A Case Report of a Dactylaria Fungal Infection in a Lung Transplant Patient*

Joseph E. Mazur, PharmD, and Marc A. Judson, MD, FCCP

Dematiaceous fungi such as Dactylaria gallopava are becoming more prevalent in transplant patients, with 50% of outcomes being fatal. In this report, we describe a 32-year-old woman who presented with swelling in the right shoulder area and right lateral neck. On further investigation with a CT scan, a fluid collection in the shoulder was identified, drained, and subsequently grew D. gallopava. We report the successful treatment of an invasive Dactylaria infection in a lung transplant patient predominantly by medical chemotherapy, although surgical incision and drainage was performed on one of the fungal lesions.

**Key words:** amphotericin B; Dactylaria; immunosuppression; itraconazole; lung transplantation

The heterogeneous group of dematiaceous fungi contribute significantly to the morbidity and mortality of solid-organ transplant recipients. Although Candida and Aspergillus species remain the most prevalent fungi affecting these patients, dematiaceous fungi are becoming common pathogens. *Dactylaria gallopava* is one such dematiaceous fungus reported in solid-organ transplant recipients. Dactylaria infections are known to be fatal in approximately 50% of cases, yet there are no standardized treatments for these fungi. We report successful treatment of an invasive Dactylaria infection in a lung transplant patient.

**CASE REPORT**

A 32-year-old white woman was hospitalized with a chief complaint of swelling in the right shoulder and right lateral neck. Her medical history was significant for a right single-lung transplant in 1994 secondary to bronchiolitis obliterans due to rheumatoid arthritis. Medications on admission included tacrolimus, 2 mg bid; prednisone, 15 mg qd; and azathioprine, 100 mg qd. Her most recent tacrolimus whole blood level was 10.4 ng/mL. A CT scan done after admission (Fig 1) revealed a large fluid collection (8 × 4 × 6 cm) in the right shoulder with extension into the apical region of her transplanted lung. Lesions were also detected in the left and right lateral neck.

CT-guided drainage of the right-shoulder collection initially revealed fungal elements. The patient was subsequently started on amphotericin cholesteryl sulfate. On the following day, surgical exploration of the right shoulder was performed with drainage of purulent fluid and removal of necrotic debris. Cultures from the fluid collection grew *D. gallopava*. Fluconazole, 1,500 mg po tid, was added to the regimen. Because of the propensity of this mold to seed other anatomic areas, MRI imaging of the head showed enhancing lesions in the right frontal and parietal areas. The patient complained of severe bilateral neck and shoulder pain for the first week of hospitalization and required patient-controlled analgesia.

Cultures were sent to the Fungus Testing Laboratory at the University of Texas Health Science Center for identification and susceptibility testing (Table 1). On the basis of these results, fluconazole was discontinued after 14 days of therapy, and itraconazole oral solution in cyclodextrin was begun at the standard loading dose of 200 mg po tid for 3 days, which was lowered to the maintenance dose of 200 mg bid. Lipid-based amphotericin B preparations were used for a total of 22 days. A total of 7,540 mg of amphotericin cholesteryl sulfate preparation was given over 19 days and was replaced for administrative reasons with amphotericin liposome for injection for 3 more days, with 1,005 mg being administered.

On hospital discharge approximately 1 month after admission, the patient’s subjective symptoms and pain had resolved. Follow-up CT scans of the neck and shoulder (Fig 2) showed marked improvement. The patient was discharged on itraconazole oral solution, 200 mg bid, and an itraconazole serum level obtained at that time was 2.31 g/mL. In addition, her immunosuppressive medication dosages were reduced to tacrolimus, 1 mg po every other day, and prednisone, 10 mg po qd. Six months later, a repeat itraconazole level was 0.53 g/mL. The patient is alive and well 21 months after admission. An MRI scan, performed 4 months after admission, showed nearly complete resolution of the brain lesions. A CT performed 12 months after admission revealed resolution of the neck lesions and residual scarring in the right lung apex.

**DISCUSSION**

Because of the rarity of dematiaceous fungal infections in immunocompromised hosts, few outcome data have been collected concerning the efficacy of treatment. The use of itraconazole has been well demonstrated in treatment of mycotic systemic infections such as phaeohyphomycosis. The use of amphotericin B colloidal dispersion and itraconazole has been successful in treatment of cerebral phaeohyphomycosis caused by *D. gallopava* in a liver transplant recipient. To our knowledge, there have been no published cases of a lung transplant recipient surviving an infection with *D. gallopava* that was cured without complete excision of fungal lesions. Although surgical drainage of the right shoulder and neck was performed, there was extensive residual disease in the left neck and the left lung apex that responded to chemotherapy alone. This is first lung transplant recipient to acquire this infection in which medical chemotherapy was effective in the treatment of several of these fungal lesions. Although chemotherapy alone cannot be routinely recommended for the treatment of an abscess, the fact that the abscess at the lung apex responded to chemotherapy without surgical incision and drainage suggests chemotherapy alone may have been effective in this case.

Dematiaceous fungal infections are often indolent and develop late after transplantation, with a median time to onset being 22 months after surgery. Our patient’s symptoms began 44 months after transplantation. Two patterns of infections occur that are characterized by either soft-tissue or systemic involvement.

