Pulmonary Complications of HIV Infection*
Autopsy Findings

Bekele Afessa, MD, FCCP; William Green, MD; Joseph Chiao, MD; and Winston Frederick, MD

Study objectives: To describe the pulmonary complications in patients with HIV infection, and the changes in the incidence of these complications over a 12-year period.
Design: Retrospective review of autopsy records.
Setting: Two university-affiliated medical centers.
Patients: We studied autopsy findings from 233 patients with HIV infection who died between 1985 and 1996. Demographic data, risk factors for HIV infection, and the lengths of hospital stay were obtained. The histologic and microbiological findings of the respiratory system, and the extrapulmonary organ involvement by Kaposi’s sarcoma (KS), Pneumocystis carinii, Mycobacterium avium complex, and Mycobacterium tuberculosis complex were reviewed.
Results: Ninety-two percent of the patients were black and 75% were male. Two of the two common identified risk factors for HIV infection were homosexuality (34%) and injection drug use (27%). Bacterial pneumonia was the most frequent pulmonary complication (42%). The two most common causes of bacterial pneumonia were Pseudomonas aeruginosa and Staphylococcus aureus. P carinii pneumonia (PCP) was found in 24%, with extrapulmonary involvement in 13%. Pulmonary mycobacterial infections were seen in 33%, with multiple extrapulmonary involvement. The most common site affected was KS. Of all pulmonary complications, only the incidence of PCP decreased over the 12-year period.
Conclusions: Recognizing the high incidence rate of bacterial pneumonia, the high frequency of pulmonary KS and the not uncommon occurrence of extrapulmonary P carinii infection in patients with HIV helps in improving their care.

Key words: acquired immunodeficiency syndrome; autopsy; bacterial pneumonia; cryptococcosis; cytomegalovirus infections; human immunodeficiency virus; Kaposi’s sarcoma; Mycobacterium infections; Pneumocystis carinii infections

Abbreviations: KS=Kaposi’s sarcoma; MAC=Mycobacterium avium complex; MTB=Mycobacterium tuberculosis; PCP=Pneumocystis carinii pneumonia

Millions of people worldwide are infected with HIV. By December 1996, 573,800 cases of AIDS had been reported in the United States.1 HIV infection has become the leading cause of death among persons aged 25 to 44 years in this country.1 Since the beginning of the AIDS epidemic, it has been recognized that infectious and noninfectious pulmonary complications are common in patients with HIV infection.2 Despite the change in trends of some of these complications as a result of antiretroviral therapy and prophylactic antibiotics over the years,3-5 the lung remains the most frequent organ involved by AIDS-associated diseases leading to death.6 We performed this retrospective study to describe the various pulmonary complications and the changes in their incidence over a 12-year period, from 1985 through 1996.

Materials and Methods

We reviewed the autopsy records of 233 adult patients with HIV-1 infection who died over the 12-year period from 1985 through 1996. Three patients were excluded from the study because the autopsy did not include the chest. One hundred eighty-five patients were from Howard University Hospital, Washington, DC, and 48 were from the University Medical Center, Jacksonville, Fla. Howard University Hospital is a 500-bed teaching hospital serving a predominantly African-American population in the District of Columbia. The Uni-
University Medical Center is a 528-bed teaching hospital affiliated with the University of Florida and located in Jacksonville, northern Florida. Demographic data and risk factors for HIV infection were retrieved. The histologic and microbiological findings of lung tissues were reviewed. The presence of pulmonary embolism and extrapulmonary organ involvement by Kaposi’s sarcoma (KS), Pneumocystis carinii, Mycobacterium tuberculosis (MTB), and Mycobacterium avium complex (MAC) were noted. Bacterial bronchopneumonia was defined as the presence of consolidation with polymorphonuclear leukocyte accumulation in bronchioles and adjacent alveoli. For the diagnosis of cytomegalovirus and fungal pneumonia, histologic evidence of lung involvement was required with or without tissue culture. To assess the trend of the main disease entities over time, the 12 years were divided into three 4-year periods. Eighty-two autopsy cases were included in the first period of the study, 80 in the second period, and 62 in the third period. Student’s t, Mann-Whitney U, and \( \chi^2 \) tests were used for comparison between groups. \( p \) values of <0.05 were considered significant. All statistical analyses were performed on software (StatView Software, version 1.5; Abacus Concepts, Inc; Berkeley, Calif).

