Pulmonary mucormycosis is relatively uncommon but an important opportunistic fungal infection in immunocompromised persons. The literature on the subject is sparse. We describe a recent case and review the literature to delineate the clinical characteristics of this infection. We searched the MEDLINE database for articles published in the English-language literature since 1970 and carefully analyzed 87 cases. The main risk factors were diabetes mellitus, hematologic cancers, renal insufficiency, and organ transplantation. Several patients had no apparent immune compromise. There was a predilection for involvement of the upper lobes. Air crescent signs on chest x-ray films were predictors of pulmonary hemorrhage and death from hemoptysis. Fiberoptic bronchoscopy was a useful diagnostic method, and histopathologic examination was more sensitive than fungal cultures. The overall survival rate was 44%. Patients treated with a combined medical-surgical approach had a better outcome than patients who did not undergo surgery. Thus, this relatively rare but often fatal disease should be suspected in immunocompromised patients who fail to respond to antibacterial therapy. Early recognition and aggressive management are warranted to maximize chances for cure. Optimal therapy requires systemic antifungal therapy, surgical resection, and, when possible, control of the patient’s underlying disease.

Pulmonary mucormycosis is a relatively uncommon infection that occurs mostly in immunocompromised persons. The first case of pulmonary mucormycosis was described in 1876 by Furbringer. In a classic review in 1971, Baker thoroughly describes all cases of mucormycosis previously reported. Since then, only scattered reports have been published, except for a review by Tedder et al, who describe 30 patients treated at their institution and 225 additional patients described in the literature. They include many patients with disseminated mucormycosis in their analysis, thus weakening the applicability of their findings and conclusions to isolated pulmonary disease. In this article, we describe an immunocompromised patient with localized pulmonary mucormycosis and review 86 other cases reported in the literature since 1970, when bronchoscopy became widely available. Because a high index of suspicion, earlier diagnosis, and aggressive management, often involving surgical resection, can lead to a cure in selected patients, the goal of our review is to better characterize the population at risk, presenting symptoms, radiological appearance, diagnostic methods, therapy, and outcome.

ILLUSTRATIVE CASE

The patient, a 39-year-old white man with a medical history of hypertension, myelodysplastic syndrome, and type 1 diabetes mellitus of 18 years’ duration complicated by retinopathy and renal failure, had received a cadaveric renal transplant in 1991. He was seen in the outpatient clinic September 15, 1995, with a 2-week history of sore throat, nonproductive cough, dyspnea on exertion, fever, chills, generalized malaise, and myalgias. Medications at presentation included predni-

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sone, 5 mg daily; cyclosporine, 125 mg twice a day; ofloxacin, 400 mg daily; ferrous polysaccharide; and insulin. On physical examination on admission to the hospital, he had a temperature of 38.4°C, and his lung fields were normal to auscultation. His chest radiograph revealed a new right upper lobe infiltrate that was not present on a radiograph taken 10 days before. His white blood cell count was $4.19 \times 10^9/L$; hemoglobin level, 69 g/L; and platelet count, $52 \times 10^9/L$; with serum levels of urea nitrogen, 9.3 mmol/L (26 mg/dL), and creatinine, 133 µmol/L (1.5 mg/dL). He had defervescence, with lessening of his symptoms, with the administration of intravenous vancomycin and ceftazidime. Blood and sputum cultures remained negative for pathogens. He was discharged from the hospital 4 days later with oral clarithromycin.

