CASE REPORT

Cryptococcus laurentii fungemia in a patient with chronic kidney disease on hemodialysis

Fungemia por cryptococcus laurentii em paciente com doença renal crônica em hemodiálise

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Abstract

Introduction: Chronic Kidney Disease (CKD) is a relevant comorbidity from clinical and public health perspectives. Infections are an important cause of death in those patients. Although rare, fungal infections are increasing in incidence. **Case report**: a 45-year-old female patient with CKD due to systemic lupus erythematosus (SLE) was admitted to a tertiary hospital due to a bloodstream infection (BSI) caused by Cryptococcus laurentii. She received treatment with anidulafungin with good initial response but presented clinical and laboratory worsening after a few days, and the treatment was switched to amphotericin B. The hemodialysis access was changed. Chest tomography, echocardiogram, eye fundus examination, and cerebrospinal fluid study did not show changes. After 32 days of amphotericin B, the patient presented clinical improvement and was discharged to take oral fluconazole for three (3) months. **Conclusion**: BSI due to Cryptococcus laurentii is rare in patients on chronic hemodialysis with a high potential for complications. Physicians should have clinical suspicion for those infrequent infections infractions, and culture evaluation should always be performed. The diagnosis is still a challenge, as well as the therapeutic regimen.

Keywords: chronic kidney disease; fungemia; cryptococcus.

Resumo

Introdução: a doença renal crônica (DRC) é uma comorbidade relevante do ponto de vista clínico e de saúde pública. As infecções configuram importante causa de morte nesses pacientes. Embora raras, as infecções por fungos têm incidência crescente. **Relato de caso**: uma paciente do sexo feminino, 45 anos, com DRC por lúpus eritematoso sistêmico (LES) foi internada em hospital terciário devido à infecção de corrente sanguínea (ICS) por Cryptococcus laurentii. Recebeu tratamento com anidulafungina com boa resposta inicial, porém, devido à piora clínica e laboratorial, o tratamento foi modificado para anfotericina B, assim como foi realizada a troca do acesso para hemodiálise. A tomografia de tórax, o ecocardiograma, o exame de fundo de olho e o estudo do líquido cefalorraquidiano não evidenciaram alterações. Após 32 dias de anfotericina B, a paciente apresentou melhora clínica e recebeu alta hospitalar com fluconazol via oral por 3 meses. **Conclusão**: a ICS por Cryptococcus Laurentii é rara nos pacientes em hemodiálise crônica, porém com alto potencial de complicações. Há a necessidade de suspeição clínica e avaliação por culturas, sendo o diagnóstico ainda um desafio, bem como o esquema terapêutico.

Palavras-Chave: doença renal crônica; fungemia; cryptococcus.

INTRODUCTION

Chronic Kidney Disease (CKD) is a relevant comorbidity from a clinical and public health point of view, with around 3 to 6 million people affected in Brazil[1] and approximately 150 thousand people on renal replacement therapy (RRT)[2]. These data may be underestimated due to the difficulty in diagnosing the disease. According to the 2021 Brazilian Dialysis Census, the most used dialysis method is hemodialysis (HD) (94%)[2]. The available venous access for hemodialysis are tunneled catheters and native or prosthetic arteriovenous fistulas (AVF).

Infectious diseases account for approximately 10% of the causes of death among hemodialysis patients[3]. Patients who undergo HD through a tunneled venous catheter have up to 10 times greater chances of developing bacteremia than those undergoing dialysis through an arteriovenous fistula (AVF)[4].

Fungal infections have become more common. Candida spp is the most fungal isolated, and the Cryptococcus genus is the second most frequent causative agent5. Cryptococcosis is a life-threatening fungal infection usually presented in immunocompromised patients, such as organ transplant recipients, AIDS patients, and those on long-term corticosteroids and/or immunosuppressive. Cryptococcus laurentii is a ubiquitous encapsulated yeast-like fungus and an extremely rare human pathogen. Infections caused by Cryptococcus in non-HIV RRT patients have only a few cases reported in the literature. The largest study is a retrospective analysis with 18 cases5. We present a case of a patient with lupus and CKD on HD using immunosuppression therapy who presented a bloodstream infection caused by Cryptococcus laurentii.

CASE REPORT

A 45-year-old woman with CKD due to systemic lupus

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erythematosus (SLE) on HD for five (5) years and multiple venous accesses was admitted to the emergency department complaining about non-specific malaise, chills, and fever while undergoing HD sessions for about one (1) month. She was on immunosuppressive therapy with azathioprine. She brought a blood culture from the hemodialysis unit that isolated Candida spp (without sensitivity profile). Upon admission, her blood pressure was 130 x 70 mmHg, axillary temperature 37ºC, heart rate 102 bpm, and respiratory rate 22 bpm. Cardiopulmonary and abdominal examination was unremarkable. She had a tunneled hemodialysis catheter in the right internal jugular vein without local inflammation. The laboratory revealed hemoglobin 7.2 g/dl, hematocrit 20.9%, leukocytes 3,000/mm3, platelets 74,000/mm3, urea 60 mg/dL, creatinine 5.49 mg/dL, C-reactive protein 97.1 mg/dL (normal range < 5 mg/dL). The laboratory tests performed during hospitalization are shown in table 1. An anidulafungin regimen was started. After three (3) days, the patient persisted with fever, drowsiness, and worsening of her general status as well as pancytopenia (hemoglobin 7 g/dl, leukocytes 2,000/mm3, segmented cells 1,432/mm3 and platelets 58,000/mm3). Azathioprine was withdrawn, and empirical antibiotic therapy with piperacillin-tazobactam and vancomycin was started. The subsequent blood culture revealed Cryptococcus laurentii (sensitivity profile not performed due to technical limitations of the microbiology laboratory). The echocardiogram, eye fundus examination, cerebrospinal fluid analysis, and chest tomography showed no changes. The HD catheter was removed, and a new catheter was implanted in a different site (right femoral vein) at the same surgical time. Antifungal therapy was switched to amphotericin B and antibiotics for pyogenic germs were discontinued. The patient was treated with amphotericin B for four (4) weeks. She was discharged with clinical improvement and completed outpatient treatment with fluconazole for three (3) months. The patient evolved stable, without new episodes of BSI, was listed for kidney transplantation, and remains on RRT in an external unit.