**RESULTS**

The demographic data and risk factors for HIV infection are listed in Tables 1 and 2. The patients’ mean (±SD) length of hospital stay was 20.7±22.5 days and median was 15 days. There were more blacks (90% vs 67%; \( p<0.0001 \)) and homosexuals (40% vs 13%; \( p=0.0016 \)) at Howard University Hospital than the University Medical Center. The median length of hospital stay during their terminal hospital admission was longer for patients at Howard University Hospital compared with the University Medical Center (16 vs 8 days; \( p=0.0163 \)). There were no significant differences in patients’ age, sex, risk factor for HIV infection, and the length of hospital stay among the first, second, and third 4-year periods of the study.

The pulmonary complications found at autopsy are listed in Tables 3 through 5. At least one pulmonary complication was seen in 90% (210/233), and two or more were seen in 52% (121/233) of the patients. The mean number of pulmonary complications was 1.61±0.93 and median was two per patient. There was no significant difference in the number of pulmonary complications per patient among the three 4-year periods.

Bacterial bronchopneumonia, the most common pulmonary complication found at autopsy, was present in 42% (98/233). Thirty-seven percent (36/98) of the patients with bacterial bronchopneumonia were bacteremic. Bacterial bronchopneumonia was seen in 41% (32/79) of homosexuals, 50% (31/62) of injection drug users, 43% (92/215) of blacks, and 35% (6/17) of whites. Neither race nor risk factor for HIV infection was associated with the occurrence of bacterial bronchopneumonia. The commonly identified bacterial organisms causing bronchopneumonia were Pseudomonas aeruginosa (16), Staphylococcus aureus (14), Klebsiella pneumoniae (7), and enterococcus (7). Only one case of pneumococcal pneumonia was found. One patient had P aeruginosa empyema. Bacterial pneumonia was found at autopsy in 43% (35/82) of the patients in the first 4-year period compared with 42% (37/89) in the second and 42% (26/62) in the third 4-year periods (\( p=0.9890 \)).

*P carinii* pneumonia (PCP) was seen in 24% (56/233) of the patients: in 33% (27/82) in the first, 20% (18/89) in the second, and 18% (11/62) in the third 4-year periods. There was a significant decrease in the PCP incidence rate in the third period com-

### Table 2—Autopsy Findings: Risk Factors for HIV Infection Among 233 Patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>Howard University Hospital (n=185)</th>
<th>University Medical Center (n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homosexuality</td>
<td>74</td>
<td>5</td>
</tr>
<tr>
<td>Injection drug use</td>
<td>53</td>
<td>9</td>
</tr>
<tr>
<td>Heterosexual contact</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Injection drug use/ homosexuality</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Unidentified</td>
<td>26</td>
<td>28</td>
</tr>
</tbody>
</table>

### Table 3—Infectious Pulmonary Complications of 233 Patients With HIV Infection

<table>
<thead>
<tr>
<th>Complication</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial bronchopneumonia</td>
<td>98</td>
</tr>
<tr>
<td>Empyema</td>
<td>2</td>
</tr>
<tr>
<td>PCP</td>
<td>56</td>
</tr>
<tr>
<td>Mycobacterial infections</td>
<td>54</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>40</td>
</tr>
<tr>
<td>Cryptococcus</td>
<td>23</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>6</td>
</tr>
<tr>
<td>Aspergillus</td>
<td>2</td>
</tr>
<tr>
<td>Histoplasma</td>
<td>2</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>1</td>
</tr>
</tbody>
</table>
pared with the first (p=0.0406). Extrapulmonary involvement by P carinii infection was seen in 13% (7/56). The extrapulmonary involvement included lymph nodes (six), adrenal gland (one), liver (one), and spleen (one).

There was evidence of mycobacterial infection in 33% (78/233) of the autopsies: 32% (26/82) in the first 4-year period compared with 35% (31/89) in the second and 34% (21/62) in the third 4-year period (p=0.9080). Fifty-four patients had lung involvement with mycobacterial infection. The types of mycobacterial infections affecting the lungs are listed in Table 4. Thirty-one of the 47 MAC infections affected the lung. The lung involvement by MAC infection was confirmed only by histology in 3, only by tissue culture in 23, and both by tissue culture and histology in 5. Eighty-one percent (25/31) of the patients with pulmonary MAC infection also had another, coexistent, nonmycobacterial pulmonary disease. Extrapulmonary dissemination of MTB and MAC was common. MTB infection was noted in lymph nodes (11), spleen (9), liver (8), kidney (5), CNS (3), GI tract (3), heart (2), adrenal (2), thyroid (1), and bone marrow (1). MAC infection was noted in lymph nodes (25), spleen (24), liver (20), GI tract (8), kidney (2), adrenal gland (2), heart (1), pancreas (1), bone marrow (1), breast (1), and skin (1).

Cytomegalovirus pneumonia was found at autopsy in 11% (9/82) of the patients in the first 4-year period compared with 20% (18/89) in the second and 21% (13/62) in the third 4-year period (p=0.1804). Cryptococcal pneumonia was found at autopsy in 10% (8/82) of the patients in the first 4-year period compared with 12% (11/89) in the second and 6% (4/62) in the third 4-year period (p=0.4878).

