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Case Report

Case Report: Cryptococcal Meningitis in a Long-Term Kidney Transplant Recipient

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Abstract

Cryptococcosis is an opportunistic fungal infection primarily caused by *Cryptococcus neoformans* and *C. gattii*, which poses significant risks for immunocompromised individuals, particularly kidney transplant recipients. This case report describes a 55-year-old female patient with a history of end-stage renal disease who underwent living donor kidney transplantation seven years prior. She presented with severe headache, fever, and altered mental status indicative of cryptococcal meningitis. Initial diagnostic evaluations included imaging studies that returned normal results, while cerebrospinal fluid analysis revealed elevated opening pressure, lymphocytic pleocytosis, and positive CrAg testing for *C. neoformans*. Notably, the patient exhibited a false-negative serum CrAg result attributed to the postzone phenomenon, emphasizing the need for careful interpretation of diagnostic tests in immunocompromised patients. Treatment involved induction therapy with liposomal amphotericin B and flucytosine, followed by fluconazole maintenance therapy. This case highlights the complexities of diagnosing and managing cryptococcal infections in kidney transplant recipients, underscoring the importance of early recognition, tailored treatment strategies, and the potential need for dilutional testing in cases of suspected cryptococcal disease.

Keywords: *Cryptococcal Meningitis; Kidney Transplant Recipient; Cryptococcosis*

Introduction

Cryptococcosis is an opportunistic fungal infection primarily caused by *Cryptococcus neoformans* and *C. gattii*, which are encapsulated yeasts found in the environment, particularly in soil and bird droppings. While the global population is frequently exposed to these fungi, symptomatic disease predominantly occurs in immunocompromised individuals, such as solid organ transplant recipients [1]. In these patients, cryptococcal infections can lead to significant morbidity, often presenting as pulmonary or central nervous system (CNS) disease.

The gold standard for diagnosing cryptococcal infections has traditionally been fungal culture; however, this method can be time-consuming and may delay timely treatment [2]. The introduction of rapid diagnostic tests, such as the lateral flow assay (LFA) for cryptococcal antigen (CrAg), has significantly improved our ability to detect these infections early, demonstrating high sensitivity and specificity [3]. This case report presents the clinical course of a 55-year-old female kidney transplant recipient who developed cryptococcal meningitis, emphasizing the importance of early diagnosis and tailored management strategies in this vulnerable population.

Case Presentation

A 55-year-old woman with a history of end-stage renal disease secondary to polycystic kidney disease underwent a living donor kidney transplantation seven years prior. She was maintained on an immunosuppressive regimen that included tacrolimus, mycophenolate mofetil (MMF), and prednisone. The patient presented to the emergency department with severe headache, fever, and altered mental status, suggestive of increased intracranial pressure (ICP).

Upon examination, the patient exhibited fever (38.5°C), hypertension (160/95 mmHg), and tachycardia (110 beats per minute). Neurological assessment revealed confusion and mild neck stiffness, though no focal neurological deficits were noted. Laboratory studies indicated leukocytosis and elevated inflammatory markers, prompting further investigation.

Imaging studies

A non-contrast computed tomography (CT) scan of the brain was performed, revealing no acute intracranial abnormalities. However, due to persistent symptoms and high clinical suspicion for meningitis, a magnetic resonance imaging (MRI) of the brain was conducted, which also returned normal results.

Cerebrospinal fluid analysis

Given the clinical presentation of meningitis, a lumbar puncture was performed on admission day nine. The analysis of the cerebrospinal fluid (CSF) revealed:

- Elevated opening pressure: 30 cm H_2O.
- White blood cell count: 150 cells/µL (predominantly lymphocytes).
- Elevated protein level: 1.5 g/L.
- Low glucose level: 1.5 mg/dL (normal range: >60% of serum glucose).

An India ink preparation was positive for encapsulated yeasts, and CrAg testing confirmed the presence of *Cryptococcus neoformans* in the CSF with a titer of 1:1 dilution. Notably, a multiplex polymerase chain reaction (PCR) test performed on the CSF was negative for all organisms, including *Cryptococcus* spp. Additionally, bronchoalveolar lavage (BAL) culture grew *C. neoformans* after six days of incubation.

