Pulmonary Aspergillosis in Patients With AIDS*

Clinical and Radiographic Correlations

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Objective: To evaluate the clinical and radiographic features of pulmonary aspergillosis as they present in AIDS patients; in particular, to determine similarities and differences between Aspergillus infection in patients with AIDS vs those without AIDS.

Subjects and Methods: Six new cases of confirmed or probable pulmonary aspergillosis were discovered during a search of hospital records. These are reviewed with 30 previously reported cases with special attention to radiographic appearance of disease and how radiographic appearance influences clinical outcome.

Results: Symptoms of pulmonary aspergillosis in AIDS were nonspecific, most often including fever, cough, and dyspnea, and less commonly, chest pain or hemoptysis. Major risk factors for the development of pulmonary aspergillosis in patients with AIDS were steroid administration and neutropenia. Neutropenia was often a complication of therapies for AIDS, in particular, ganciclovir and zidovudine. Radiographic appearance of disease could be divided into three general categories. One third of the patients (13/36) presented with cavitary upper lobe disease resembling noninvasive or chronic necrotizing aspergillosis. Fatal hemoptysis occurred in 42 percent of patients with this form of disease. Twenty-two percent (8/36) of the cases presented as a nondescript focal alveolar opacity similar to invasive aspergillosis. In several patients, the focal infiltrate remained stable for several months, a feature that is unusual for aspergillosis in non-AIDS patients. The air crescent sign was present in none of the 36 reported cases. Patients with only focal disease had the best prognosis of patients with pulmonary aspergillosis. Bilateral alveolar or interstitial disease similar to invasive aspergillosis was present in 23 percent (9/36) of the patients. Bilateral disease appears to be a marker for disseminated infection and was associated with a high mortality due to aspergillosis. Two new forms of bronchial aspergillosis (5/36 cases) have been described previously. These patients presented with either obstructing fungal casts or bronchial pseudomembranes demonstrated bronchoscopically. In some patients with the bronchial forms of aspergillosis, transient alveolar opacities were seen on chest radiographs. These opacities may represent regions of atelectasis due to airway obstruction. One patient who had bilateral pneumothoraces without parenchymal opacities did not correspond to any of the three previously mentioned categories. Mortality due to aspergillosis was greater than 50 percent among AIDS patients. Death was subsequent to fatal hemoptysis or widespread pulmonary or systemic infection.

Conclusion: Unlike other risk groups that tend to contract only one form of pulmonary aspergillosis, AIDS patients can develop the whole spectrum of aspergillosis-related pulmonary disorders, including chronic cavitary, invasive, and bronchial forms of aspergillosis. Clinical symptoms are nonspecific and major risk factors include neutropenia, which is often a side effect of various therapies for AIDS, and steroid administration. Patients with the chronic cavitary form of disease have an unusually high mortality due to fatal hemoptysis. Patients with bilateral pulmonary infiltrates and aspergillosis have a high mortality due to disseminated infection.

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Aspergillus has become an increasingly common pathogen among immunocompromised patients. This is particularly true of those with prolonged neutropenia from chemotherapy for lymphoproliferative or solid neoplasms. Despite the severe immunosuppression seen among patients with AIDS, Aspergillus is a relatively uncommon pathogen among patients with HIV infection, and in 1984 was removed from the list of AIDS-defining illnesses.1 This report reviews our experience with pulmonary Aspergillus infection among the population of patients with HIV infection at 2 university medical centers over the last 6 years, in conjunction with a review of previously reported cases and with particular attention to radiographic manifestations as this impacts on clinical outcome.

Materials and Methods

A computerized search of the inpatient records of the Hospital of the University of Pennsylvania for patients with the diagnosis of both HIV infection or AIDS and Aspergillus infection was performed for the years 1990 to 1991. Five cases of confirmed or probable Aspergillus infection were obtained in this fashion. An additional case was obtained from the Jackson Memorial Hospital in Miami. The inpatient and outpatient records and radiology files were reviewed in detail to determine the clinical and radiographic

CMV = cytomegalovirus; OBA = obstructing bronchial aspergillosis; PNB = pseudomembranous necrotizing bronchial aspergillosis

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Table 1 — Epidemiologic Characteristics of Six Patients

