First Report of Cryptococcus Albidus—Induced Disseminated Cryptococcosis in a Renal Transplant Recipient

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Cryptococcus albidus, a non-neofomrans species of the genus Cryptococcus, is generally regarded as a rare cause of disease. There have been only 14 previously reported cases in which this organism has been isolated as a pathogen, none of which occurred in a renal transplant recipient. A 23-year-old renal transplant recipient taking medication consisting of cyclosporine and prednisolone was admitted with a 10-day history of dry cough, fever and progressive dyspnea. The next day, his respiratory status deteriorated dramatically, and he developed acute respiratory distress syndrome (ARDS) and fulminant septic shock. On the eighth hospital day, tender macules on both his shins coalesced to form erythematous patches. Cryptococcus albidus was isolated by skin biopsy and tissue culture. We report here the first case of disseminated cryptococcosis caused by C. albidus in a renal transplant recipient who had been successfully treated with fluconazole monotherapy.

Key Words: Cryptococcus albidus, Fluconazole, Kidney transplantation

INTRODUCTION

Cryptococcosis is a serious opportunistic fungal infection often occurring in immunocompromised patients.1,2 Despite the recognition of several species of the genus, the non-C. neofomrans including C. albidus are generally regarded as non-pathogenic saprophytes3. Infections due to other species of Cryptococcus are extremely rare and poorly substantiated.

There have only been 14 previously reported cases in which Cryptococcus albidus has been isolated as a pathogen, none of which occurred in a renal transplant recipient. To the best of our knowledge, this is the first reported case of disseminated cryptococcosis presenting cutaneous infection, septic shock, and acute respiratory distress syndrome (ARDS) caused by C. albidus in a renal transplant recipient. Our experience with this case is instructive since it was treated successfully with fluconazole alone despite the serious multiorgan involvement. We have reviewed and compared all known cases of infection with C. albidus.

CASE REPORT

A 23-year-old Asian man with chronic renal allograft dysfunction was admitted to our hospital in May 2001 with a 10-day history of fever, intermittent chills, dry cough and progressive dyspnea. He underwent renal transplantation in 1994 for end-stage renal disease of unknown cause diagnosed in 1993. He had been on a medication of cyclosporine 200 mg/day and prednisolone 5−20 mg/day. His temperature was 40°C, blood pressure 120/70 mmHg supine, pulse rate 120/min and respiratory rate 20/min. Respiratory examination revealed mildly decreased breathing sounds on the right lower chest. We also noted several erythematous tender macules measuring 0.5 cm in diameter on both shins. He had no neurological signs of meningitis. Chest radiograph obtained on admission demonstrated increased opacity on the right lower lobe. Arterial blood gas analysis on room air revealed a pH of 7.38, PaCO2 22.1 mmHg, PaO2 49.4 mmHg, and SaO2 85.3%. A complete blood count yielded a leukocyte count of 5,600/mm3 (91.6% neutrophils), hemoglobin 5.6 g/dL, and platelet count

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267,000/mm³. The renal allograft function was in acute exacerbation on chronic dysfunction: BUN 113 mg/dL, Cr 8.5 mg/dL, Na 125 mmol/L, K 6.4 mmol/L, protein 5.2 g/dL, albumin 2.9 g/dL, glucose 102 mg/dL. The patient had been treated with empirical antibiotics for the presumed diagnosis of severe community-acquired pneumonia. On the next day, his respiratory status deteriorated dramatically with a rapid development of hypotension. A repeat chest radiograph showed nearly complete opacification of both lung fields (Figure 1). The patient was intubated and placed on mechanical ventilation. Dobutamine and dopamine were administered. Urgent anti-CMV IgM, CMV PCR and anti-HIV were negative. Anti-mycoplasma antibody titer was <1:20. Acid-fast bacillus smear and methenamine silver stain of sputum yielded negative results. The initial three sputum and blood cultures were sterile. On the eighth hospital day, tender macules on both shins coalesced to form erythematous patches. Skin biopsy showed granulomatous inflammation in the dermis and numerous yeast organisms with clear thick capsules (Figure 2). The cerebrospinal fluid (CSF) exam was clear with normal glucose and slightly increased protein (95 mg/dL). The cryptococcal antigen titer was elevated in CSF at >1:256 and at >1:516 in serum. However, the microscopic examination of CSF preparations with India ink was negative for encapsulated yeasts and CSF cultures were negative. The culture of skin biopsy isolated a yeast organism, which was identified as Cryptococcus albidus by characteristic morphology, fermentation, and carbon assimilation tests using the API 20c AUX system (bioMérieux, Marcy-l’Etoile, France). The patient was treated intravenously with fluconazole immediately after the skin biopsy. After 10 days of fluconazole therapy, his chest radiograph and CT scan showed marked clearing with only one cavitary nodular lesion on the left upper lobe (Figure 3). Percutaneous needle aspiration was performed for the left upper pulmonary nodule. Cytologic examination of the aspirates also revealed a typical morphology of the numerous cryptococci (Figure 4). The patient was discharged on an oral regimen of fluconazole (200 mg/day). Fluconazole maintenance therapy was continued for 12 months on a long-term basis for prevention of cryptococcosis. At the time of the most recent follow-up, July 2002, his chest radiograph was stable and we detected no evidence of recurrent cryptococcal infection.

**Figure 1.** Chest X-ray on second hospital day, shows rapidly aggravated bilateral airspace consolidation.

**Figure 2.** Skin biopsy showing numerous encapsulated yeast-like organisms surrounded by large clear spaces and inflammatory cells consisting of lymphoid cells in subcutis (H&E stain, ×400).

**Figure 3.** Chest CT showed a irregular, spiculated nodule with cavity at the apicoposterior segment of the left upper lobe.