Paecilomyces Sinusitis in an Immunocompromised Adult Patient: Case Report and Review

R. Gucalp, P. Carlisle, P. Gialanella, S. Mitsudo, J. McKitrick, and J. Dutcher

From the Departments of Oncology, Microbiology, and Pathology. Montefiore Medical Center/Albert Einstein Cancer Center, Bronx, New York

A case of fungal sinusitis caused by *Paecilomyces lilacinus* that was unresponsive to amphotericin B and involved a patient with acute myeloid leukemia is described. Histologic examination of sinus tissue and periorbital bone demonstrated invasion by a fungus with septate hyphae, which was identified in culture as *P. lilacinus*. The isolate was resistant to amphotericin B but susceptible to itraconazole. The patient responded clinically when itraconazole was added to the treatment regimen. Invasive aspergillar infections are frequently diagnosed by histology. Other fungi such as *Fusarium, Pseudallescheria,* and *Paecilomyces* species also produce hyphae in tissue and can be confused with *Aspergillus* species. However, these pathogens may be resistant to amphotericin B. Since alternative therapy is now available for infections with some of the amphotericin B-resistant fungi, such as *P. lilacinus,* every effort should be made to recover the fungal pathogen so that effective treatment can be administered.

Most fungal sinusitis in immunosuppressed patients is caused by *Aspergillus* species. Unusual fungi such as *Fusarium* and *Penicillium* species have now emerged as significant pathogens. Recently, infections with *Paecilomyces* species in immunosuppressed patients have been reported [1–9]. Fungi such as *Fusarium, Pseudallescheria,* and *Paecilomyces* species also produce hyphae in tissue and can be confused with *Aspergillus* species. These pathogens may be resistant to amphotericin B. In this report, we describe a patient who had fungal sinusitis with *Paecilomyces lilacinus.*

Case Report

A 22-year-old female with acute myeloid leukemia presented because of a relapse. She received taxol, followed by doxorubicin and cytosine arabinoside, but this did not lead to remission. *Escherichia coli* bacteremia associated with neutropenia (WBC count, 900/mm³, with 6% granulocytes) developed on hospital day 9, and she was treated for 18 days with cefoperazone and gentamicin.

On hospital day 23, left facial pain, swelling, and toothache developed. Roentgenography of the paranasal sinuses revealed complete opacification of the left maxillary sinus. A CT scan confirmed opacification of the left maxillary sinus, with involvement of the ethmoid, frontal, and sphenoид sinuses (figure 1a). A roentgenogram of the chest did not show any abnormalities.

Therapy with amphotericin B (1 mg/[kg·d]) was initiated for presumed aspergillar sinusitis; however, the left facial swelling progressed, involving the periorbital area with chemosis of the left eye. Administration of granulocyte-macrophage colony-stimulating factor (250 µg/m²) was initiated on hospital day 32. She underwent a Caldwell-Luc procedure the next day.

Histology showed multiple fragments of respiratory mucosa, partially necrotic and hemorrhagic, with diffuse invasion by fungi characterized by branching septate. Small fragments of cortical bone also revealed fungal hyphae (diagnosed as *Aspergillus* species) in haversian canals. Fungal culture isolates, however, were identified as *Paecilomyces* species (figure 1d) several days later.

Repeated CT scanning of the paranasal sinuses showed an air-fluid level within the left maxillary sinus and increased soft-tissue density in the premaxillary space, which was enhancing and extended to the medial orbit, causing lateral deviation of the left eye (figure 1b). Despite surgical debridement on day 44 and treatment with amphotericin B, the orbital infection progressed and diplopia developed.

Her right-upper molar loosened and whitish mucosa formed over the gingiva and palate of the anterior maxilla, with dehiscence of the mucosal incision (figure 1c). Repeated fungal culture yielded *Candida albicans,* while histologic specimens still showed fragments of necrotic tissue completely invaded by a branching septate fungus. Fluconazole was added to the regimen after 23 days of therapy with amphotericin B.

Fungal pathogens were typed as *P. lilacinus* in the Fungus Testing Laboratory at the University of Texas Health Sciences Center, in San Antonio. Fungal susceptibility testing was performed according to protocol [10]. The 48-hour MICs of amphotericin B and fluconazole were 4.62 µg/mL and 64 µg/mL, respectively. The minimum lethal concentration (MLC) of fluconazole was >64 µg/mL. The 48-hour MIC of itraconazole was 0.5 µg/mL, and the MLC was 4 µg/mL.
Figure 1. Images of a female with acute myeloid leukemia and paecilomyces sinusitis: a, nodular appearance of mucosa in the maxillary sinus (large arrow), extension of disease into the nasal cavity with areas of bony sequestration (arrowhead), and extension into the surrounding soft tissues (small arrow); b, extension into the orbit (small arrowhead) and ethmoid bone, with probable bone destruction of posterior ethmoid cells (large arrowhead), and the sphenoid sinus (arrow); c, Erosion of the hard palate; and d, Grocott-Gomori methenamine-silver nitrate stain of septate hyphae, with acute angle branching, of Paecilomyces (original magnification, ×400).

