ORIGINAL RESEARCH

Septicemia in Patients With AIDS Admitted to a University Health System: A Case Series of Eighty-Three Patients

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Background: **Patients with AIDS incur higher rates of infection than the general population. However, little evidence exists to guide family physicians in selecting antibiotics for initial empiric therapy for suspected septicemia.**

Methods: **We recorded the causative organisms of septicemia (defined here as bacteremia, fungemia, or both) in 83 patients with AIDS admitted to the teaching hospitals of the University of Louisville from 1996 to 2006. All patients fulfilled the requirements for a diagnosis of AIDS on the basis of the 1993 Centers for Disease Control criteria. In addition to the causative organism, demographic information, immunologic data, portal of entry, and mortality were collected.**

Results: **Only 53% of the patients presented with fever and the median leukocyte count was 4400 cells/mm^3. The most common organisms causing septicemia were, in decreasing order, methicillin-sensitive *Staphylococcus aureus* (MRSA; n = 21; 21.4%), *Mycobacterium avium* complex (n = 10; 10.2%), coagulase-negative staphylococci (n = 9; 9.2%) and *Streptococcus pneumoniae* (n = 9; 9.2%). Other pathogens included *Escherichia coli*, *Pseudomonas aeruginosa*, and MRSA. Polymicrobial septicemia was identified in 12 cases (14.5% of the episodes). The portals of entry of the organism were (in decreasing order) primary, lung, intravascular line, and skin. The types of organisms found in patients with primary septicemia patterned those found overall. The mortality rate was 12.1%.**

Conclusions: **AIDS patients with septicemia may not present with the signs that would a non-AIDS patient with septicemia. On the basis of the range of organisms identified in this study, antibiotic coverage of AIDS patients with suspected septicemia, both in primary septicemia and septicemia overall, should take into consideration bacteremia with a wide range of organisms: Gram-positive organisms including MRSA and *M. avium* complex and Gram-negative organisms including *Pseudomonas* species. In addition, physicians should be aware that polymicrobial septicemia may be present. (J Am Board Fam Med 2012;25:318–322.)**

Keywords: **AIDS, Bacteremia, Case Reports, Septicemia**

Patients with AIDS acquire more infections and more atypical infections than does the normal population. Family physicians and especially family medicine residency programs frequently admit patients with AIDS who have fever of undetermined etiology to the hospital, and this may pose a diagnostic problem for them. The task of the physician is then to find the etiology of the fever. Although the etiology of the fever often is not bacterial or fungal septicemia, these patients usually must be treated empirically with antibiotics until blood cultures are reported. Although this problem has been studied in the past,[1–4] little recent empiric evidence

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guides the family physician in selecting antibiotics for initial treatment. The objective of this study was to determine the most common organisms infecting patients with AIDS and septicemia and thus determine the most appropriate treatment for these patients.

Methods

We reviewed patient charts from the teaching hospitals of the Louisville Medical Center to determine the most common pathogens of bacterial and fungal septicemia in patients with AIDS who were admitted. In addition, we collected demographic data to gain a more complete understanding of AIDS-related septicemia.

We searched the medical records departments of 3 University of Louisville School of Medicine teaching hospitals (University of Louisville Hospital, Norton Hospital, and Jewish Hospital) from 1996 through 2006 for charts displaying diagnoses of AIDS (*International Classification of Diseases, Ninth Revision*, [*ICD-9*] code 042), septicemia (*ICD-9* code 038.9), and bacteremia (*ICD-9* code 790.7). Data were extracted from records by 3 of the authors (BWR, FMT, and KZF), who also determined if study criteria were met. For our study, we defined AIDS by the 1993 Centers for Disease Control criteria: the patient had to be serologically positive for HIV with a CD4 count of $\leq$200 cells/mm^2 or an AIDS-defining condition.[5] We defined septicemia as at least one blood culture positive for a pathogenic bacterium or fungus in a patient displaying one or more clinical signs for septicemia, which include fever, chills, vomiting, somnolence, or confusion. Patients with septic shock were not excluded. Fever was defined as a temperature higher than 100.5°F within 24 hours before or after the positive blood cultures. The causative organism was noted, as well as the patient's age, sex, ethnicity, and leukocyte count at admission. The most recent CD4 count and viral load were recorded when available. When viral load was reported as a range, the median of the range was used. For example, when viral load was reported as being above or below a number (eg, >100,000 copies/mL), the number reported was used (ie, 100,000 copies/mL). The portal of entry then was recorded. For example, the source of the infection was noted as "lung" if the blood pathogen also was present in the patient's sputum (via culture or DNA probe) or if the patient's chest imaging demonstrated a new pulmonary infiltrate. The source was noted as "urinary tract" if the bacterium with the same sensitivity pattern also was found in the patient's urine, "wound" if the same organism also was cultured from a skin wound, or "catheter tip" if the organism also was cultured from a catheter tip. The portal of entry was considered "primary" if no portal of entry was found. Coagulase-negative staphylococci only were considered to be the cause of sepsis when they were grown in 2 separate cultures taken at a single time or 1 of 2 sets on 3 separate occasions. The patient was considered to have died from septicemia if he or she died within 7 days of the positive blood culture with no intervening events to explain the death.

