-negative male patients.

<table>
<thead>
<tr>
<th>No. of predisposing factors</th>
<th>In HIV-positive patients (n = 32)</th>
<th>In HIV-negative patients (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3 (9)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>1</td>
<td>10 (31)</td>
<td>9 (36)</td>
</tr>
<tr>
<td>2</td>
<td>14 (44)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>3</td>
<td>5 (16)</td>
<td>3 (12)</td>
</tr>
</tbody>
</table>

Table 3. Summary of types of catheters associated with episodes of Staphylococcus aureus bacteremia (SAB) in HIV-positive and HIV-negative male patients.

<table>
<thead>
<tr>
<th>Catheter type</th>
<th>In HIV-positive patients (n = 32)</th>
<th>In HIV-negative patients (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial line</td>
<td>0</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Groshong (Bard Access)</td>
<td>10 (31)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>ICPM</td>
<td>0</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Perma-Cath (Quinton)</td>
<td>1 (3)</td>
<td>0</td>
</tr>
<tr>
<td>PICC</td>
<td>11 (34)</td>
<td>0</td>
</tr>
<tr>
<td>Port-a-Cath (Deltec)</td>
<td>1 (3)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Quinton</td>
<td>1 (3)</td>
<td>4 (16)</td>
</tr>
<tr>
<td>Swan-Ganz</td>
<td>0</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Triple-lumen</td>
<td>1 (3)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>Hickman (Bard Access)</td>
<td>1 (3)</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

NOTE. ICPM, intracranial pressure monitor; PICC, peripherally inserted central venous catheter.
HIV-negative patients, respectively, and mean (SD) cholesterol values were 219 (21) mg/dL. Among HIV-negative patients (table 4), all laboratory values were otherwise similar in the 2 groups. Biochemical indicators of nutritional status in both groups were similar: mean (±SD) albumin values were 2.8 (±0.2) and 3.2 (±0.4) g/dL in HIV-positive and HIV-negative patients, respectively, and mean (±SD) cholesterol values were 118 (±13) and 150 (±21) mg/dL.

Laboratory data. HIV-positive patients had significantly lower mean WBC and platelet counts at admission than did the HIV-negative patients (table 4). All laboratory values were otherwise similar in the 2 groups. Biochemical indicators of nutritional status in both groups were similar: mean (±SD) albumin values were 2.8 (±0.2) and 3.2 (±0.4) g/dL in HIV-positive and HIV-negative patients, respectively, and mean (±SD) cholesterol values were 118 (±13) and 150 (±21) mg/dL.

Outcomes. Empirical antibiotic therapy administered to patients is shown in table 5. Among patients who were found to have β-lactam antibiotic-resistant S. aureus in the blood, antibiotic selection was appropriate for only 3 (38%) of 8 HIV-negative patients, but the overall outcome for patients in each group was comparable.

The mean (±SD) number of days of antibiotic use was similar among HIV-positive and HIV-negative patients (18 ± 4 and 23 ± 6 days, respectively). Antibiotics were administered in the hospital for comparable mean durations (±SD) of 14 ± 3 and 16 ± 5 days in the 2 groups. Table 6 shows the outcomes, complications (which included metastatic seeding, pneumonia, endocarditis, relapsed osteomyelitis, sternal wound infection, septic shock, disseminated intravascular coagulation, multiorgan dysfunction syndrome, and acute renal failure), and mortality associated with episodes of SAB caused by MRSA in the 2 groups of patients. The mortality (22% for HIV-positive patients and 20% for HIV-negative patients), complication rates (9% and 12%, respectively), and duration of hospitalization (19 and 16 days, respectively) were essentially similar for patients with SAB in both groups.

**DISCUSSION**

Infection with HIV dramatically increases the odds that an individual will develop SAB. The possible reasons for this increased risk of bacterial infection have been thoroughly reviewed elsewhere in the literature [1]. The fact that all of the HIV-positive patients with SAB in our study were men reflected our local selection of HIV-positive patients; the primary risk factor for acquiring HIV infection for the majority of HIV-positive patients treated at the IMMC is to be a man who is sexually active with men. Further studies will be needed to assess the nature of SAB in HIV-positive female patients. Use of IV drugs was found to be less common than skin conditions and catheters as a predisposing factor for SAB. It was quite common in both groups for patients to have a skin condition that was the primary source of the SAB. Catheters played an important role in SAB in both HIV-positive and HIV-negative patients, a finding similar to that of studies published elsewhere [7]. Prior episodes of SAB seemed predictive of future episodes among HIV-positive patients, more so than among the HIV-negative patients (table 1); this finding was not unexpected, because overwhelming data show that chronic carriers are at constant risk of being infected by the organisms they carry [8].

