

Fungal Discitis Due to *Aspergillus terreus* in a Patient with Acute Lymphoblastic Leukemia

We report a case of *Aspergillus terreus* discitis which developed in a patient with acute lymphoblastic leukemia following induction chemotherapy. *A. terreus* was isolated from sputum, one month earlier, but the physician did not consider it significant at the time. Magnetic resonance imaging study showed the involvement of L3-4, L4-5 and L5-S1 intervertebral discs. Etiology was established by means of histology and culturing a surgical specimen of disc materials. Our patient survived after a surgical debridement and amphotericin B administration with a total dose of 2.0 g. Discitis caused by *Aspergillus terreus* is a very rare event. *A. terreus* is one of the invasive *Aspergillus* species. The pathogenetic mechanism is discussed and the literature is reviewed.

Key Words: *Aspergillus*; Discitis; Aspergillosis; Immunocompromised Host

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INTRODUCTION

As the number of immunocompromised patients increases, there has been a concomitant increase in patient morbidity and mortality due to fungi. The etiologic microorganisms vary depending on the type of immune dysfunction. Patients with malignancies and chemotherapy-induced neutropenia are commonly infected with *Candida* and *Aspergillus* (1).

The *Aspergillus* species consists of widespread molds, which causes systemic disease only in immunocompromised hosts. More than 200 species of *Aspergillus* are known, but only a few are considered to be pathogenic to humans. *Aspergillus fumigatus* and *Aspergillus flavus* are the most frequently isolated species. *Aspergillus terreus* is ubiquitous in the environment, but has rarely been found to be pathogenic. Invasive infection with *A. terreus* is a rare disease, and bone and joint infection with *A. terreus* is even rarer (2).

We report a case of fungal discitis caused by *A. terreus* in a patient with acute lymphoblastic leukemia following induction chemotherapy, and a review of the literature. To our knowledge, a review of the literature revealed only two previous cases (3,4) of vertebral osteomyelitis due to *A. terreus* in humans.

CASE REPORT

A 37-year-old man was admitted in November 1998

with fluctuating fever, nonproductive cough, and headache. Physical examination confirmed non-tender hepatomegaly. Chest radiograph revealed right lower lobe haziness, but no organisms were cultured from several sputum or blood specimens. Routine complete blood count (CBC) disclosed severe anemia (hemoglobin, 6.3 g/dL), slightly decreased leukocyte counts (3,700/ μ L), and normal platelet counts (161,000/ μ L). A differential blood count showed 80% lymphoblastic cells. A bone marrow aspirate was hypercellular with 98.0% of the lymphoblasts negative for peroxidase staining. The case was diagnosed as acute lymphoblastic leukemia (ALL, L1). Chemotherapy was initiated, and complete remission was achieved in December 1998. Apart from an episode of Staphylococcal pneumonia, the chemotherapy was well tolerated. Chest radiograph showed staphylococcal pneumatocele, and *Staphylococcus aureus* were cultured from sputum specimens. Cefprozil and vancomycin were administered. At the end of December 1998, *Aspergillus terreus* was isolated from the sputum of the patient. At the time, the physician did not consider the significance of isolating of *A. terreus* from sputum.

Although the patient achieved complete remission, he complained of severe lower back pain in January 1999. He had no neurologic deficits. A bone scan revealed a faint uptake around the sacroiliac joint. Magnetic resonance imaging (MRI) of the lumbar spine showed changes in the intervertebral discs and vertebrae at levels L3-4, L4-5, and L5-S1, consistent with discitis (Fig. 1).

On February 1, surgical debridement and fusion with



Fig. 1. Infectious discitis at levels L3-4, L4-5, and L5-S1, extended to the vertebral body end plates (T1-weighted sagittal magnetic resonance image).

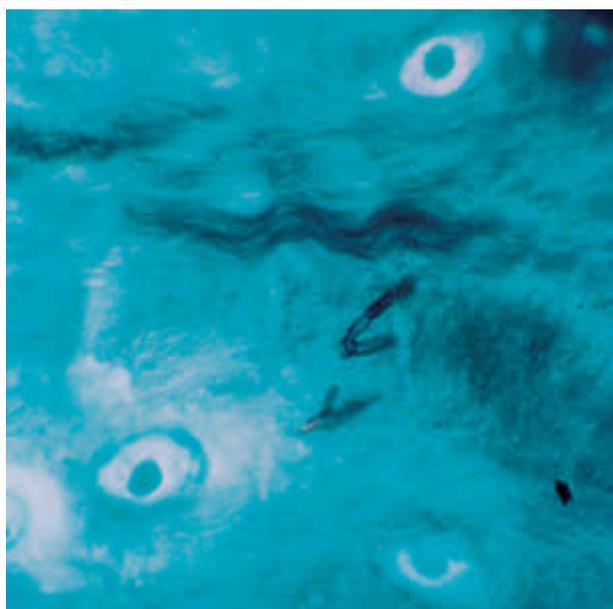


Fig. 2. Dichotomously branched septated hyphae in the disc materials, consistent with *Aspergillus* species (Gomori methenamine silver stain, $\times 400$).