Results

Demographic Data

Eighty-three patients met criteria for the study. Of these, 41 patients were from the University of Louisville Hospital, 27 were from the Jewish Hospital, and 15 were from the Norton Hospital. The average age was 41 years. Sixty-one patients (73.5%) were men and 22 (26.5%) were women. Forty-five patients (54.2%) were African American, 32 (38.6%) were white, and 6 (7.2%) were of unknown ethnicity.

Clinical Data

Forty-four patients (53.0%) displayed fever, 30 (36.2%) displayed no fever, and 9 (10.8%) had no temperature recorded. Median leukocyte count was 4400 cells/mm^3, median CD4 count was 34 cells/mm^3, and median viral load was 81,273 copies/mL (Table 1). Ten patients died, for a mortality rate of 12.1%.

Table1. Leukocyte count, CD4 Count, and Viral Load Determinations in AIDS Patients With Septicemia

	Reported, n (%)	Median	Range
Leukocyte count (cells/mm^3)	82 (98.8)	4.4	<1–20.6
CD4 (cells/mm^3)	69 (83.1)	34	0–396
Viral load (copies/mL)	33 (39.8)	81,273	<50–750,000

Microbiologic Data

Methicillin-sensitive *Staphylococcus aureus* (n = 21; 21.4%), *Mycobacterium avium* complex (MAC; n = 10; 10.2%), coagulase-negative staphylococci (n = 9; 9.2%), and *Streptococcus pneumoniae* (n = 9; 9.2%) were the most frequent causes of septicemia in this group of patients with AIDS. Other organisms are listed in Table 2. *Cryptococcus neoformans* was isolated in 2 cases. Polymicrobial septicemia occurred 12 times (14.5% of the episodes) in this study; the causative organisms are listed in Table 3. Polymicrobial septicemia with both *S. aureus* and MAC occurred in 2 episodes. *S. aureus* frequently was involved in polymicrobial septicemia. The mortality rate of AIDS patients with polymicrobial septicemia (n = 3; 25.0%) was not significantly higher than that of AIDS patients with monomicrobial septicemia (n = 6; 8.5%) (Fisher's exact test, P = .1180).

Portals of Entry

The most common portal of entry was primary, followed by lung, intravascular line, and skin (Table 4).

Discussion

The average patient age (41 years) and predominance of men in this study have been observed previously, as has our finding that *S. aureus* and *S. pneumoniae* are common causes of bacterial sepsis in AIDS patients.[1] The finding that only slightly more than half of the patients displayed fever and the median leukocyte count was 4400 cells/mm^3 at the onset of septicemia suggests that patients with AIDS may not present with classic signs (eg, fever and leukocytosis) when septicemic and that the physician must keep a high index of suspicion for septicemia to diagnose this disease in AIDS patients. In a general study of 213 bacteremic patients in a community hospital, leukocyte counts were

Table 2. Totals of Organisms and Totals in Patients With Unknown Portal of Entry (Primary Septicemia)*