With regard to specific antibiotic effects, the use of trimethoprim-sulfamethoxazole as prophylaxis against opportunistic infections in HIV-positive patients is likely to be associated with MRSA infection. Prophylaxis with trimethoprim-sulfamethoxazole was used for 13 (40%) of 32 HIV-positive patients.

Episodes of SAB in both groups of men were more likely to have been acquired in a community rather than a hospital setting, which can probably be explained by the success of stricter infection control efforts in the hospital and improved in-hospital catheter maintenance. In addition, patients are increasingly being cared for in the outpatient setting, with long-term indwelling catheters in place.

Blood count data revealed significantly lower admission WBC and platelet counts in the HIV-positive patients. Zidovudine was administered to 5 (16%) of 32 HIV-positive patients, which may have contributed to this difference, as may other bone marrow–suppressive medications.

Antibiotics were administered in the hospital for a mean (±SD) duration of 14 ± 3 and 16 ± 5 days in the HIV-positive and HIV-negative groups, respectively. One possible reason for

### Table 4. Data for complete blood cell counts (CBCs) for HIV-positive and HIV-negative male patients with *Staphylococcus aureus* bacteremia (SAB).

<table>
<thead>
<tr>
<th>CBC data</th>
<th>Results of CBCs, mean ± SD</th>
<th>In HIV-positive patients (n = 32)</th>
<th>In HIV-negative patients (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBCs, ×10^3 cells/mm³</td>
<td>6 ± 2.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14 ± 2.2</td>
<td></td>
</tr>
<tr>
<td>Polymorphonuclear lymphocytes, %</td>
<td>61 ± 8</td>
<td>73 ± 5</td>
<td></td>
</tr>
<tr>
<td>Bands, %</td>
<td>9 ± 3</td>
<td>9 ± 4</td>
<td></td>
</tr>
<tr>
<td>Platelets&lt;sup&gt;a&lt;/sup&gt; ×10^3 cells/mm³</td>
<td>133 ± 26</td>
<td>220 ± 35</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> P < .05.

(6.1 ± 1.8 and 5.4 ± 1.6 days, respectively). Three patients in the former group and 2 patients in the latter group remained febrile throughout the entire hospitalization, despite isolation of *S. aureus* from their blood samples.

### Table 5. Empirical antibiotic therapy for episodes of *Staphylococcus aureus* bacteremia (SAB) in HIV-positive and HIV-negative male patients.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>In HIV-positive patients (n = 32)</th>
<th>In HIV-negative patients (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-Lactam antibiotic</td>
<td>15 (47)</td>
<td>18 (72)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>20 (63)</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Other(s)</td>
<td>19 (59)</td>
<td>16 (64)</td>
</tr>
<tr>
<td>Appropriate</td>
<td>25 (78)</td>
<td>22 (88)</td>
</tr>
</tbody>
</table>
what seems to be a long duration of therapy was that the initial antibiotic coverage was empirical; subsequent changes were made in some cases after culture results were received. Finally, in 1996–1997, a hospital policy was developed to attempt to minimize the use of vancomycin because of concern about a potential increase in vancomycin-resistant enterococci. Thus, the managing physicians were under increasing pressure to limit the empirical use of vancomycin, and, as a result, some patients who did not receive vancomycin ultimately were found to have blood cultures that were positive for MRSA. It was reassuring that the lack of vancomycin in the initial coverage for such patients did not seem to affect the outcome of their treatment.

In conclusion, the frequency of episodes of SAB among hospitalized HIV-positive patients is 16.5-fold greater than the frequency of episodes among HIV-negative patients. However, clinical factors in the 2 groups, such as community acquisition of infection and the presence of indwelling catheters, were similar. HIV-positive patients were more likely to have received antibiotics previously, and a trend toward higher incidence of infection with MRSA was seen among those patients. Outcomes did not differ between HIV-positive and HIV-negative patients. A better understanding of clinical factors associated with the development of SAB in both HIV-positive and HIV-negative patients will offer important opportunities for prevention of this frequent and potentially morbid and expensive complication.

Acknowledgments

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