

Unusual fatal presentation of invasive cryptococcal infection after 25 years of immunosuppressive therapy

Abstract

Cryptococcosis is an opportunistic systemic mycosis commonly associated with immune compromised solid organ transplant recipients. In these patients, the diagnosis of fungal infections can be very challenging due to the variety of clinical presentations.^{1,2} This case describes a kidney transplant recipient diagnosed with invasive cryptococcal infection after 25 years of immunosuppressive therapy presenting with Dysphagia, a symptom that has not been reported in the literature.

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Case report

A 52-year-old Caucasian man with significant history of CHF (class IV), severe COPD, unilateral kidney transplant in 1995 on chronic immunosuppressive therapy (Azathioprine 150mg/day and Prednisone 10mg/day), was admitted with complaints of Dysphasia and shortness of breath. Physical examination revealed a respiratory rate of 26 breaths-per-minute and blood pressure 89/42. The physical exam was otherwise unremarkable. Chest x-ray showed diffuse bilateral granular infiltrates. Laboratory showed moderate anemia, white blood cell count of 1200/mm³, serum creatinine of 1.6mg/dl. Sputum cultures grew *Cryptococcus neoformans*. Pharyngeal tissue biopsy showed extensive necrosis with diffuse cryptococcal infiltration. Blood cultures and cerebrospinal fluid cultures tested negative for cryptococcal antigen. Intravenous amphotericin B was initiated but despite medical treatment and intensive supportive care he developed multi-organ failure and expired.

Discussion

Cryptococcosis is the third most common fungal infection in renal transplant recipients and it usually presents as a late complication after transplantation (>1year).^{3,4} The literature describes a variety of clinical presentations of cryptococcal infection mainly affecting the brain, lungs, skin and soft tissues; but also uncommon sites like the liver, lymph nodes, peritoneum, adrenals, bones and eyes have been described.^{5,6}

Apart from an isolated elevation of serum creatinine levels, which is characteristic of both a state of chronic rejection and an opportunistic infection; renal transplant recipients usually exhibit fewer clinical manifestations and few or no findings on conventional imaging studies and laboratory tests.⁷ To increase the awareness of a possible fungal infection, Badiee et al.³ recommends that in these patients, the presence of unexplained fever despite broad-spectrum antibiotic treatment for more than 3 to 6 days, recurring febrile episodes or the presence of pulmonary infiltrates during antibiotic treatment, should place a fungal infection very high in the differential, and trigger the initiation of more invasive diagnostic procedures and management.

This new presentation and the time of onset since renal transplantation should alert the physician of a possible fungal infection and lead to a direct endoscopic evaluation and biopsy. There are not specific guidelines for the management of extra pulmonary or extra neural Cryptococcosis, and curiously these patients have the worst prognosis and the highest percentage of failed therapy.⁸ Nonetheless, severe cryptococcal infection without CNS involvement should be treated empirically as a cryptococcal CNS disease; and in order to minimize the risk of immune reconstitution inflammatory syndrome, the immunosuppressive management in renal transplant recipients should include a step-wise reduction of immunosuppressant's with consideration of lowering the corticosteroid dose first.^{8,9}

Early diagnosis remains difficult to achieve and by the time it is confirmed the patient may expire despite antifungal therapy.³ To improve the prognosis of these patients, a high index of suspicion is necessary, and prompt initiation of treatment should be based in very little clinical and microbiological information, even before obtaining definite results.

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Conflict of interest

The author declares no conflict of interest.

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