Successful Therapy for Cerebral Phaeohyphomycosis Due to *Dactylaria gallopava* in a Liver Transplant Recipient

Rade B. Vukmir, Shimon Kusne, Peter Linden, William Pasculle, Annette W. Fothergill, John Sheaffer, Jose Nieto, Ricardo Segal, Hadar Merhav, A. Julio Martinez, and Michael G. Rinaldi

From the Departments of Anesthesiology and Critical Care Medicine, Infectious Diseases, Neurological Surgery, Pathology, and Surgery and the Clinical Microbiology Laboratory, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; and the University of Texas Health Science Center at San Antonio, San Antonio, Texas

A 68-year-old liver transplant recipient who was being treated with FK 506 and immunosuppressive steroid therapy was admitted to our medical center because of a tonic-clonic seizure. Computed tomography of the head revealed multiple discrete cerebral abscesses, and culture of fluid drained intraoperatively yielded a dematiaceous fungus. The isolate was susceptible to amphotericin B and itraconazole but was resistant to flucytosine and fluconazole. The patient was successfully treated with a prolonged course of amphotericin B colloidal dispersion and itraconazole, as evidenced by both clinical and radiographic resolution of disease over a 2-year follow-up.

Dactylaria constricta variety *gallopava* sensu Georg et al. is a thermophilic dematiaceous hyphomycete (this organism is also known as *D. gallopava*) [1]. Recently, this fungus has undergone taxonomic evaluation by several investigators and has been reclassified as *D. constricta* variety *gallopava* sensu Dixon and Salkin [2] and *Ochroconis gallopavum* sensu Cannon [3]. It has been isolated from heated environments (30°C–70°C) and acidic environments (pH, 2–6) [4] including thermal-spring and nuclear-reactor effluents, self-heated waste piles, thermal soils, and chicken litter [5, 6]. The fungus has caused neurological infections, such as encephalitis and brain abscesses, in young captive or domesticated birds, including turkey poults, chickens, owls, and gray trumpeter swans [1, 7, 8]. To our knowledge, only three cases of *D. gallopava* infection in humans have been reported previously [9–11]. We describe a liver transplant recipient with cerebral abscesses caused by *D. gallopava* who was successfully treated with amphotericin B colloidal dispersion and itraconazole. This is the fourth report of human infection (and the third report of neurological infection) caused by this organism.

Case Report

A 68-year-old man for whom cryptogenic cirrhosis was diagnosed underwent orthotopic liver transplantation in July 1990. His postoperative course was uneventful, and allograft function while he received a maintenance immunosuppressive regimen of FK 506 (8 mg/d) and prednisone (5 mg/d) was excellent. He was discharged on the 45th day after surgery and then was examined monthly in the outpatient clinic.

He was well until February 1992, when he experienced a tonic-clonic seizure after bruising the left side of his forehead. On admission to our medical center, the patient was alert and coherent. His vital signs were normal: blood pressure, 158/90 mm Hg; pulse rate, 84; respiratory rate, 24; and temperature, 36.1°C. Physical examination revealed an apical grade 2/6 systolic ejection murmur, a palpable spleen tip, and contusions of the left forehead and left elbow. The chest was clear to auscultation. A funduscopic examination revealed no retinal pathology. No focal sensorimotor deficit was observed.

Laboratory studies indicated the following: mild leukopenia (total white blood count, 3.6×10^9/L [3,600/mm^3]; normal differential blood cell count [absolute neutrophil count, 2,448/mm^3]); platelet count, 140×10^9/L; creatinine level, 200 mmol/L; and glucose level, 10.3 mmol/L. Serum electrolyte levels and results of liver function tests and coagulation studies were all within normal limits. Chest radiography demonstrated a new noncavitary nodule in the left midlung, subsegmental atelectasis in the left lower lobe, and a slight pleural effusion in the right lobe.

On the day of admission, contrast-enhanced computed tomography (CT) of the head revealed three hypodense, ring-enhancing lesions (1–1.7 cm in diameter) in the left frontal, left parietal, and right periventricular white matter adjacent to the corona radiata (figure 1). All three lesions were located <1 cm from the lateral ventricles. Mild surrounding edema was evident, but no mass effect was present. A lumbar puncture yielded clear fluid; analysis of the fluid revealed 4 leukocytes, a glucose concentration of 7.0 mmol/L (126 mg/dL), and a mildly increased protein concentration of 1.26 g/L. Gram and acid-fast staining of the fluid did not show

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Reprints or correspondence: Dr. Shimon Kusne, Division of Infectious Diseases, University of Pittsburgh, Transplantation Institute, 3601 Fifth Avenue, 4C Falk Clinic, Pittsburgh, Pennsylvania 15213.