Organism	Patients With Unknown Portal of Entry, n (%)	Total Patients, n (%)
Methicillin-sensitive *Staphylococcus aureus*	15 (23.1)	21 (21.4)
Mycobacterium avium complex	4 (6.2)	10 (10.2)
Coagulase-negative Staphylococci	4 (6.2)	9 (9.2)
Streptococcus pneumoniae	5 (7.7)	9 (9.2)
Escherichia coli	4 (6.2)	7 (7.1)
Pseudomonas aerugenosa	3 (4.6)	4 (4.1)
Candida albicans	3 (4.6)	3 (3.1)
Candida sp.	1 (1.5)	3 (3.1)
Gram-negative bacilli, unspecified	3 (4.6)	3 (3.1)
Gram-positive cocci, unspecified	3 (4.6)	3 (3.1)
Histoplasma capsulatum	2 (3.1)	3 (3.1)
Methicillin-resistant *Staphylococcus aureus*	2 (3.1)	3 (3.1)
Mycobacterium tuberculosis	2 (3.1)	3 (3.1)
Alpha-hemolytic streptococci	2 (3.1)	2 (2.0)
Cryptococcus neoformans	2 (3.1)	2 (2.0)
Group B beta-hemolytic streptococci	1 (1.5)	2 (2.0)
Streptococcus feacalis	1 (1.5)	2 (2.0)
Coagulase-negative Gram-positive cocci	1 (1.5)	1 (1.0)
Cryptococcus vs *Histoplasma* sp.	1 (1.5)	1 (1.0)
Enterobacter cloacae	1 (1.5)	1 (1.0)
Group D *Salmonella* sp.	1 (1.5)	1 (1.0)
Helicobacter pylori	1 (1.5)	1 (1.0)
Hemophilus influenzae	1 (1.5)	1 (1.0)
Micrococcus sp.	1 (1.5)	1 (1.0)
Spirochetes	1 (1.5)	1 (1.0)
Totals	65	98

*The total number of isolates (98) is greater than the number of patients (83) because some cases of septicemia were polymicrobial.

Table 3. Polymicrobial Septicemia in Patients With AIDS

Organisms	No.
Staphylococcus aureus, Mycobacterium avium complex	2
Streptococcus pneumoniae, *S. aureus*	1
Group D *Salmonella* sp., Gram-negative bacilli (unspecified)	1
Cryptococcus neoformans, alpha-hemolytic streptococci	1
Coagulase-negative Staphylococcus, Gram-positive cocci (unspecified)	1
Coagulase-negative staphylococci, *Histoplasma* sp.	1
Coagulase-negative *S. aureus*, *Streptococcus faecalis*	1
S. aureus, *Streptococcus viridens*	1
Candida albicans, *S. aureus*	1
Mycobacterium tuberculosis, *Mycobacterium avium* complex	1
Candida albicans, "spirochetes"	1
Total	12

elevated in 43.6% of the patients, normal in 31.9% of the patients, and low in 10.8%.[6] In previous studies of *Enterobacter* (Dayton, OH; n = 75; 1991)[7] and *Klebsiella* bacteremia (Gainsville, FL; n = 46; 1989),[8] 61% and 57% of the patients, respectively, presented with fever; the rest had no fever. This suggests that septicemia in both AIDS patients and other patients may not present with classic signs; perhaps this occurs more so in AIDS patients. The most common organisms causing septicemia in our study (methicillin-sensitive *S. aureus*, MAC, coagulase-negative staphylococci, and *S. pneumoniae*) compared with coagulase-negative staphylococci, *S. aureus*, *S. pneumoniae*, nontyphi *Salmonella*, and *Pseudomonas aeruginosa* in one study (Spain; n = 274; 1996);[2] *P. aeruginosa*, *S. aureus*, and *S. pneumoniae* in another (Ann Arbor, Michigan; n = 102; 1996)[3]; nontyphi *Salmonella* species, *S. pneumoniae*, and *Mycobacterium tuberculosis* in a hospital in Nairobi, Kenya (n = 117; 1997).[1] The organisms in each of these studies are similar with the order of commonness being different. The reasons for the high numbers of *M. tuberculosis* septicemia in the Kenya study may be because of poorer living conditions tend less access to medical care in Kenya. The high incidence of pseudomonas bactermia in the study by Rosenberg et al[3] may be accounted for by the study being limited to intensive care unit (ICU) patients who may have been more debilitated and more susceptible to this opportunistic organism and that *P. aeruginosa* is a common hospital-acquired organism. We would expect fewer cases of *Pseudomonas* septicemia in our study, which probably consists of more community-acquired infections. Fungemia by *C. neoformans* is uncommon but has been observed previously in HIV-positive patients.[1]

In the majority of patients, the portal of entry for the pathogens into the bloodstream was primary. This highlights the necessity of obtaining blood cultures in AIDS patients with fever even when no obvious portal of entry exists. The common portals of entry in our study (in decreasing order: primary, lung, intravascular line, and skin) compared with intravascular catheter, primary, skin and soft tissue, and respiratory in one study[2] and pneumonia, catheter-related, and primary in the study of ICU patients.[3]

Mortality caused by septicemia was 12.1%, much lower than the 54% mortality in ICU patients reported by Rosenberg et al[3] in 2001 and slightly lower than the 17.5% found in immunocompetent patients in1996.[5] Because Rosenberg's study only included patients admitted to the ICU, it is likely that these patients were more physically debilitated before their infection and therefore more likely to acquire and die from a septicemic episode. Our lower mortality rate also may be because we defined mortality secondary to septicemia more rigorously than the other studies; we used a shorter time from positive blood culture to death. Because of our small sample size, we cannot assume our overall lower mortality rate is due to improvements in therapy.