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Our patient had predominantly soft-tissue disease, although two small brain lesions seen on MRI were assumed to be caused by *D. gallopava*. Mortality is high, ranging from 7 to 57%, depending on dissemination.²

Treatment of systemic phaeohyphomycosis (including dactylariosis) is thought to require surgical resection followed by systemic amphotericin B therapy, itraconazole, or flucytosine treatment. Because there are no data in lung transplant patients, the use of these agents is extrapolated from treatment of cerebral²³⁴ and pulmonary phaeohyphomycosis,⁵⁶ where amphotericin B served as first-line therapy, followed by either itraconazole or flucytosine. Our case suggests that properly selected antifungal agents in certain patients may be effective without surgery. Patients who may be good candidates for chemotherapy alone depend on various characteristics, such as anatomic location of the dactylariosis, previous prophylactic antifungals, knowledge of susceptibility of fungi to antifungal agents, and the pharmacokinetics/pharmacodynamics of the antifungal treatments that are used. If infection with dactylariosis is confined to the skin and/or soft-tissue and systemic involvement is not suspected, antifungal therapy should be considered for a trial period. The development of dactylariosis while receiving itraconazole prophylaxis suggests that the fungus is resistant to azoles or is protected from penetration by antifungal chemother-

apy, and amphotericin B therapy or surgical resection should be considered in these cases. Itraconazole oral solution⁸ and the new liposomal amphotericin B preparations (amphotericin B liposomal complex, amphotericin B cholesteryl sulfate complex, and amphotericin B liposome) offer theoretical advantages of increased bioavailability, higher area under the curves after standardized dosing, and possibly higher tissue concentrations.⁹¹⁰ This may result in greater activity and better efficacy against superficial mycoses. Itraconazole oral capsules and traditional amphotericin B deoxycholate have not been compared to the newer preparations in case series, and it may be advantageous to consider these newer agents as first-line treatment prior to considering surgical resection.

There are various reasons why our patient may have been treated successfully with medical therapy. First, the patient

### Table 1—Results of Antifungal Susceptibility Testing From the University of Texas Health Science Center at San Antonio

<table>
<thead>
<tr>
<th>Drugs</th>
<th>MIC, μg/mL</th>
<th>24 h</th>
<th>48 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>0.25</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>5-Flucytosine</td>
<td>2</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td>0.06</td>
<td>0.125</td>
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*MIC = minimum inhibitory concentration.*

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**Figure 1.** Chest CT scan of the patient at the level of the lung apices. A large necrotic area (double arrows) is seen in the right soft tissues at the base of the neck. This necrotic process extended into the right lung apex (single arrow).

**Figure 2.** Follow-up chest CT scan shows complete resolution of neck and lung lesions, at a level similar to that in Figure 1 (top), and residual right upper lobe scarring at a higher level (bottom).
had primarily soft-tissue involvement. She did have two small brain lesions, but did not have evidence of extensive disseminated disease. Second, an aggressive chemotherapy regimen was combined with a reduction in the immunosuppressive regimen, which may have added to antifungal efficacy.

Obtaining itraconazole serum or plasma concentrations has been recommended to: (1) avoid potential drug interactions, (2) determine adequate clinical response, (3) assess compliance, and (4) determine GI absorption.9 Recommended concentrations of itraconazole based on high-performance liquid chromatography should be in a detectable concentration (reference ranges of 0.1 to 2.2 g/mL; Specialty Laboratories; Santa Monica, CA).

In summary, this case describes the successful treatment of *D gallopava* in a lung transplant patient without complete surgical excision of the fungal lesions. It is possible that the surgical incision and drainage of the right shoulder lesion were required for cure of this patient, but clearly multiple other lesions, including a lung abscess, were successfully treated with chemotherapy. We believe that successful treatment was related, in part, to combination chemotherapy, drug susceptibility testing, and reduction of immunosuppression. Itraconazole has been shown to penetrate the CNS poorly11; therefore, obtaining itraconazole levels may be helpful in adjusting doses.12 The itraconazole solution in cyclodextrin (used in this case) has better absorption and relative bioavailability in either a postprandial or fasting state as compared with the similar dose of oral capsules that may improve efficacy.11 The advent of liposomal amphotericin B preparations has resulted in a class of agents that achieve higher serum and tissue concentrations, with presumably fewer side effects.13 The use of drug susceptibility testing definitely aided the clinician’s choice of antifungal agents in this case.

References
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**Benign Mediastinal Lymphadenopathy in Congestive Heart Failure**

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We report three cases of benign mediastinal lymphadenopathy revealed by chest radiography in patients ranging in age from 61 to 75 years. All three patients had severe coronary heart disease and a history of several episodes of acute cardiac decompensation. Chest CT scanning contributed to the diagnosis by revealing the existence of multiple enlarged lymph nodes, mostly 10 to 17 mm in short-axis diameter. CT scanning also confirmed the disappearance of the mediastinal lymph nodes in one patient on follow-up after treatment with diuretics and digitalis. Histopathology investigations of biopsy samples obtained by mediastinoscopy consistently revealed noninflammatory, benign lesions that did not affect the node structure. Our report draws attention to the particular nosology of left heart disease represented by benign enlarged lymph nodes of the mediastinum and pulmonary edema. The diagnostic approach to such lymphadenopathy should be guided by the radiologic regression seen on follow-up CT scanning while the patient was undergoing appropriate therapy for congestive heart failure, which constitutes a decisive argument for the congestive heart failure origin.

*(CHEST 2001; 119:653–656)*

**Key words**: left heart failure; mediastinal lymph node

**Abbreviation**: SaO2 = arterial oxygen saturation

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Manuscript received December 16, 1999; revision accepted July 11, 2000.

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