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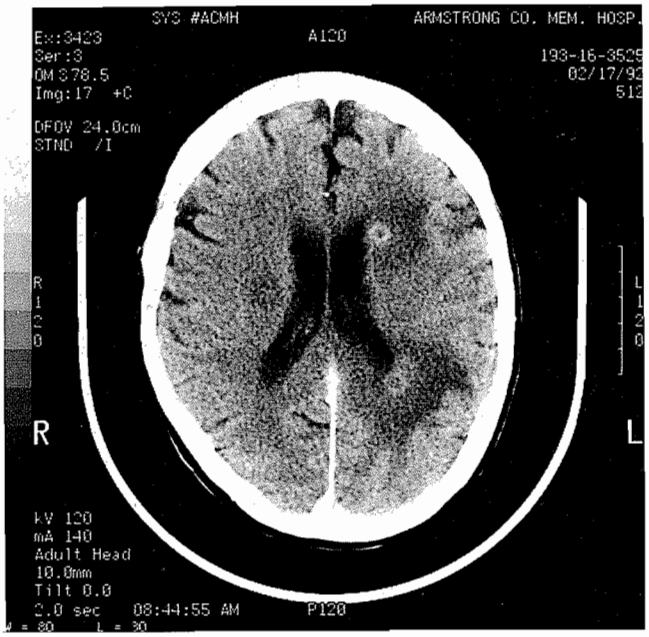

Figure 1. Computed tomogram of the brain of a liver transplant recipient with cerebral phaeohyphomycosis due to *Dactylaria gallopava;* this scan demonstrates the extent of disease at the time of admission.

any microorganisms. A test for CSF cryptococcal antigen was negative. Serum titers of antibody to toxoplasma and human immunodeficiency virus type 1 were negative. Transthoracic two-dimensional echocardiography revealed no cardiac vegetations.

On the second day of hospitalization, 0.5 mL of thick brown pus was aspirated through a CT-guided stereotactic needle from the left parieto-occipital lesion. Gram staining of the material showed numerous white blood cells and septate hyphal elements with acute-angle branching; these hyphal elements were initially thought to be an *Aspergillus* species. Grocott-Gomori methenamine–silver nitrate staining revealed similar findings (figure 2). Therapy with intravenous amphotericin B (50 mg/d) was begun immediately. However, progressive azotemia developed by the fourth day of therapy, and the patient's treatment was changed to an investigational preparation of amphotericin B (amphotericin B colloidal dispersion [Liposome Technology, Menlo Park, CA]) under a compassionate protocol approved by the University of Pittsburgh's Institutional Review Board. The maintenance dosage of amphotericin B colloidal dispersion was 2 mg/(kg · d).

In addition, flucytosine (1.5 g every 8 hours) was added to the therapeutic regimen during the first week of treatment. The dose of FK 506 was tapered to 2 mg/d, and prednisone therapy was continued at a dose of 5 mg/d. On the eighth day of hospitalization, the fungal isolate was identified as *D. gallopava* by definitive analysis of morphological criteria and thermal or cycloheximide tolerance criteria. During discussions with the patient's family, we learned that he kept a pet parakeet at home and used mail-order potting soil to graft plants. Samples of potting soil and litter from the parakeet's cage were cultured [12].

Subsequently, the patient's condition in the hospital stabilized, and he did not have any further seizures or other neurological sequelae. On hospital day 28 CT demonstrated slight shrinkage of the abscesses and partial resolution of the edema. The patient received a total dose of amphotericin B colloidal dispersion of 8.5 g and a 4-week course of flucytosine therapy. His medication was switched to itraconazole (200 mg twice per day) during the last week of hospitalization, and he was discharged 57 days after admission. He received maintenance doses of itraconazole over the subsequent year and remained asymptomatic. Follow-up CT performed 18 months after hospital discharge revealed progressive resolution of the cerebral abscesses.

Methods

The abscess aspirate was cultured using standard laboratory methods on 5% sheep blood agar, Columbia colistin–nalidixic acid (CNA) agar, and eosin–methylene blue agar (BBL Microbiology Systems, Cockeysville, MD) for facultative bacteria and on CDC (Centers for Disease Control and Prevention) anaerobic and Columbia CNA agars incubated in Gas Pack jars (BBL Microbiology Systems) for anaerobic bacteria. Fungal cultures were performed on Sabouraud dextrose (SAB) agar and mycophil agar with penicillin (100

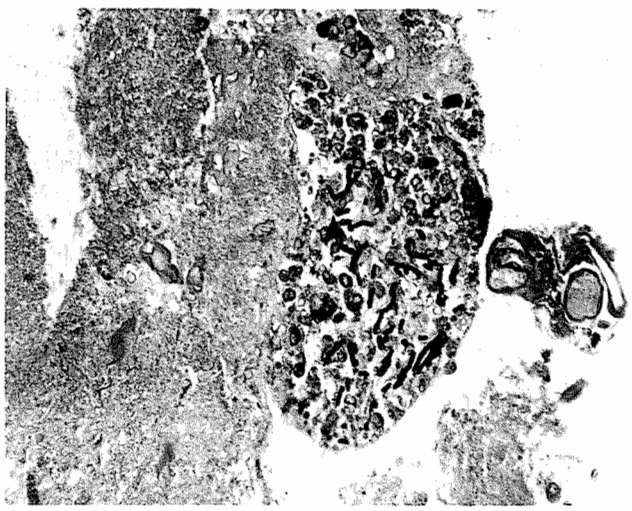

Figure 2. Stereotactic brain biopsy specimen of the parieto-occipital lesion in a liver transplant recipient with cerebral phaeohyphomycosis due to *Dactylaria gallopava;* the specimen demonstrates collections of darkly stained fungal elements within necrotic tissue (Grocott-Gomori methenamine–silver nitrate stain; original magnification, × 500).