The patient returned to the emergency department 4 days later with recrudescence of his previous symptoms and pleuritic chest pain. He was again febrile to 38.2°C, with bronchial breath sounds and a localized wheeze heard over the right upper lung. His blood pressure on admission was 132/64 mm Hg; respirations, 20/min; and oxygen saturation, 100% with the patient breathing room air. His chest radiograph revealed persistence of the right upper lobe infiltrate, which now extended to the right hilum, with volume loss and the development of a hilar mass (Figure 1). His white blood cell count was $5.8 \times 10^9/L$ with 0.74 neutrophils. The intravenous administration of a combination of ticarcillin and clavulanate, and erythromycin was started. Flexible fiberoptic bronchoscopy performed on day 3 of his second hospital admission revealed narrowing of the anterior and posterior segments of the right upper lobe associated with mucosal edema. Computed tomography of the sinuses revealed no abnormalities. Computed tomography of the chest on the same day revealed right upper lobe consolidation and necrosis extending to the right hilum (Figure 2). The right upper lobe and right main bronchi were both narrowed. A small right pleural effusion was also noted. Cytologic analysis of endobronchial brushings and histological examination of a biopsy specimen revealed broad nonseptate hyphae with right-angle branching, consistent with mucormycosis. His absolute neutrophil cell count fell to $1.02 \times 10^9/L$. A course of intravenous amphotericin B (1 mg/kg of body weight) was initiated that evening. At thoracotomy on September 29, the right main pulmonary artery was found to be invaded by a fungating mass, and a pneumonectomy was performed.

Figure 1. A chest radiograph showing a right upper lobe infiltrate.

Figure 2. A computed tomographic scan of the chest showing an infiltrative mass in the right upper lobe involving the right hilum.

Histopathologic analysis of the lung confirmed widespread angioinvasive infection with Mucorales (Figure 3 and Figure 4). The organism grew and was found to be Rhizopus arrhizus. His postoperative course was complicated by a rise in the serum creatinine level to 212 µmol/L (2.4 mg/dL). His amphotericin preparation was changed on October 3 to a colloidal dispersion (Amphotec; 4 mg/kg) to minimize nephrotoxic effects. A nosocomial left lower lobe pneumonia devel-
oped that progressed despite broad-spectrum antibiotic therapy, necessitating mechanical ventilation. He died of sepsis on October 9. An autopsy revealed pneumonitis of the left lower lobe, with silver staining failing to show fungi. There was no evidence of disseminated mucor.

METHODS

Our retrospective review focuses on patients with localized pulmonary mucormycosis who did not have evidence of dissemination. Pulmonary mucormycosis was defined as disease localized to the lungs or mediastinum. Disease was defined as disseminated when 2 or more non-contiguous organ systems were involved or blood cultures grew the causative organism. The presence of sinus disease in addition to pulmonary disease was not considered dissemination because it reflected focal involvement of the respiratory tract, and a case of rhinocerebral disease in the presence of pulmonary lesions was accepted only if it was obvious that the cerebral lesion was due to direct extension from the sinuses. The diagnosis was accepted only if it was established by histological or cytologic examination or by a culture positive for the causative organism.

We searched the MEDLINE database for articles published in the English-language literature since 1970 using mucormycosis and pulmonary as keywords or text words. We used 1970 as a cutoff because of the year of publication of Baker’s article (1971) and because of the introduction of flexible fiberoptic bronchoscopy. Where applicable, we reviewed references cited in the above studies. Care was taken to ensure that the same patient was not included twice in our analysis, as some patients were described more than once in the literature. Incomplete case reports with limited clinical information were not included in our analysis. The data were analyzed with a database program (Reflex 2.0; Borland [now Inprise Corp], Scotts Valley, Calif).

RESULTS

Eighty-six cases in the literature met our criteria for localized pulmonary mucormycosis without evidence of dissemination, leading to a total of 87 cases when our patient’s case is added.

DEMOGRAPHICS AND UNDERLYING CONDITIONS

Sixty-five patients were male and 22 were female, for a male-female ratio of 3:1. The mean age was 44 years (range, 2 months to 83 years). The ethnic group was not recorded consistently in the literature, being reported for only 36 of 87 patients, with the following distribution: 16 whites, 10 African Americans, 7 Asians, 2 Hispanics, and 1 Middle Eastern patient.