Despite the initial negative serum CrAg result, subsequent dilutions of serum were performed, ultimately yielding a positive CrAg with a titer of 1:2560, indicating a postzone phenomenon.

Treatment and follow-up

The patient was initiated on induction therapy with liposomal amphotericin B (4 mg/kg IV daily) and flucytosine (25 mg/kg orally four times daily). Due to a rise in creatinine levels to 1.6 mg/dL, flucytosine was discontinued after five days. The patient completed two weeks of amphotericin B therapy before transitioning to oral fluconazole. A follow-up CT scan on day 15 showed increased inflammation around the cavitary lung lesion, likely representing an immune reconstitution inflammatory reaction rather than treatment failure. The patient's renal function normalized, and she was discharged on an eight-week course of fluconazole (800 mg daily), followed by maintenance therapy at 400 mg daily with plans for gradual tapering based on repeat serum CrAg titers.

Discussion

This case illustrates the complexities of diagnosing and managing cryptococcal meningitis in kidney transplant recipients, a population at heightened risk for opportunistic infections. The clinical presentation of our patient underscores the need for a high index of suspicion for cryptococcal disease in immunocompromised individuals, particularly those presenting with neurological symptoms.

Diagnostic considerations

The diagnosis of cryptococcal meningitis can be challenging, especially when relying solely on traditional methods such as fungal culture, which may take several days to yield results. In our patient, the initial negative serum CrAg result was attributed to the postzone phenomenon, where an excess of antigen relative to antibodies leads to a false-negative result [6]. This phenomenon is critical to recognize, as it emphasizes the importance of considering dilutional testing in patients with high clinical suspicion for cryptococcal infection. Previous studies have demonstrated that dilution of serum samples can significantly enhance the sensitivity of CrAg detection, making it a valuable approach in ambiguous cases [7].

The LFA for CrAg detection has revolutionized the diagnostic process for cryptococcal infections by providing rapid results with high sensitivity and specificity. In a meta-analysis, the pooled sensitivity of the LFA was reported at 97.6%, making it a cornerstone in the early diagnosis of cryptococcal disease, particularly in resource-limited settings [5]. However, clinicians should remain vigilant for the possibility of false negatives, particularly in the context of high antigen loads.

Treatment strategies

The management of cryptococcal meningitis in kidney transplant recipients must be approached with caution due to the potential for drug interactions and the nephrotoxic effects of antifungal agents. In our case, the decision to discontinue flucytosine after five days was made to safeguard renal function, as elevated creatinine levels were observed. The use of liposomal amphotericin B as the initial therapy is consistent with current guidelines, which recommend this formulation due to its efficacy and reduced nephrotoxicity compared to conventional amphotericin B [4].

Furthermore, the interactions between antifungal agents and immunosuppressants warrant careful monitoring. Fluconazole, a key component of maintenance therapy, can influence tacrolimus levels, necessitating close observation to prevent potential toxicity [4]. This case exemplifies the delicate balance required in managing immunosuppression while effectively treating opportunistic infections.

Implications of immunosuppression

The immunosuppressive therapies employed in kidney transplant recipients, while essential for preventing graft rejection, significantly increase the risk of infections, including cryptococcosis. The interplay between immunosuppression and the host's ability to respond to infections is a critical consideration in the management of these patients. In this case, the long-term use of immunosuppressants likely contributed to the development of cryptococcal meningitis, highlighting the need for ongoing vigilance in this population.

Conclusion

This case of a long-term kidney transplant recipient with cryptococcal meningitis emphasizes the importance of early recognition, appropriate diagnostic strategies, and tailored treatment approaches in managing opportunistic infections. Clinicians should maintain a high level of suspicion for cryptococcal disease in immunocompromised patients, particularly in the presence of neurological symptoms. The potential for false-negative results in CrAg testing underscores the necessity of considering dilutional testing in cases with high pretest probability. Ultimately, a multidisciplinary approach that includes nephrology and infectious disease expertise is essential for optimizing patient outcomes in this complex clinical scenario.

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