Progressive Cutaneous Hyalohyphomycosis Due to *Paecilomyces lilacinus*: Rapid Response to Treatment with Caspofungin and Itraconazole

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A case of rapidly progressive cutaneous infection due to *Paecilomyces lilacinus* developed in a woman with advanced pancreatic cancer who did not have granulocytopenia. The infection responded favorably to caspofungin and itraconazole combination therapy.

*Paecilomyces lilacinus* is an emerging opportunistic pathogen in humans [1–3]. In patients with intact immunity, *Paecilomyces* organisms occasionally cause localized infection related to penetrating trauma or implantation of surgical prosthetic devices, such as a prosthetic heart valves, intraocular lenses, and peritoneal catheters for dialysis [4, 5]. In patients who are immunocompromised, *Paecilomyces* organisms sometimes cause extensive infection, especially of the skin [2, 3, 6]. Erythematous macules, vesicles, pustules, and refractory nodular lesions are among the variable clinical manifestations of such infection [2, 3]. A case of rapidly progressive cutaneous *P. lilacinus* infection that responded to combination antifungal therapy is presented.

A 64-year-old diabetic woman with metastatic adenocarcinoma of the pancreas developed a cluster of painful red nodules over the distal right lower extremity. During a 2-week period, this cluster evolved into excoriated nodules and draining pustular lesions. Six months before the cluster of nodules developed, the patient had received induction therapy with gemcitabine, 1000 mg/m^2 weekly, which was discontinued after chemotherapy-related acute hemolytic uremic syndrome and azotemia developed. In the months before presentation, the patient had required hospitalization for exacerbation of bronchial asthma, and she had followed a regimen of high-dose corticosteroid therapy that included methylprednisolone, 80 mg q6h for 5 days, followed by prednisone, 30 mg q.d. initially but then reduced to 20 mg q.d. (the dosage at the time of presentation).

Physical examination revealed, over an extensive area of the right lower leg, excoriated pustules and tender nodules overlying an erythematous and indurated base. An isolated cluster of subcutaneous nodules was also present on the right anterior-medial midthigh. Severe onychomycosis (i.e., tinea unguium) was observed on both feet.

Laboratory studies revealed the following findings: WBC count, 10,800 cells/µL; platelet count, 178,000 platelets/µL; blood urea nitrogen, 68 mg/dL; creatinine, 3.3 mg/dL; glucose, 75 mg/dL; lactic dehydrogenase, 389 U/L; aspartate aminotransferase, 46 U/L; and erythrocyte sedimentation rate, 16 mm/h. No acute pulmonary process was noted on a CT scan. Blood cultures were found to be sterile. Prominent growth of *P. lilacinus* (5–10 cfu) occurred on samples obtained from 4 lesions on the lower leg.

Antifungal susceptibilities (MIC values) were determined at The University of Texas Health Science Center at San Antonio, according to the guidelines of the National Committee for Clinical Laboratory Standards [7]. The MIC values determined at 2 intervals (at 48 and 72 h after incubation, respectively) were as follows: for amphotericin B, 16.0 and 16.0 µg/mL; for ketoconazole, 1.0 and 1.0 µg/mL; for itraconazole, 1.0 and 4.0 µg/mL; for voriconazole/UK-109,496, 0.25 and 0.25 µg/mL; for posaconazole/SCH-56592, 0.125 and 0.125 µg/mL; for ravuconazole/BMS-207147, 0.5 and 1.0 µg/mL; and for caspofungin/MK-0991, 1.0 and 4.0 µg/mL.

Initial treatment consisted of oral itraconazole, 600 mg q.d. for 3 days, followed by 400 mg q.d. (maintenance dose). Seven days after treatment with itraconazole commenced, caspofungin, 70 mg on the first day and then 50 mg q.d. thereafter [8–10], was added to the regimen because of the lack of clinical response, as was demonstrated by the development of new lesions. During the week after caspofungin was added to oral itraconazole therapy, no new lesions were noted, and the nodules on the midthigh disappeared. The excoriated nodules on the lower leg resolved, although pustular eruptions persisted (figure 1, left). A complete resolution of the *P. lilacinus* infection was observed after 4 weeks of therapy (figure 1, right). Treatment...
was continued for ~3 months, and there were no significant side effects of combined therapy.

Since 1977 [11], nearly 25 cases of cutaneous infection due to Paecilomyces species have been reported [2, 3]. The source of such cutaneous infection may be the contamination of implantable or semi-implantable surgical prosthetic devices with these ubiquitous molds. A recent outbreak of nosocomial cutaneous Paecilomyces lilacinus infection in highly compromised individuals was traced to a contaminated topical moisturizing agent [2]. In the present report, the long-standing onychomycosis probably served as the reservoir and the portal of entry for the rapidly progressive infection. Involvement of the adjoining tissue occurs through the contiguous spread of the infection, although local dissemination of infection by the lymphatic system has also been noticed [12] and may be responsible for an isolated cluster of nodules on the proximal ipsilateral leg of this patient.

P. lilacinus, unlike Paecilomyces variotii, often shows variable resistance to amphotericin B, flucytosine, and the triazole-based drugs [2, 3, 13, 14]. In most cases, treatment is extremely difficult, and the in vitro susceptibility of P. lilacinus to currently available alternative agents, such as itraconazole and caspofungin, is uncertain [3, 14]. Treatment with ketoconazole and/or terbinafine has produced a durable response in patients with disease that is refractory to amphotericin B [2–5]. For the patient described in the present report, the in vitro susceptibility of P. lilacinus to the upcoming new generation of broad-spectrum triazoles (e.g., voriconazole/UK-109,496, posaconazole/SCH-56592, and ravuconazole/BMS-207147) was excellent. Voriconazole/UK-109,496 recently has been shown to have fungicidal activity against P. lilacinus, a finding that is in contrast to the fungistatic effect of amphotericin B and itraconazole [13]. The limited clinical experience with voriconazole/UK-109,496 in such cases has been promising [15]. In the patient described here, the response to itraconazole and caspofungin therapy was rapid resolution of progressive cutaneous and subcutaneous P. lilacinus infection, and combined antifungal therapy was well tolerated. At present, appropriate treatment for invasive, life-threatening infections due to yeasts and/or dermatophyte molds that are not susceptible to amphotericin B...
is uncertain. As clinical validation of future treatment options, including the next generation of broad-spectrum triazoles and pneumocandin/echinocandins, becomes available, combination antifungal therapy [16, 17] may evolve into a suitable treatment option for patients with severe invasive mycosis.

References