The pulmonary malignancies found at autopsy are listed in Table 5. KS was seen in 12% (29/233) of the patients: 12% (10/82) of the patients in the first 4-year period compared with 11% (10/89) in the second and 15% (9/62) in the third 4-year period (p=0.8319). The most common site affected by KS was the lung (Table 6). Six of the 19 patients with pulmonary KS had no evidence of skin involvement at autopsy. The main organs affected by KS are listed in Table 6. The other organs affected by KS and not listed in Table 6 were pancreas (three), genitourinary (two), bone (two), bone marrow (one), and adrenal gland (one).

Pulmonary emboli were seen in 40 patients and the sources were thrombotic (30), bone marrow (5), septic (4), and tumor (1).

**Discussion**

Despite the advances in diagnostic radiology, laboratory analyses, and endoscopy, autopsy has remained a valuable tool for the identification and understanding of diseases for hundreds of years. Recent autopsy-based studies have highlighted the discrepancies between autopsy findings and ante-mortem clinical diagnoses and the changing patterns of the diseases affecting patients with HIV infection. In this retrospective review of 233 autopsy cases from two medical centers, we found that bacterial infections were the most frequent pulmonary complications. We confirmed the declining incidence of PCP over the years. We also described the extrapulmonary dissemination by P carinii infection and the incidence of pulmonary KS as well as the incidence of thrombotic and nonthrombotic pulmonary emboli. Our findings may be biased

---

### Table 4—Mycobacterial Pulmonary Complications Seen in 54 Patients With HIV Infection

<table>
<thead>
<tr>
<th>Complications</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAC</td>
<td>31</td>
</tr>
<tr>
<td>M tuberculosis</td>
<td>13</td>
</tr>
<tr>
<td>Mycobacterium kansasii</td>
<td>5</td>
</tr>
<tr>
<td>Mycobacterium chelonis-fortuitum</td>
<td>1</td>
</tr>
<tr>
<td>Mycobacterium fortuitum</td>
<td>1</td>
</tr>
<tr>
<td>M genkense/MAC</td>
<td>1</td>
</tr>
<tr>
<td>Unidentified</td>
<td>2</td>
</tr>
</tbody>
</table>

---

### Table 5—Pulmonary Malignancies of 233 Patients With HIV Infection

<table>
<thead>
<tr>
<th>Malignancies</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>KS</td>
<td>19</td>
</tr>
<tr>
<td>Non-Hodgkin's lymphoma</td>
<td>3</td>
</tr>
<tr>
<td>Hodgkin's lymphoma</td>
<td>2</td>
</tr>
<tr>
<td>Metastasis</td>
<td>3</td>
</tr>
<tr>
<td>Breast</td>
<td>1</td>
</tr>
<tr>
<td>Germ cell tumor</td>
<td>1</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>1</td>
</tr>
<tr>
<td>Bronchogenic carcinoma</td>
<td>1</td>
</tr>
</tbody>
</table>

---

### Table 6—The Main Sites Involved by KS

<table>
<thead>
<tr>
<th>Site</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>19</td>
</tr>
<tr>
<td>Parenchyma only</td>
<td>15</td>
</tr>
<tr>
<td>Airway only</td>
<td>1</td>
</tr>
<tr>
<td>Both airway and parenchyma</td>
<td>3</td>
</tr>
<tr>
<td>Skin</td>
<td>16</td>
</tr>
<tr>
<td>Lymph node</td>
<td>13</td>
</tr>
<tr>
<td>GI tract</td>
<td>9</td>
</tr>
<tr>
<td>Spleen</td>
<td>7</td>
</tr>
<tr>
<td>Liver</td>
<td>6</td>
</tr>
</tbody>
</table>

---
by the larger number of blacks and women and fewer homosexuals than the national AIDS population.1

Since the initial AIDS cases were associated with opportunistic infections such as PCP, the importance of bacterial infections, including bacterial pneumonia, was not fully recognized at the beginning of the epidemic. However, recent studies have shown that bacterial infections occur more frequently than other opportunistic infections in patients with HIV.12,13 Since the occurrence of bacterial infection in patients with HIV is a reflection of their immunosuppression, the Centers for Disease Control and Prevention added recurrent bacterial pneumonia in the revised 1993 case definition of AIDS.14 Recent cohort studies of patients with HIV13,15 showed that bacterial pneumonia was more common in injection drug users, and that Streptococcus pneumoniae, S. aureus and Haemophilus influenzae were the most frequent pathogens causing bacterial pneumonia. We did not find injection drug use to be a risk factor for bacterial bronchopneumonia, and P. aeruginosa and S. aureus were the most common pathogens in our study. In another autopsy-based study of patients with AIDS by Lyon et al,16 P. aeruginosa and S. aureus were the most frequent pathogens causing bacterial infections.16 All our patients had been hospitalized, and their mean (±SD) length of hospital stay was 20.5±22.4 and median was 15 days before they died. Thus, the difference between our study and that of Lyon et al and others can be partly explained by the nosocomial acquisition of the bacterial bronchopneumonia in autopsy-based studies. Even in nonautopsy studies, P. aeruginosa has become a common cause of bacterial infection in patients with HIV infection.17-22