When we analyzed underlying conditions in our study population, the largest group consisted of 49 patients (56%) with diabetes mellitus, of whom 10 (20%) presented with ketoacidosis. The next largest group consisted of 28 patients (32%) with hematologic cancers, of whom 13 (46%) had neutropenia. Of the 28 patients, 17 (61%) had acute leukemia (8 with acute myeloid leukemia, 7 with acute lymphocytic leukemia, and 2 with acute promyelocytic leukemia),
Table 1. Presenting Symptoms and Physical Findings in 87 Patients With Pulmonary Mucormycosis

<table>
<thead>
<tr>
<th>Presenting Symptoms</th>
<th>Patients, No. (%)</th>
<th>Physical Findings</th>
<th>Patients, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>56 (64)</td>
<td>Fever (temperature &gt;38°C)</td>
<td>55 (63)</td>
</tr>
<tr>
<td>Cough</td>
<td>53 (61)</td>
<td>Tachypnea</td>
<td>20 (23)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>32 (37)</td>
<td>Crackles</td>
<td>21 (24)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>25 (29)</td>
<td>Decreased breath sounds</td>
<td>15 (17)</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>23 (26)</td>
<td>Wheezing</td>
<td>13 (15)</td>
</tr>
<tr>
<td>Sputum production</td>
<td>18 (21)</td>
<td>Dullness to percussion</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Malaise</td>
<td>16 (18)</td>
<td>Normal findings on examination</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>14 (16)</td>
<td>Pleural rub</td>
<td>3 (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Superior vena cava obstruction</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cervical adenopathy</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

whereas 7 (25%) had chronic leukemia (5 with chronic lymphocytic leukemia and 2 with chronic myeloid leukemia), and 1 each had hairy cell leukemia, Hodgkin lymphoma, myelodysplastic syndrome, and agammaglobulinemia. Of the 11 patients (13%) with renal insufficiency, 6 were receiving dialysis. Ten patients (11%) were organ transplant recipients. Of these, 6 received renal transplants, 2 bone marrow transplants, 1 a heart transplant, and 1 a liver transplant. Of note, 8 patients (9%) had metabolic acidosis, including 1 patient with long-term salicylate ingestion, 1 with renal insufficiency, 2 with diabetes mellitus without ketosis, and 2 diabetic patients receiving dialysis. One patient was taking deferoxamine and another was taking iron supplements. Finally, 11 patients (13%) had no apparent underlying illness.

**CLINICAL PRESENTATION**

Table 1 summarizes presenting symptoms and physical findings. These were mostly nonspecific. Cough was present in 53 patients (61%) only, and 23 (26%) presented with hemoptysis. The most prominent physical finding was fever in 55 patients (63%). The findings otherwise were sparse, including 8 patients with normal findings on clinical examination. Unusual presentations included 1 patient with superior vena cava obstruction who was found at autopsy to have lung infarcts and invasion of the superior vena cava and pulmonary artery by mucor and another patient with cervical lymphadenopathy who died of stridor due to granulomatous and fibrous mediastinitis. One patient was seen because of left shoulder pain due to the Pancoast tumor and survived surgical resection of the lesions.

We arbitrarily defined onset as acute if symptoms were present for 30 days or less before presentation and chronic if present for more than 30 days. Most patients (68 [78%]) had an acute onset, but a substantial number (16 [18%]) had chronic symptoms. Both groups had similar bacterial coinfection rates (34% vs 29%) and survival rates (44% vs 41%).

**MICROBIOLOGIC ASSESSMENT**

A total of 59 specimens were submitted to the microbiology laboratory for culture. Only 29 (49%) were positive for the causative organism. Of these, the most common isolates belonged to the genus *Rhizopus* in 12 patients (41%). Our patient's organism was identified as *R. arhizus*. Mucor was identified in 7 patients (24%), although it is unclear whether these organisms truly belonged to the genus *Mucor* or if this was simply a generic designation. *Cunninghamella bertholletiae* was identified in 6 patients (21%), and in 1 patient, the pathogen was *Cunninghamella elegans*, now reclassified as *Apophysomyces elegans*. Two patients grew organisms belonging to the genus *Absidia* and 1 to the genus *Syncphaulastrum*.