<table>
<thead>
<tr>
<th>Patient/Age, yr/Sex</th>
<th>HIV Risk Factor*</th>
<th>Time From Diagnosis of AIDS to Diagnosis of Aspergillosis</th>
<th>CD4† Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/43/M</td>
<td>Homosexual</td>
<td>4 yr</td>
<td>40</td>
</tr>
<tr>
<td>2/53/M</td>
<td>NK</td>
<td>7 mo</td>
<td>&lt;25</td>
</tr>
<tr>
<td>3/28/F</td>
<td>Haitian</td>
<td>0 mo</td>
<td>NK</td>
</tr>
<tr>
<td>4/25/M</td>
<td>Homosexual</td>
<td>12 mo</td>
<td>10</td>
</tr>
<tr>
<td>5/39/M</td>
<td>NK</td>
<td>4 yr</td>
<td>63</td>
</tr>
<tr>
<td>6/28/M</td>
<td>Homosexual</td>
<td>12 mo</td>
<td>NK</td>
</tr>
</tbody>
</table>

*NK = not known.
†Absolute CD4 count in cells per microliter.

features of these patients.

Confirmed pulmonary aspergillosis cases were those with histologically proven pulmonary infiltration with Aspergillus organisms or with positive culture for Aspergillus species obtained via percutaneous aspiration of the lung. Patients 1, 2, and 3 met these criteria. Probable pulmonary aspergillosis describes those patients with (1) a new pulmonary infiltrate and sputum cultures or pulmonary lavage cultures positive for Aspergillus species without another pathogen recovered (patient 5), or (2) a cavitary infiltrate from which Aspergillus species are recovered (patient 4). Similar criteria were used by the largest reported series to date.1

A literature search for pulmonary aspergillosis and HIV infection or AIDS was also performed, yielding for review an additional 31 cases that described the radiographic findings.2-4 One case of proven pulmonary aspergillosis from Jones et al56 was excluded from this report because the most recent chest radiograph, a normal study, was 2 months prior to the patient’s death at a time when the patient had no pulmonary symptoms and Aspergillus had not been recovered from any of the patient’s tissues or secretions.

RESULTS

Clinical Features

Of the 36 cases reviewed, 2 were women and 34 were men. Ages ranged from 15 to 70 years with a mean of 35 years and a median of 37 years. Among the 20 with reported HIV risk factors, 12 were homosexual or bisexual, 6 were intravenous drug users, 1 was a hemophiliac, and 1 was a heterosexual partner of a person with AIDS. One patient was Haitian without other known risk factors. In 16 patients the risk factors were not reported or not known. Table 1 reviews the epidemiologic characteristics of the six new cases reported herein.

Fever (77 percent), cough (71 percent), and dyspnea (60 percent) were the most common symptoms. Cough was productive in some cases and nonproductive in others. Chest pain (31 percent) and hemoptysis (26 percent) were encountered less frequently.

Table 2 lists the relative frequencies of the more common clinical features relative to the radiographic appearance of disease. These were similar for each radiographic manifestation with a few exceptions. Hemoptysis was almost exclusively seen in patients with cavitary upper lobe disease or obstructing bronchial aspergillosis. Chest pain was more frequent with cavitary upper lobe disease or focal disease. Dyspnea was more common with noncavitary disease, especially bilateral disease.

Neutropenia (absolute neutrophil count less than 1,000), the most commonly reported predisposing risk factor for aspergillosis in AIDS patients,1,2,5 was seen in only two (33 percent) of our patients and was present in 41 percent of all reported cases (including the current series). None of our patients had received steroids; however, 25 percent of the total series of described patients had received them prior to development of aspergillosis. Of all reported cases, neutropenia and steroid administration were believed to be important factors contributing to infection in 64 percent.

Radiographic Features

1. Cavitary Upper Lobe Disease: Cavitary upper lobe disease was the most common radiographic presentation, occurring in 13 of 36 patients. It was bilateral in two patients and exhibited multiple cavities in the same lobe in one patient (Fig 1). It was unilateral with only one cavity in nine patients. An intracavitary mass was noted in three patients and was demon-