Because we observed a polymicrobial septicemia rate of 14.5%, physicians should consider this possibility when treating AIDS patients. These data indicate that the mortality rate for AIDS patients

Table 4. Portals of Entry for Septicemia in Patients With AIDS

Portal of Entry	No. (%)
Primary	51 (61.5)
Lung	10 (15.9)
Intravascular line	7 (8.4)
Skin	4 (4.8)
Urinary tract	3 (3.6)
Bone marrow	3 (3.6)
Meninges	2 (2.4)
Urinary catheter	1 (1.2)
Knee	1 (1.2)
Liver	1 (1.2)

with polymicrobial septicemia (25.0%) is not significantly higher than AIDS patients with monomicrobial septicemia (8.5%). This seems to conflict with a study by Kiani[9] of 88 patients with polymicrobial bacteremia but without AIDS. In their study, the mortality rate of patients with polymicrobial bacteremia was 45% compared with 18% of patients with monomicrobial bacteremia. The reason for this discrepancy may be that patients debilitated with AIDS were already severely ill, making the number of organisms they acquire when they have septicemia less important in the cause of death. That is, septicemia, whether monomicrobial or polymicrobial, may simply be a marker of how ill the AIDS patient is. Another reason for our lack of significant difference in mortality rate between patients with polymicrobial bacteremia and monomicrobial bacteremia may simply be the low numbers of patients in both categories.

One obvious limitation to this study may be that some AIDS patients with septicemia may have had negative blood cultures. This, however, would be a limitation for any study of bacteremia or septicemia. Another may be that the patterns of microbial infection may have changed over the time of the study, though we are not aware of a reason this might have happened.

Conclusions

Given the variety of pathogens that may cause sepsis in HIV-positive patients, we believe antibiotic use that covers most of the organisms found in this and similar studies is indicated when the clinical presentation does not suggest a specific pathogen. Initial antibiotic coverage in these patients should take into consideration bacteremia with Gram-positive organisms including MRSA, MAC, and Gram-negative organisms including *P. aeruginosa*. When all cultures are negative and it is apparent that the cause of the fever is not bacterial or fungal, antibiotics should be discontinued. These conclusions would obviously not apply to nonimmunosuppressed septic patients without AIDS. Appropriate antibiotics for likely infecting organisms may be decided on in the latter patients on the basis of signs, symptoms, age, and likely portal of entry.

References

1. Arthur G, Nduba UN, Kriaki SM, Kimari J, Bhatt SM, Gilks CF. Trends in bloodstream infections among human immunodeficiency virus–infected adults admitted to a hospital in Nairobi, Kenya, during the last decade. Clin Inf Dis 2001;33:248–56.
2. Torres-Tortosa M, Canueto J, Bascunana A, et al. Prognostic evaluation of bacteremia and fungemia in patients with acquired immunodeficiency syndrome. Eur J Clin Microbiol Infect Dis 2002;21:262–8.
3. Rosenberg AL, Seneff MG, Aliyeh L, Wagner R, Bojanowski L, Zimmerman JE. The importance of bacterial sepsis in intensive care units with acquired immunodeficiency syndrome: implication for future care in the age of increasing antiretroviral resistance. Crit Care Med 2001;29:548–56.
4. Proctor RA. Bacterial sepsis in patients with acquired immunodeficiency syndrome. Crit Care Med 2001; 29:693–84.
5. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Recomm Rep 1992;41(RR-17):1–19.
6. Haddy RI, Klimberg S, Epting RJ. A two-center review of bacteremia in the community hospital. J Fam Pract 1987;24:253–9.
7. Haddy RI, Cecil ML, Norris LL, Markert RJ. Enterobacter bacteremia in the community hospital. J Fam Pract 1991;32:601–6.
8. Haddy RI, Lee M III, Sangal SP, Walbroel GS, Hambrick CS. Klebsiella pneumoniae in the community hospital. J Fam Pract 1089;28:686–90.
9. Kiani D, Quinn EL, Burch KH, Madhaven T, Saravolatz LD, Neblett TR. The increasing importance of polymicrobial bacteremia. JAMA 1979;242: 1044–7.