Coinfection was a feature in 28 patients (32%) only. Of these, 27 had bacterial pneumonia, and 1 patient had *Pneumocystis carinii* pneumonia. All 28 patients had received chemotherapy or steroids for their underlying condition, and 23 patients (82%) presented with acute symptoms.

**RADIOLOGICAL PRESENTATION**

Table 2 outlines the radiographic manifestations of pulmonary mucormycosis. Most patients (37 [43%]) had involvement of the upper part of the chest, with the right upper lobe (23 patients) more commonly implicated than the left upper lobe (16 patients), followed by the lower part of the chest (21%)—equally divided between right and left lungs (9 patients each)—and, rarely, the middle part of the chest (3 patients). The findings of a chest radiograph were rarely normal: 1 patient had tracheal mucor presenting with stridor, another had endobronchial disease with right pulmonary artery involvement at autopsy, and a third died of multiple mucor-related pulmonary infarcts.
Thirty-four patients (39%) were described as having an infiltrate or consolidation, and 23 (26%) had a cavitory lesion. An air crescent sign was described on chest radiograph in 7 patients, all with upper lobe disease. The presence of an air crescent sign seems to be significantly associated with an increased risk for massive hemoptysis. Chest pain, hemoptysis, or both were a feature in 10 patients (43%) with a cavity only on chest radiograph, as opposed to 5 patients (71%) with an air crescent sign, suggesting that the latter may herald the onset of pulmonary infarction and the erosion of pulmonary vessels. More specifically, only 1 patient (5%) with a cavity, but 3 patients (43%) with an air crescent sign, died of massive hemoptysis.

Pleural effusions seem to be relatively uncommon in pulmonary mucormycosis, with only 7 patients (8%) exhibiting this finding on chest radiograph. One report described only bilateral effusions on chest radiograph, but a computed tomographic scan of the thorax revealed a left lower lobe cavity, illustrating the value of computed tomographic imaging in selected cases.

Fistulas were uncommon, occurring in 5 patients (6%) only, but they were fatal in 3 of the patients. The types of fistulas described include bronchocutaneous, bronchopleural, and bronchoarterial with pseudoaneurysm.

**DIAGNOSIS**

The most common method used to make the diagnosis of pulmonary mucormycosis in our review was flexible fiberoptic bronchoscopy, which was used in 33 (40%) of 87 patients, and 34 of these had visible endobronchial disease. Our review also confirms the hypothesis of Donahue et al. that diabetic patients have a predilection for endobronchial disease because the most common predisposing factor was diabetes mellitus in 29 (85%) of these 34 patients. Table 3 outlines the variety of features seen with bronchoscopy in these 34 patients. Stenosis and obstruction were seen in 12 patients (35%).

Seventeen patients (20%) required open lung biopsy or surgical resection for diagnosis. Transbronchial needle aspiration and thoracentesis were successfully used for diagnosis in 6 and 3 patients, respectively. Sputum culture was a remarkably insensitive method, leading to the diagnosis in only 2 patients. Direct laryngoscopy was used in a diabetic patient with tracheal mucormycosis who eventually required laryngotracheal resection and primary reanastomosis. The diagnosis was made at autopsy in 23 patients.

The diagnosis was established by histological examination in 71 (93%) of 76 patients for whom it was done and by cytologic examination in 18 (62%) of 29 patients for whom it was done, whereas cultures were positive for fungi in only 29 (49%) of 59 specimens submitted. In one report, “dicing” or homogenizing of the specimen was noted to result in a negative culture result because of the aseptate nature of the fungus. This may explain, at least in part, why fungal cultures provided the lowest yield among the 3 modalities.