Table 2—Clinical Features

<table>
<thead>
<tr>
<th></th>
<th>Fever</th>
<th>Cough</th>
<th>Dyspnea</th>
<th>Chest Pain</th>
<th>Hemoptysis</th>
<th>Steroids or Neutropenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper lobe cavitary disease (n = 13)</td>
<td>11 (85)*</td>
<td>9 (69)</td>
<td>4 (31)</td>
<td>5 (38)</td>
<td>6 (46)</td>
<td>6 (46)</td>
</tr>
<tr>
<td>Focal infiltrate (n = 8)</td>
<td>5 (63)</td>
<td>5 (63)</td>
<td>5 (63)</td>
<td>2 (25)</td>
<td>1 (12)</td>
<td>4 (50)</td>
</tr>
<tr>
<td>Bilateral infiltrate (n = 9)</td>
<td>7 (78)</td>
<td>7 (78)</td>
<td>8 (89)</td>
<td>1 (11)</td>
<td>0 (0)</td>
<td>5 (55)</td>
</tr>
<tr>
<td>Obstructing bronchial aspergillosis (n = 3)</td>
<td>2 (67)</td>
<td>3 (100)</td>
<td>2 (67)</td>
<td>2 (67)</td>
<td>2 (67)</td>
<td>2 (67)</td>
</tr>
<tr>
<td>Other (n = 2)†</td>
<td>2 (100)</td>
<td>1 (50)</td>
<td>2 (100)</td>
<td>1 (50)</td>
<td>0 (0)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>Total (n = 35)</td>
<td>27 (77)</td>
<td>25 (71)</td>
<td>21 (60)</td>
<td>11 (31)</td>
<td>9 (26)</td>
<td>18 (51)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are percentages.
†A third case, Marchevsky et al., did not detail the clinical aspects of the case and therefore is not included in this table.
strated to be mobile in two instances. There was a known preexisting cavity that was subsequently involved by Aspergillus in two instances: one was a pneumococcal pneumatocele and the second was residua from prior Mycobacterium kansasii infection (case 2). In one of these patients, the cavity enlarged and the surrounding infiltrate increased following the development of aspergillosis. A third individual with multiple cystic spaces resembling premature emphysema may have had a thin-walled cyst at the site of subsequent Aspergillus infection. In two individuals with initial cavitary upper lobe disease, Aspergillus progressed to involve other nonapical regions of lung (and case 4). In those cases that were illustrated, cavitary disease was predominantly in the more apical regions of the upper lobe. Only one case was reported in the lingula.

An autopsy was performed in only one of 13 cases and demonstrated local pulmonary parenchymal invasion by Aspergillus without evidence of distant pulmonary or other organ system involvement.

Clinical outcome of patients with this form of disease was variable. Seven patients died as a result of Aspergillus infection. Hemothysis was seen in 6 of 13 patients with cavitary upper lobe disease and was fatal in 5 patients. Hemothysis occurred within 2-1/2 to 6 months of presentation of the cavitary lesion. Two patients died within a month of hospital admission of disseminated aspergillosis. One patient was cured of aspergillosis following surgical resection of a lingular cavitary infiltrate. Three patients died of other causes. One patient’s condition was improving after 2 months of therapy with itraconazole. In one patient, the clinical outcome is unknown.

2. Focal Alveolar Opacity: Eight of 36 cases of pulmonary aspergillosis presented with a nondescript focal alveolar process resembling bacterial pneumonia (Fig 2). Several cases were noted to be “pleural based,” a known feature of aspergillosis in non-AIDS patients. In three cases focal disease progressed to bilateral alveolar opacities (Fig 3). The patients who progressed to bilateral alveolar infiltrates died soon after: one with widespread disseminated infection of lung, bone, and meninges; the second died of respiratory failure from widespread pulmonary aspergillosis in conjunction with Pneumocystis, Escherichia coli, and Pseudomonas pneumonias; and the third died of a respiratory failure (case 3).

Three patients responded clinically and radiographically to amphotericin B or itraconazole therapy. One was completely free of disease with resolution of radiographic infiltrate 10 months later (case 1). Two showed partial radiographic and clinical response several months later. One was unavailable for follow-up and the second died of causes unrelated to Aspergillus infection.

Two patients progressed focally while receiving no therapy. One was unavailable for follow-up after 3 months (moved to another city) (case 5). A second died 2 months later of unknown cause (case 6).

3. Bilateral Opacities: Twelve of the 36 described patients noted bilateral opacities at presentation; they had known or suspected pulmonary aspergillosis. The
majority of these cases (8 of 12) were alveolar, some diffuse, and some patchy in distribution. One patient had diffuse nodular infiltrates. Two patients had reticular or reticular-nodular interstitial opacities.

Patchy bilateral alveolar opacities in three patients were due to an unusual and newly reported form of aspergillosis, "obstructing bronchial aspergillosis." 

In this disease, fungal casts occlude the central airways leading to airway compromise. The authors believed that the alveolar infiltrates represented atelectasis secondary to airway obstruction. Two of the three patients were cured of their aspergillosis with a combination of lavage and antifungal chemotherapy. One patient developed disseminated aspergillosis and died.

