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Single Case

Cellulitis in a Liver Transplant Patient as an Initial Manifestation of Disseminated Cryptococcal Disease

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Keywords
Skin and soft tissue infections · Cutaneous cryptococcosis · Liver transplantation

Abstract
A 50-year-old male underwent liver transplantation due to cryptogenic cirrhosis and was admitted with severe pain in the left leg as well as phlogosis. Amoxicillin/clavulanic acid was prescribed, assuming bullous erysipelas. Among the tests performed, the latex agglutination test for the *Cryptococcus* sp. antigen was positive, and in both the blood culture and blister culture *Cryptococcus* sp. was isolated. Daily fluconazole was started. Even though liposomal amphotericin B has been started on the fifth day of hospitalization, the patient progressed to death.

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Introduction

Cryptococcosis is a significant infection with high mortality in solid organ transplant recipients [1]. Most cases occur in immunosuppressed hosts, including patients with HIV/AIDS, patients receiving immunosuppressing drugs, and solid organ transplant recipients [2, 3]. Primary cryptococcosis of the skin is very rare, and cryptococcal skin disease should therefore be interpreted as a sign of systemic cryptococcal infection [4]. Cryptococcal skin disease can manifest itself in a variety of ways, each of which is uncharacteristic for *Cryptococcus* sp. [4, 5]. Erysipelas is a very uncommon form [2, 6].

We describe a case of disseminated cryptococcal infection in a liver transplantation patient with a clinical presentation of bullous erysipelas in the lower limb that rapidly culminated to a fatal outcome.

Case Report

A 50-year-old male underwent liver transplantation in October 2010 due to cryptogenic cirrhosis. After 13 months, he started to present clinical and laboratory signs consistent with liver rejection, such as fever, abdominal pain, jaundice and an increase in hepatic enzymes. After 7 days of hospitalization and readjustment of immunosuppressive therapy doses, he was discharged with clinical and laboratory regression of liver rejection. After 4 months, he sought the hospital with a 1-week history of severe pain in the left leg, associated with edema, local heat and redness with discrete blisters in the distal third of this limb (fig. 1). Amoxicillin/clavulanic acid 1,000/200 mg EV, three times a day, was prescribed due to the assumption of bullous erysipelas; 3 days after starting antibiotic treatment, there was persistence of severe pain in the left leg and emergence of extensive ecchymosis and erosion of blisters.

Among the tests performed, the latex agglutination test for the *Cryptococcus* sp. antigen was positive, and in both the blood culture and blister culture *Cryptococcus* sp. was isolated. Fluconazole 800 mg daily was started. Even though liposomal amphotericin B 5 mg/kg/day were started on the fifth day of hospitalization, in less than 12 h, the patient had a decreased level of consciousness (Glasgow Coma Scale 4) and was transferred to the intensive care unit. A cranial computed tomography scan with contrast was normal, and a lumbar puncture was performed. The cerebrospinal fluid was clear and colorless, no cells, 75 mg/ml protein, 25 mg/ml glucose and the direct microscopy with Indian ink revealed structures consistent with *Cryptococcus* sp. The patient had onset of status epilepticus and on the 6 day of hospital admission; 36 h after the beginning of neurological symptoms, he progressed to death.

Discussion

Cutaneous lesions occur in 10–20% of all cryptococcal infections and are often an indication of disseminated infection [2, 7]. Clinical recognition is essential for timely initiation of therapy to minimize the morbidity and mortality of this potentially lethal fungal infection [1, 3]. There is no pathognomonic finding for cryptococcal skin disease and incorrect initial diagnosis because atypical presentations may lead to inappropriate or significantly delayed treatment, thereby having an impact on the outcomes [2]. Initially, our patient was treated

for presumed bacterial erysipelas but due to the absence of response, direct examination and culture of a blister skin lesion showed the correct diagnosis.

Treatment of cryptococcal erysipelas has been based on recommendations for disseminated disease and central nervous system disease, as no data from clinical trials are available [7]. Current recommendations suggest liposomal amphotericin B 3–6 mg/kg/day or amphotericin B deoxycholate 0.5–1 mg/kg/day plus flucytosine 100 mg/kg/day for at least 14 days or until blood and cerebrospinal fluid cultures became sterile [7, 8].

Diagnosis of cutaneous manifestations of cryptococcosis can be challenging, as it can resemble more common bacterial infections, and a delay in appropriate diagnosis can lead to high morbidity and mortality rates. Clinicians should maintain a high index of suspicion for atypical pathogens, especially fungi, among patients with skin infection not responding to antimicrobial therapy.

Statement of Ethics

Informed consent for publishing the case was obtained from the patient. No animal experiments were performed, nor was human research committee approval needed.

Disclosure Statement

The authors declare that there are no conflicts of interest.

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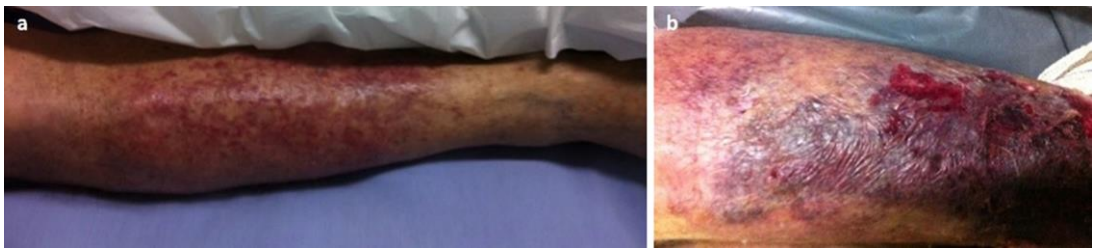

Fig. 1. **a** Initial aspect of erysipelas and **b** after the diagnosis of disseminated cryptococcosis.