**THERAPY AND OUTCOME**

Of the 87 patients, 38 (44%) survived. Twenty-two patients (25%) died of the infection, and 15 (17%) died of massive hemoptysis. The remaining 12 patients (14%) died of unrelated causes. If we exclude deaths unrelated to the fungal infection or hemoptysis, the overall survival rate was 51% (38 of 75 patients). We also looked at the effects of predisposing factors on the outcome (Table 4). Patients with renal insufficiency or metabolic acidosis did the worst, with no survivors. Patients with hematologic conditions had a survival rate of only 25% (7 of 28 patients). Within this group, only 1 (8%) of 13 patients with neutropenia survived, compared with 6 (40%) of 15 patients without neutropenia. Diabetic patients, organ transplant recipients, and patients with no predisposing factors had similar survival rates—between 45% and 60%.

**Table 3. Endobronchial Appearance in 34 Patients With Pulmonary Mucormycosis Diagnosed by Fiberoptic Bronchoscopy**

<table>
<thead>
<tr>
<th>Findings</th>
<th>Patients, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenosis</td>
<td>8 (24)</td>
</tr>
<tr>
<td>Erythematous mucosa</td>
<td>6 (18)</td>
</tr>
<tr>
<td>Obstruction of airway</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Gelatinous or mucoid secretions</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Fungating or polyoid mass</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Granulation tissue</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Mucosal ulceration</td>
<td>2 (6)</td>
</tr>
<tr>
<td>White and creamy, or purulent</td>
<td>2 (6)</td>
</tr>
<tr>
<td>exudate</td>
<td></td>
</tr>
<tr>
<td>Toothpaste-like exudate</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Tracheitis</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Fibrinoid necrotic slough</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Plaques</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Vocal cord paralysis</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

**Table 4. Underlying Condition and Outcome in 87 Patients With Pulmonary Mucormycosis* **

<table>
<thead>
<tr>
<th>Underlying Condition (No. of Patients)</th>
<th>Death From Progression of Mucormycosis</th>
<th>Death From Massive Hemoptysis</th>
<th>Unrelated Death</th>
<th>Alive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus (49), No. (%)</td>
<td>5 (10)</td>
<td>12 (24)</td>
<td>4 (8)</td>
<td>28 (57)</td>
</tr>
<tr>
<td>Hematologic condition (28), No. (%)</td>
<td>9 (32)</td>
<td>4 (14)</td>
<td>8 (29)</td>
<td>7 (25)</td>
</tr>
<tr>
<td>Renal insufficiency (11), No.†</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Organ transplant (10), No.†</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Metabolic acidosis (8), No.†</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Deferoxamine or iron supplements (2), No.†</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>No underlying condition (11), No.†</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

*Some patients had more than 1 underlying condition.
†Percentages are not given because of the small number of patients in this category (<15).
Table 5. Treatment and Outcome in 87 Patients With Pulmonary Mucormycosis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients, Deaths, No. (%)</th>
<th>Patients, Deaths, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical therapy only*</td>
<td>31 (36) 17 (55)</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>30 (34) 8 (27)</td>
<td></td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>6 2</td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>22 5</td>
<td></td>
</tr>
<tr>
<td>Debridement and cavernostomy</td>
<td>1 1</td>
<td></td>
</tr>
<tr>
<td>Laryngotraheal resection</td>
<td>1 0</td>
<td></td>
</tr>
<tr>
<td>Drainage procedure</td>
<td>3 (3) 2 (67)</td>
<td></td>
</tr>
<tr>
<td>Chest tube</td>
<td>2 2</td>
<td></td>
</tr>
<tr>
<td>Removal of mass with bronchoscope</td>
<td>1 0</td>
<td></td>
</tr>
<tr>
<td>No therapy</td>
<td>23 (26) 22 (96)</td>
<td></td>
</tr>
</tbody>
</table>

* See the subsection “Therapy and Outcome” in the “Results” section for details.

receiving medical therapy alone, 17 patients (55%) died: 6 with massive hemoptysis, 7 of overwhelming fungal sepsis, and the remaining 4 of unrelated causes. Thirty patients were treated surgically with or without antifungal therapy, and 3 underwent an adjunctive drainage procedure. Patients who underwent surgery had a mortality of 27%, with 5 of the 8 deaths due to unrelated causes. Twenty-three patients, most of whose diagnosis was made at autopsy, received no specific antifungal therapy or surgery. All but 1 died: 12 of the infection, 8 of massive hemoptysis, and 2 of unrelated causes.