iliac bone graft was performed. Histopathological findings, using periodic acid-Schiff stain and Gomori methenamine silver stain (Fig. 2), revealed dichotomously branched septated hyphae in the disc materials, which was consistent with the *Aspergillus* species and confirmed the diagnosis of fungal discitis. The disc materials were inoculated on blood agar, MacConkey agar, and Sabouraud's dextrose agar. After inoculation, blood agar

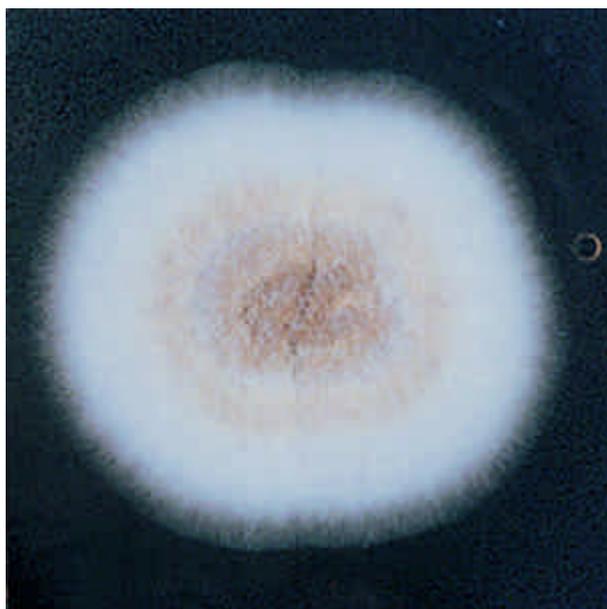


Fig. 3. Cinnamon-brown colonies with granular to velvety textures on Sabouraud's dextrose agar, consistent with *Aspergillus terreus*.

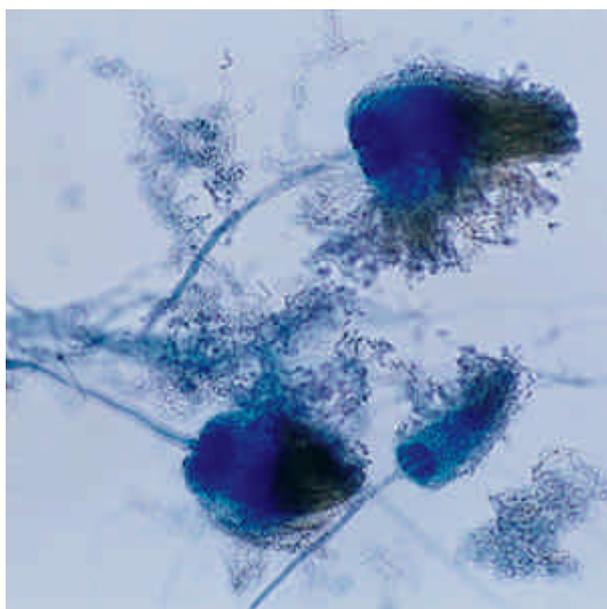


Fig. 4. Long slender conidiophores, as well as elliptical conidia with biserial phialides, consistent with *Aspergillus terreus* (lactophenol blue stain, $\times 200$).

and MacConkey agar were incubated at 35°C in a 5% CO₂ incubator, and Sabouraud's dextrose agar was incubated at 30°C in a CO₂-free incubator. A culture of the disc materials on Sabouraud's dextrose agar yielded *Aspergillus*, and the fungus was further identified as *Aspergillus terreus*. No other organisms were cultured from the disc materials. Cinnamon-brown colonies with granular to velvety textures were observed on the Sabouraud's

dextrose agar after four days of incubation (Fig. 3). Microscopically, the colonies showed long slender conidiophores, as well as elliptical conidia with biseriata phialides (Fig. 4). No fungi were cultured from several sputum or blood specimens, with the exception of *Aspergillus terreus* that had been isolated from the sputum of the patient at the end of December 1998. The patient was treated with amphotericin B intravenously with a total dose of 2.0 g. He has remained asymptomatic and without signs of infection.