The clinical outcome of patients with bilateral opacities that were not due to obstructing bronchial aspergillosis was the poorest of all the groups. Six of nine patients died of aspergillosis, one due to aspergillosis alone and five patients due to Aspergillus infection in conjunction with other pulmonary illnesses. Accompanying illnesses included Pneumocystis carinii pneumonia (two cases), cytomegalovirus (CMV) pneumonia (two cases), aspiration pneumonia, and Kaposi's sarcoma. One patient died of causes unrelated to aspergillosis but with persistent untreated pulmonary aspergillosis. In two cases the clinical significance of aspergillosis was uncertain.

4. Other Manifestations: Three patients initially presented without pulmonary infiltrate. One was a 15-year-old hemophiliac with an entity termed "pseudo-membranous necrotizing bronchial aspergillosis." He presented with cough, severe dyspnea, and wheezing with a normal chest radiograph. He subsequently progressed to respiratory failure and died. In the days prior to his death, the chest radiograph demonstrated minimal patchy opacities in the right lower lobe and extensive subcutaneous emphysema. Autopsy revealed pseudomembranes obstructing the central airways. Microscopically there was invasion of the bronchial walls and peribronchial tissue by Aspergillus organisms but no presence of Aspergillus in the remaining pulmonary parenchyma.

A second patient with similar pseudomembranes at post-mortem evaluation also died of respiratory failure with a normal chest radiograph.

The last patient initially presented with fever, cough, and pleuritic chest pain. Chest radiograph revealed bilateral pneumothoraces. Post-mortem examination demonstrated invasive aspergillosis of the lungs and pleura as well as CMV and P. carinii pneumonitis.

Clinical outcome as a function of radiographic appearance is listed in Table 3.

**Discussion**

As shown by the paucity of reported cases, aspergillosis in patients with HIV infection is an uncommon occurrence. Of 3,170 AIDS cases reported to the Centers for Disease Control between May 1983 and June 1984, only five patients (0.16 percent) were reported to have aspergillosis.

The Immunodeficiency Clinic at the Hospital of the University of Pennsylvania has cared for 470 patients from July 1988 to December
**Table 3—Clinical Outcome**

<table>
<thead>
<tr>
<th>Clinical Outcome</th>
<th>Cavity (n = 13)</th>
<th>Focal Infiltrate (n = 8)</th>
<th>Bilateral* (n = 9)</th>
<th>OBA†</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death due to Aspergillus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Nonhemoptysis</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Death due to other causes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspergillus absent</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Aspergillus persistent</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Alive with resolution of aspergillosis</td>
<td>1†</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Alive with disease</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Unknown§</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

*Not including obstructing bronchial aspergillosis.
†OBA = obstructing bronchial aspergillosis.
§Surgical resection for cure.

This category includes those whose clinical outcome is unknown.

1991. Four of our patients with aspergillosis were seen in this time interval, a 0.9 percent incidence in our population. This is in contrast to the relative frequency of cases in certain other immunocompromised patients: 70 percent of patients with leukemia and neutropenia of greater than 30 days, 11 15 to 20 percent of all patients with leukemia, 12 and 14 percent of heart transplant patients. 13 These profound differences in susceptibility to Aspergillus infection are most likely related to the differences in immune dysfunction among these groups. The majority of patients who develop aspergillosis, those with lymphoproliferative disorders, organ transplants, etc, have deficiencies in phagocyte function. This may be due to absolute deficiencies in numbers of granulocytes or may be secondary to decreased activity of granulocytes and pulmonary macrophages as seen following high-dose steroid use. 14-17 Neutropenia and steroid use are well-established risk factors for the development of aspergillosis. 18 Laboratory data support the importance of phagocytes, granulocytes, and tissue macrophages in the normal host defense against Aspergillus infection. 19-22 Barrier host defenses may also play a role in preventing aspergillosis. 20-21

Since AIDS patients primarily have deficiencies in T-cell function, not granulocytes or macrophages, they are less susceptible to infection by Aspergillus species. As such, AIDS is probably not an independent risk factor for the development of aspergillosis. 5,19,23 Many of the AIDS patients who developed aspergillosis had other traditional risk factors for acquiring aspergillosis. Most important of these risk factors, neutropenia or steroid use, were seen in 54 percent of reported cases. This has been noted by others. 1,2,6 Of interest is the fact that neutropenia was often the result of AIDS-related therapies such as zidovudine and ganciclovir. 1,2 These were a factor in 9 of 13 cases of neutropenia reviewed herein. Thus, aspergillosis in AIDS patients may be due largely to the various toxic therapies (including steroids) employed in the management of AIDS, rather than a direct result of HIV infection.1,2