Table 1. Main laboratory tests performed during hospitalization.

Laboratory test	Days		
	D1	D3	D31
Hemoglobin (g/dL)	7,3	8,3	9,6
Leukocytes (/mm³)	3,000	12,900	2,900
Platelets (/mm³)	74,000	70,000	111,000
C-reactive protein (mg/L)	97,1	238	19
Urea (mg/dL)	60	190	19
Creatinine (mg/dL)	5,49	10,88	2,48
Potassium (meq/L)	3,6	4,0	3,1
AST/ALT	44/20	93/39	-
Blood culture	Negative	Cryptococcus laurentii	Negative

D1: admission; D3: clinical worsening; D31: hospital discharge; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

DISCUSSION

Bloodstream infection related to hemodialysis access is the association of clinical manifestations and at least one positive peripheral blood culture and a quantitative catheter segment culture > 10^2 units colony forming (CFU) or semiquantitative > 15 CFU6. The same microorganism, with the same antibiogram, must be isolated from the culture of the catheter segment and from peripheral blood culture. There must be no other apparent infectious source. The quantitative ratio of the culture obtained from the dialysis circuit versus the peripheral vein must be greater than or equal to 3:1, and the differential time of at least 2 hours between the positivity of the blood culture obtained from the catheter lumen and the peripheral blood culture[6].

Patients who undergo HD have a ten (10) times higher risk of developing fungal infection when compared to the general population7. Infections are common complications for HD patients. The annual incidence of hospitalization for infectious causes in the United States is as high as 31%8. In addition to antimicrobial therapy, the removal of access for hemodialysis should be evaluated. Patients who present local infection signs, tunnelitis, septic shock, persistent fever or bacteremia 48 to 72 hours after the start of culture-guided therapy, evidence of septic embolization, isolation of multidrug-resistant pathogens, infections by Staphylococcus aureus, Pseudomonas, or Candida must have access removed9. The patient in this report had persistent fever and clinical worsening despite antifungal treatment. Thus, she underwent the removal of the catheter, new access for HD was obtained, and the antifungal treatment was changed to amphotericin B.

Fungal infections have become more frequent. The genus Cryptococcus is the second most frequently causative agent[5]. Cryptococci reach the human body through the inhalation of spores or desiccated yeast cells from the environment. In immunocompromised patients, it can be spread to various organs (such as lungs, central nervous system, bowel, eyes, and skin) through haematologic dissemination[10,11,12]. Cryptococcus laurentii is considered a saprophyte, and its pathogenicity in humans usually occurs mainly in immunosuppressed patients[13]. An increase in infections caused by these organisms has been observed among HD patients[5]. There is little data about cryptococcosis in dialysis patients. The clinical presentation varies depending on the organ affected. Fever is the most common symptom and may be accompanied by skin lesions, respiratory symptoms, and headache, reflecting the main affected sites (central nervous system, bloodstream, lung and pleura, skin)[5]. This presentation is similar to infections caused by Cryptococcus neoformans and Cryptococcus gattii. Nevertheless, the diagnosis is most commonly performed through culture as the cryptococcal antigen is typically negative[14]. The patient was taking immunosuppression, and the blood culture isolated Cryptococcus laurentii. The main symptoms were fever and chills, mainly during hemodialysis, and there was no involvement of other sites.

Data about the involvement of remote sites by Cryptococcus laurentii are also scarce. In the central nervous system, the classic presentation is meningitis, and the main complication is intracranial hypertension, which may be difficult to control. Besides antifungal therapy, daily lumbar punctures must be considered if the intracranial pressure is greater than 25 mmHg. The aim is to maintain intracranial pressure below 20 mmHg. When there is lung involvement, the clinical presentation varies from coughing to acute respiratory failure. Treatment of severe cases should be with intravenous amphotericin B, followed by oral fluconazole. In mild cases, treatment is with fluconazole[15]. The patient in this report had no evidence of distant infection related to fungemia. She was treated with anidulafungin, but it was necessary to switch to amphotericin B due to clinical worsening.

There is no consensus on the antifungal choice and duration of therapy. The most commonly used medication is amphotericin B, associated or not with fluconazole, voriconazole, or flucytosine. Hong et al.[5] reported 18 patients on RRT, eight (8) on hemodialysis, and ten (10) on peritoneal dialysis (PD). In addition to the antifungal medication, the PD catheter was removed in all patients. On the other hand, hemodialysis access was removed in only one (1) patient. The patient in this report began treatment with anidulafungin for approximately 20 days. Meanwhile, due to a lack of response, the treatment was switched to amphotericin B, and the HD access was changed. She has completed fluconazole treatment for three (3) months with a good response.

In summary, cryptococcus infection has an increasing incidence and may be associated with serious complications. The diagnosis is still challenging, and clinicians should be aware of this differential diagnosis while evaluating CKD patients on hemodialysis.

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