At the onset of the AIDS epidemic, PCP was the most common serious complication, affecting nearly 75% of patients with the syndrome at least once in their lifetime.23 However, the incidence of PCP has been declining as a result of chemoprophylaxis and antiretroviral therapy.3,24 A recent longitudinal, prospective, multicenter study showed that the frequency of PCP as the index AIDS diagnosis had decreased from 47% in 1988 to 25% in 1991.25 The lower incidence of PCP in the last two 4-year periods of our study compared with the first 4-year period is consistent with the national trend. We found a significant decline in the autopsy incidence rate of PCP, but not in KS, mycobacterial infections, and bacterial bronchopneumonia during the 12-year period. This reflects the implementation of successful PCP prophylaxis during the later periods of the study. Klatt et al6 found PCP in 54% (305/565) and Marchevsky et al26 found it in 47% (9/19) of autopsy cases. However, the frequency of PCP in our study and that of Lyon et al16 was lower probably due to the fact that our study populations consisted of fewer homosexuals.27 Klatt et al6 reported 308 cases of P. carinii infection in 565 autopsies and described the sites involved, including lung (305), lymph node (12), spleen (4), kidney (3), liver and gallbladder (3), adrenal gland (3), heart (2), pancreas (2), eye (2), pituitary gland (2), thyroid gland (2), male genital gland (1), lower urinary tract (1), bone marrow (1), and skin (1). In the review of the literature by Cohen and Stoeckle,28 there were 37 patients with AIDS and extrapulmonary P. carinii infections, 18 of which had no pulmonary involvement. Nonpulmonary sites were affected in 13% of the P. carinii infections in our study, all of them with pulmonary involvement.

KS is the most common malignancy affecting patients with HIV infection. Although KS presents usually with cutaneous disease, pulmonary involvement is also common.6 It is not easy to determine the real incidence of pulmonary KS antemortem because of the need for invasive, diagnostic procedures, especially if only parenchymal disease is present. A recent autopsy study has shown KS to be present in 24% (138/565) of patients with AIDS, with 41% (56/138) lung and 90% (110/138) skin involvement.6 In our study, KS was present in only 12% of the patients and the most frequent site affected was the lung, followed by the skin. The low frequency of KS in our study may be explained by the relatively fewer number of homosexuals in our autopsy series.29 Our finding of the high incidence of pulmonary parenchymal KS, without airway involvement, underlines the low diagnostic yield of bronchoscopy in the diagnosis of pulmonary KS.

Most of the patients with pulmonary mycobacterial infection had extrapulmonary involvement in the present study. This is similar to other studies.6,30 Disseminated MAC occurs in 15 to 24% of AIDS patients in the developed countries.31 Despite the colonization of the respiratory tract, pneumonia caused by MAC is uncommon.32 A recent study has shown pulmonary MAC disease to be present in 2.5% of patients with disseminated MAC infection.33 Thirteen percent of the patients had MAC pulmonary involvement in our study. The lack of uniform criteria for the diagnosis of MAC pulmonary infection explains the differences between various studies.34 Most of our patients with positive lung tissue culture for MAC had no histologic evidence of MAC pneumonia and had other coexistent, nontuberculous mycobacterial diseases. Regardless of the histologic findings in lung tissue, the isolation of MAC from respiratory specimens in patients with HIV infection can be used as a predictor of dissemination.35

Pulmonary embolus, predominantly thrombotic, was seen in 17% of our patients. Although the emboli may not appear to have significant clinical impact on mortality, clinicians should be aware of their occurrence in hospitalized patients with HIV infection.
The lung is the organ most frequently affected by infectious and noninfectious diseases in patients with HIV infection. In this study of 233 patients with HIV infection, we used autopsy as a tool to confirm that bacterial pneumonia was the most common pulmonary complication and that the incidence of PCP has been declining over the years. We showed that the most commonly affected organ by KS was the lung. We also described extrapulmonary involvement by *P. carinii* and mycobacterial infections as well as the incidence of thrombotic and nonthrombotic pulmonary emboli.

**References**