Other reported risk factors for the development of invasive aspergillosis in patients with AIDS include prior recent broad-spectrum antibiotic administration seen in five of six of our patients and in many of the previously reported cases. 1,2,6,8 However, AIDS patients often receive broad-spectrum antibiotics because of their frequent episodes of fever and infections. Therefore, this is not a good predictor of Aspergillus infection. Recent antecedent bacterial, Pneumocystis, or CMV infection have also been associated with development of Aspergillus infection 2 and were seen in three of our patients. Like broad-spectrum antibiotics, these are common features of AIDS patients in general and do not identify particular patients at risk. Other risk factors have been reported, including marijuana use, alcohol abuse, and intravenous drug abuse. 2,6

As seen in Table 2, the most common symptoms of pulmonary aspergillosis in AIDS patients are those of pulmonary infections in general: fever, cough, dyspnea, and occasionally chest pain. They do not help in differentiating aspergillosis from other pulmonary infections. These symptoms were similar among all radiographic appearances although dyspnea was more common for individuals with bilateral disease, and chest pain was more frequently seen in patients with cavitary upper lobe disease and obstructing bronchial aspergillosis.

Hemoptysis was an infrequent but often life-threatening symptom of aspergillosis in HIV-infected patients. It was seen predominantly in two groups of patients; those with obstructing bronchial aspergillosis and those with cavitary upper lobe disease. Hemoptysis in patients with obstructing bronchial aspergillosis was minor, with little effect on the patient's prognosis. 2 This is probably similar to the hemoptysis seen in patients with other forms of bronchitis. However, in patients with cavitary upper lobe disease, hemoptysis was often fatal. Death occurred in five of six patients with cavitary upper lobe disease and hemoptysis. The 38 percent rate of fatal hemoptysis.
among HIV-infected patients with cavitary aspergillosis is significantly higher than the 0 percent to 25 percent rate of fatal hemoptysis seen in non-HIV-infected patients with cavitary upper lobe disease.\textsuperscript{1,2,4-30}

The sudden onset and high fatality rate from locally confined disease raises the question whether the infection should be surgically treated. This approach is not tenable in many HIV-infected patients because of their advanced stage of disease and short life expectancy from other causes. However, in selected individuals, surgical excision of cavitary upper lobe aspergillosis might be considered. It is interesting to note that one patient with cavitary upper lobe disease but without hemoptysis underwent resection without recurrence of aspergillosis. This was the only patient with cavitary upper lobe disease who was cured of his aspergillosis.

Our review of the 36 reported cases of pulmonary aspergillosis among HIV-infected patients discloses three major radiographic presentations: cavitary upper lobe disease, focal alveolar infiltrates, and bilateral interstitial or alveolar infiltrates. These presentations in some ways parallel the radiographic appearance in the non-AIDS population, but there are also distinct differences.

Cavitary upper lobe disease resembled noninvasive aspergillosis or semi-invasive aspergillosis seen in nonimmunocompromised hosts or those with nonspecific alterations in immune function such as sarcoidosis, malignancies, or alcoholism. Like noninvasive and semi-invasive aspergillosis in non-HIV-infected patients, progression to disseminated disease was uncommon, seen in only 2 of 12 reported cases. The rate of local progression was quite rapid in our two patients and involved much of an upper lobe within a few months of initial presentation. In our experience, this was more rapid than is usual for the non-AIDS population.

Focal alveolar opacities were present in one quarter of the cases. Similar focal opacities may be seen in leukemic patients or transplant recipients with invasive aspergillosis. These may resolve spontaneously with recovery of white blood cells or with antifungal therapy. Among the HIV-infected patients, the conditions of three improved with antifungal therapy. Interestingly, unlike most non-HIV-infected patients with invasive aspergillosis, these focal infiltrates in some cases persisted for months without progression or regression of disease.

No air crescent signs were noted among the cases reported. This is a relatively common feature of invasive aspergillosis in non-AIDS patients and is associated with the rapid rise in neutrophil counts following recovery from bone marrow suppression. Since AIDS patients are unlikely to have rapid recovery in granulocytes, it is not surprising that air crescent signs were not detected.