DISCUSSION

The *Aspergillus* species is the most common cause of invasive mold infection in immunocompromised hosts (2). The lung is the usual portal of entry, and is the organ mostly invaded. Primary infection of extrapulmonary sites most commonly affects the skin or paranasal sinuses (2). Aspergillar bone and joint infection is rare (5). Lumbar involvement is the main area of manifestation, followed by the tibia, ribs, wrist, sternum, pelvis and knee (6). These are usually secondary sites to pulmonary aspergillosis.

Invasive aspergillosis is most often caused by *A. fumigatus* and *A. flavus*. Invasive infection with *A. terreus* is very rare (2). *A. terreus* is usually a saprophyte, but the discovery of this organism in the vertebral discs should be considered pathogenic, particularly in immunocompromised hosts.

We present here a case of fungal discitis caused by *A. terreus* in a patient with acute lymphoblastic leukemia following induction chemotherapy. To our knowledge, only two cases (3, 4) of vertebral osteomyelitis due to *A. terreus* have been reported previously in humans. The clinical features of the cases reported in the literature are summarized in Table 1. In the report by Seligsohn *et al.* (3), the portal of entry of the organism was unclear, but the authors noted that the infection was probably

hematogenous in origin, and that the introduction of the organism into the blood stream may have resulted from intravenous drug abuse. According to Glotzbach (4), the exact origin of the *A. terreus* infection was also unclear. However, the prolonged febrile hospital course which followed the initial aortofemoral bypass surgery, and the localized nature of the infection, made it very likely that the organism had been acquired at the time of initial surgery.

Our patient presented with a case of localized, invasive aspergillosis. The infection was limited to the lumbar discs. Our case appears to be primary discitis with extension to the vertebral bodies. The source of the infection is unclear. There was no prior history of back pain or lumbar surgery, and the localization of the infection in the lumbar spine strongly suggests that the discitis was hematogenous in origin. Our patient showed no clinical evidence of pulmonary aspergillosis, with the exception of the *A. terreus* isolated from the sputum at the end of December 1998. However, we believe that hematogenous infection of the lumbar discs with *A. terreus* may have resulted from a primary pulmonary involvement with the fungus. Disseminated aspergillosis resulting from an asymptomatic and radiographically occult primary *Aspergillus* focus in the lung has been previously described (7).

Invasive aspergillosis is a life-threatening fungal infection which is associated with a high mortality rate despite treatment. Lass-Flörl *et al.* (8) obtained *Aspergillus* species from 29 patients with hematological diseases, the outcome of *Aspergillus* infection depended on the *in vitro* susceptibility of the isolates to amphotericin B. Survival was poor in patients with isolates resistant to amphotericin B, and good in those with amphotericin B-susceptible specimens. *A. terreus* has been associated with a high resistance to amphotericin B and with poor survival.

Aspergillus species infections of the spine have been reported infrequently (9-12). In most cases reviewed in

Table 1. Reported cases of *Aspergillus terreus* infection of the spine

	Seligsohn <i>et al.</i> (3)	Glotzbach (4)	The present case
Age (yr) / Sex	42/F	71/M	37/M
Underlying condition	Cirrhosis and IV drug abuse	Pseudoaneurysm of aortofemoral vascular graft	Acute lymphoblastic leukemia, L1
Site of infection	L1-2 vertebrae and disc space	L2-3 vertebrae and disc space	L3-4, L4-5, and L5-S intervertebral discs
Means of diagnosis	Open biopsy material	Open biopsy material	Surgical specimen of the disc materials
Treatment	Amphotericin B, total 3.0 g	Amphotericin B	Surgical debridement and Amphotericin B, total 2.0 g
Course	Survived	Died	Survived

the literature, combined surgical and medical treatment was necessary to cure the infection. Hummel et al. (6) recommended a combined surgical and medical approach, which enabled quick pain relief for the patient, histologic and microbiologic diagnosis, and stabilization of the spine. In our patient, early surgery with vigorous surgical debridement along with antifungal treatment seems to have yielded a good outcome.

In summary, a case of *Aspergillus terreus* discitis in a patient with acute lymphoblastic leukemia is described in detail. This case illustrates the variability of possible presentations of aspergillosis and the difficulties in diagnosing this infection in immunocompromised patients. A combined surgical and medical approach seems necessary to cure this infection.

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