COMMENT

The review by Baker2 in 1971 thoroughly describes all cases of mucormycosis previously reported. He reports on 49 cases of primary pulmonary mucormycosis, although, from our criteria, some of these could be classified as disseminated mucormycosis. This leaves 39 patients with mucormycosis limited to the lungs, with a mean age of 44 years (range, 11⁄2-72 years). In his series, 24 patients were male and 10 female (5 were not specified), for a male-female ratio of 2.4:1. Hematologic conditions were the most frequent underlying disease, occurring in 18 (46%) of the 39 patients, and 17 of these had leukemia. Eleven patients (28%) were taking steroids, but 10 of these had an underlying hematologic condition. Nine patients (23%) had diabetes mellitus, 6 (15%) had sarcoma or carcinoma, and 4 (10%) had uremia. Only 4 (12%) of 32 patients for whom an outcome is reported were cured. The review by Tedder et al3 in 1994 combines 30 patients treated at their institution with 225 cases from the literature. Again, they do not restrict their review to pulmonary cases and include patients with disseminated disease.

We limited our review to patients with localized pulmonary mucormycosis because we thought that it represents a different disease in outcome and therapeutic options. This strengthens the conclusions that can be deduced from such a series, with the recognition, of course, that the retrospective nature of the study has unavoidable inherent limitations, including incomplete data and selection bias in the literature to report successes more than failures. To minimize the former, we limited our series to patients with sufficient data reported.

In all 3 reviews, the mean age is in the 40s, and the male-female ratio is between 2.4:1 and 3:1. This preponderance of male patients is difficult to explain, and none of the risk factors explain it. These remain the same over the years, except for the emergence of organ transplantation as a significant underlying predisposing disease. Diabetes mellitus and hematologic cancers continue to lead the list. The finding of 12 patients with no apparent underlying illness was unexpected because mucormycosis has been traditionally considered a disease of immunocompromised patients and suggests that a heightened level of suspicion may be warranted in immunocompetent patients as well. None of the patients in our series or that of Tedder et al3 had the acquired immunodeficiency syndrome. We found only 1 case report81 in the German-language literature of a patient who had diffuse infiltrates and whose condition was diagnosed at autopsy. Patients infected with the human immunodeficiency virus are at risk for infections with Aspergillus species, another angioinvasive fungal disease,82,83 but it is unclear why more cases of mucormycosis have not been reported. Whether this reflects that such patients are not at increased risk for this particular infection or simply that mucormycosis is less common than aspergillosis remains to be determined.

The association of mucormycosis with deferoxamine therapy and iron overload states is well recognized, and several such cases have been reported.84-90 Iron availability is critical for the growth of mucor, and when transferrin is saturated with iron and more free iron becomes available to the fungus, the fungistatic capacity of serum is decreased.91 To explain why deferoxamine, an iron chelator, paradoxically increases susceptibility to mucormycosis, it has been hypothesized that the fungus use deferoxamine as a siderophore. The iron chelate of deferoxamine abolishes the fungistatic effect of serum on Rhizopus species and increases the in vitro growth of the fungus, much more than iron alone and more than the effect on Aspergillus species.92 Part of the reason that acidosis increases the susceptibility of the host to mucormycosis may be by temporarily disrupting the capacity of transferrin to bind iron.93