Bilateral disease was most often described as diffuse or patchy alveolar disease. One case noted multiple nodular opacities, a pattern that is common in non-HIV-infected patients with invasive aspergillosis. Several patients were noted to have reticular or reticulo-nodular infiltrates. This is a pattern that is unusual among non-HIV-infected patients and would be of great interest if they were caused by invasive aspergillosis. However, most of these patients had superimposed infections that are known to produce interstitial infiltrates, usually \textit{P. carinii} or CMV pneumonia. Therefore, it is unclear whether the Aspergillus or these other organisms were the cause of the interstitial opacities.

Two unusual and possibly AIDS-specific forms of aspergillosis with bronchial involvement have been reported by Denning et al.\textsuperscript{2} Perez et al.\textsuperscript{7} and Marchevski et al.\textsuperscript{9} Termed “obstructing bronchial aspergillosis” (OBA) and “pseudomembranous necrotizing bronchial aspergillosis” (PNBA), they in some ways resemble allergic bronchopulmonary aspergillosis. Patients with OBA and PNBA presented with hypoxia and acute respiratory distress. In the former entity, patients were noted to spontaneously expectorate fungal casts. In PNBA, thin membranes were noted to occlude the airways. Chest radiographs were often normal or demonstrated patchy alveolar opacities thought to represent atelectasis.\textsuperscript{2,7} In both entities, Aspergillus was isolated to the major airways, without pulmonary parenchymal involvement.

In the general population, Aspergillus species are known to produce a variety of pulmonary disorders: noninvasive, semi-invasive, invasive and allergic bronchopulmonary aspergillosis. Each of these disorders characteristically involves distinct subpopulations. Note, however, that HIV-infected patients have been subject to nearly the whole spectrum of Aspergillus-related diseases. The reason for this is not known, but it may be due to varying degrees of neutrophil dysfunction among the HIV-infected patients who develop aspergillosis.

Overall, the clinical outcome of HIV-infected patients with pulmonary aspergillosis is dismal (Table 3). Fifty-six percent of patients died from aspergillosis either due to widespread pulmonary or systemic infection or due to fatal hemoptysis. Another 14 percent died of causes unrelated to aspergillosis although the majority had persistent aspergillosis at the time of their death. Only 17 percent were known to be alive at the time of reporting. Only 11 percent of patients were cured of their aspergillosis (three alive, one dead of other causes).

Seven of 13 patients with cavitary upper lobe disease died as a result of their Aspergillus: 2 secondary to widespread dissemination and 5 as a result of hemoptysis.
Patients with focal alveolar disease had the best prognosis of all groups except obstructing bronchial aspergillosis. Three of eight patients responded to antifungal therapy: one with eradication of Aspergillus, and two others with clinical and/or radiographic improvement. The three patients who progressed to bilateral disease all died of widespread pulmonary or disseminated disease.

Patients with bilateral disease, except those with obstructing bronchial aspergillosis, had a poor prognosis. Widespread bilateral infiltrates appear to be a marker of disseminated aspergillosis in patients with AIDS and is an ominous finding. Nine of 12 patients with widespread bilateral infiltrates died of disseminated disease. (Three presented with focal opacities that subsequently became diffuse).

Both Denning et al. and Klapholtz et al. have noted that Aspergillus infection occurred predominantly in patients with advanced states of AIDS infection. This was also frequently noted in the clinical charts of our patients and is reflected in their low CD4 counts (Table 1). Thus, the high mortality rate among these individuals likely reflects not only the severity of Aspergillus infection, but also the patient's generally debilitated state, and in some cases superimposed illnesses.

In summary, we conclude that the radiographic patterns of Aspergillus infection in HIV-infected patients are quite similar to those seen in other patients. Interestingly, HIV-infected patients appear to be susceptible to the whole variety of Aspergillus-related pulmonary disorders, a feature not seen in other risk groups. Clinical symptoms are similar to those found in non-HIV-infected patients as are risk factors. Most important risk factors include neutropenia, which is often a side effect of various therapies for AIDS, and steroid administration. Focal alveolar infiltrates resembling bacterial pneumonias are seen in approximately one quarter of cases. These can resolve with therapy or progress to disseminated disease. Bilateral diffuse lung disease is often a marker for systemically disseminated aspergillosis and has a high mortality. Chronic upper lobe cavitory disease is seen in approximately one third of cases. Hemoptysis is the most common cause of death in this group, and surgical resection may be useful in selected cases. Overall prognosis is grim with more than 50 percent of patients dying of their aspergillosis and a large percentage of the remainder dying of other diseases within a few months of diagnosis of aspergillosis.

References

on AIDS, Montreal, June 4-9, 1989