Flucytosine was withdrawn on hospital day 50, and itraconazole (400 mg/d) was added to the amphotericin B regimen, after which the facial swelling diminished. The WBC count was 1,900/mm³ (with 85% neutrophils) on hospital day 48. She became neutropenic after further chemotherapy (500 WBCs/mm³, with 10% granulocytes) on hospital day 58, and she remained neutropenic thereafter.

As the infection progressed, the serum bilirubin and alkaline phosphatase levels increased (peaks, 18.5 mg/dL and 467 U/L, respectively). An abdominal sonogram revealed hepatomegaly without a focal defect. A liver biopsy during a previous admission had shown a moderate amount of hemosiderin pigment deposited in Kupffer’s cells and hepatocytes, as well as reactive changes in hepatocytes. After the second surgery, the bilirubin level slowly returned to normal. Unfortunately, the patient’s course was further complicated by varicellar infection and leukemic meningitis. She died of leukemia on hospital day 112.

At the time of death she had no symptoms related to the fungal infection. Autopsy was not permitted.

Discussion

Paecilomyces infections in immunocompromised patients have been reported sporadically. Most of these cases were localized infections and were cured with treatment (table 1). Despite prolonged neutropenia and initial inappropriate therapy, our patient’s survival was prolonged because of the low pathogenicity of the fungus. The only reported fatal case of paecilomyces infection involved a patient with acute lymphocytic leukemia [5]. In that patient, the infection began as a cutaneous infection with P. lilacinus and appeared to disseminate to the lungs; bronchoscopy did not lead to pathological or microbiological confirmation of paecilomyces pneumonia, and autopsy was not permitted.
Aspergillus is the most common cause of fungal sinusitis in cancer patients, but fungal pathogens such as Alternaria and Paecilomyces species are emerging. In tissue section the branching septate hyphae of Paecilomyces resemble those of Aspergillus (figure 1d). When Paecilomyces is recovered as a pathogen, the species should be determined. Paecilomyces varioti forms fast-growing, velvety colonies on agar that are buff-colored to olive-brown. Colonies of P. lilacinus are lavender, pink, and vinaceous. P. lilacinus and Paecilomyces marquandii are highly resistant to amphotericin B and flucytosine, while P. varioti appears universally susceptible to these agents [9]. P. lilacinus is susceptible to imidazoles. Evidence of clinical correlation with in vitro antifungal susceptibility tests is limited, but paecilomyces sinusitis in our case was also clinically resistant to amphotericin B and diminished after the addition of itraconazole to the treatment regimen. The use of itraconazole as initial antifungal treatment for paecilomyces infections has not been reported.

We have described a case of P. lilacinus sinusitis in a patient with acute myeloid leukemia in which surgical debridement and therapy guided by fungal susceptibility testing were effective despite persistent neutropenia. New fungal pathogens such as Pseudallescheria boydii and P. lilacinus may be resistant to amphotericin B while demonstrating in vivo and in vitro susceptibility to other antifungals. A histologic diagnosis of invasive fungal infection is no longer sufficient to guide therapy. Every effort should be made to identify the species of the putative fungal pathogen so that the appropriate antifungal agent can be prescribed.

### Table 1. Data from cases of paecilomyces infection involving immunocompromised hosts.

<table>
<thead>
<tr>
<th>Year [Reference]</th>
<th>Predisposing factor(s)</th>
<th>Source of isolate</th>
<th>Pathogenic Paecilomyces species</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979 [1]</td>
<td>Renal transplantation, corticosteroid therapy</td>
<td>Skin</td>
<td>marquandii</td>
<td>Mic</td>
<td>Cure</td>
</tr>
<tr>
<td>1984 [2]</td>
<td>Lymphoma, penetrating keratoplasty</td>
<td>Cornea (keratitis)</td>
<td>lilacinus</td>
<td>Mic</td>
<td>Cure</td>
</tr>
<tr>
<td>1986 [4]</td>
<td>Chronic lymphocytic leukemia, corticosteroid therapy</td>
<td>Skin</td>
<td>lilacinus</td>
<td>AmB, 5-FC</td>
<td>Progression, then cure</td>
</tr>
<tr>
<td>1990 [6]</td>
<td>Renal transplantation, therapy with corticosteroid + azathioprine</td>
<td>Skin</td>
<td>lilacinus</td>
<td>GR</td>
<td>Cure</td>
</tr>
<tr>
<td>1992 [7]</td>
<td>Chronic granulomatous disease</td>
<td>Skin</td>
<td>lilacinus</td>
<td>AmB</td>
<td>Cure</td>
</tr>
<tr>
<td>1992 [9]</td>
<td>Chronic granulomatous disease</td>
<td>Skin</td>
<td>varioti</td>
<td>AmB + Itr</td>
<td>Cure</td>
</tr>
<tr>
<td>1994 [PR]</td>
<td>Acute myeloid leukemia, prolonged neutropenia</td>
<td>Paranasal sinus</td>
<td>lilacinus</td>
<td>AmB + Itr</td>
<td>Progression, then cure</td>
</tr>
</tbody>
</table>

**NOTE.** AmB = amphotericin B; 5-FC = 5-fluorocytosine; GR = griseofulvin; Itr = itraconazole; Mic = miconazole; PR = present report.

References