Not surprisingly, the clinical presentation of pulmonary mucormycosis is not specific. The presence of hemoptysis should bring mucormycosis to mind because it is one of the angioinvasive fungi. The chronicity of the symptoms (>30 days) in no way helped rule out mucormycosis, and the duration of symptoms at the time of presentation should not be used to exclude pulmonary mucormycosis from the differential diagnosis in any patient. Similarly, none of the radiological findings were characteristic, although we found a predilection for the upper lobes, a finding not previously described on plain radiography. The presence of an air crescent sign is noteworthy and should increase the urgency of the workup because massive hemoptysis and death were more common in these patients. This sign appears to be a useful diagnostic clue for fungal infection, and aspergillosis and cryp-
Aspergillus infections, especially mucor and diagnosis of angioinvasive fungal infection appears to have some benefit in the di-
agnosis of aspergillosis, especially in patients with pulmonary mucormycosis and found a predilection for the upper lobes in 16 (84%) of 19 patients, in agreement with our findings. They also cite cavitation, air crescent sign, halo sign, and rim enhancement as radiological evidence of necrosis in these patients.

Noninvasive diagnosis with sputum cultures is difficult to achieve, and, in fact, even when culturing surgical specimens, false-negative culture results can be obtained. This may be due in part to sampling error when highly necrotic tissue is submitted for culture and no viable fungus is present or that the microbiology laboratory usually processes specimens for fungal culture after initially homogenizing the specimen. This dicing decreases the sensitivity of the sputum culture because this microorganism is aseptate and is killed by this process. This is an important concept and reinforces the high level of suspicion that one must have to notify the laboratory when submitting a specimen for appropriate processing. For that purpose, we summarize the various appearances of mucormycosis at bronchoscopy, in the hope of educating our pulmonary and surgical colleagues in that regard. Endobronchial features seen with mucormycosis may provide important clues for selecting the appropriate methods for specimen collection, preparation, and staining. Finally, the high incidence of obstruction may help explain the frequent occurrence of bacterial coinfection, likely due to postobstructive pneumonia.

Survival seems to have increased. Substantially more patients are now being diagnosed premortem, which may help explain the better outcome. In Baker's article, 12% (4/32) of the patients survived. In 1977, Murray noted in an editorial that only 6 (9%) of 70 patients with localized pulmonary involvement survived in the first 100 years since the disease was originally described. In our series, 44% of all patients (n = 38) survived, and if we exclude patients who died of unrelated causes, this percentage increases to 51% (38 of 75 patients). A premortem diagnosis was made in 62 (71%) of 87 patients. Of these, 38 patients (61%) survived, and, if we exclude deaths unrelated to mucormycosis, we come up with a survival rate of 72%. These figures compare favorably with the data by Tedder et al, where there was only a 35% survival in patients with disease confined to the lungs. In both series, renal failure portended a poor outcome, and neutropenia was clearly a predictor of death in our series. As noted by Tedder et al, although not as strikingly as in ours, the survival of patients treated only medically was much worse than for patients who underwent a surgical procedure. These observations have a great potential for bias because patients more fit for surgery and with a better possible outcome may well be the ones undergoing surgery. Despite this, the contrast between the group treated medically alone and the group treated surgically is impressive. Surgical resection is important in the treatment of pulmonary mucor because of the angiocentric nature of the fungus, with its propensity toward invading the pulmonary vascualture, often resulting in massive hemoptysis.

Pulmonary mucormycosis is a relatively rare disease, but with a growing number of immunosuppressed patients, it may become more common. Maintaining a high level of suspicion is important in any patient in the right clinical setting with a pneumatic process that fails to respond to antibacterial agents, either clinically or radiologically. In some patients, an apparent initial improvement is followed by recurrence of symptoms shortly after, maybe due to a transient response of a postobstructive bacterial pneumonitis secondary to endobronchial disease. These scenarios should heighten concerns about the possibility of a fungal infection. The diagnosis is rarely obtained by cultures because of processing in microbiology laboratories, and more aggressive bronchoscopic or surgical approaches should be pursued to obtain histopathologic specimens. The presence of an air crescent sign on radiological imaging often portends a poor prognosis if surgical therapy is delayed. We agree with recommendations that adequate treatment of pulmonary mucormycosis requires an aggressive approach, with a combination of both medical and surgical measures to effect a cure. Optimal therapy begins with an early diagnosis and, in addition to systemic antifungal therapy and surgical resection, control of the patient's underlying disease.

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