CASE REPORT

Rhino-orbital mucormycosis in a diabetes patient with renal impairment after amphotericin B deoxycholate: the role of amphotericin B lipid-complex treatment

Mucormicose rino-orbital em um paciente com diabetes e insuficiência renal após desoxicolato de anfotericina B deoxicolato: o papel do tratamento com anfotericina B complexo-lipídico

Italo Gustavo Lima Monteiro[1], Luís Arthur Brasil Gadelha Farias[2], Ruth Maria Oliveira de Araújo[3], Licia Borges Pontes[3,4]

1. Serviço de Clínica Médica, Hospital Universitário Walter Cantídeo (HUWC), Fortaleza, Ceará, Brasil. 2. Departamento de Saúde Comunitária, Faculdade de Medicina, Universidade Federal do Ceará (UFC), Fortaleza, Ceará, Brasil. 3. Serviço de Infectologia, Hospital Universitário Walter Cantídeo (HUWC), Fortaleza, Ceará, Brasil. 4. Professora do curso de Medicina, Centro Universitário Christus (UNICHRISTUS), Fortaleza, Ceará, Brasil.

Abstract

Introduction: Mucormycosis is an infection caused by the ubiquitous saprophyte fungi with rapid and aggressive progression, especially in immunocompromised patients. **Case report**: A 57-year-old woman diagnosed with rhino-orbital mucormycosis presented with decreased renal function after treatment with amphotericin B deoxycholate which was discontinued. Renal function improved after amphotericin B lipid-complex, being also treated with itraconazole, and otorhinolaryngological surgery. **Conclusion**: The use of Amphotericin B deoxycholate may result in adverse effects. In this situation, Amphotericin B lipid formulation is usually the drug of choice.

Keywords: Mucormycosis. Amphotericin B; Liposomal Formulation; Drug Therapy.

Resumo

Introdução: A mucormicose é uma infecção causada por fungos saprófitos com progressão rápida e agressiva, principalmente em pacientes imunocomprometidos. **Relato de caso:** Uma paciente de 57 anos, do sexo feminine, com diagnóstico de mucormicose rinorbital apresentou diminuição da função renal após tratamento com anfotericina B desoxicolato que foi descontinuada. A função renal foi recuperada após troca da terapia por anfotericina B complexo lipídico, sendo tratada também com itraconazol e cirurgia otorrinolaringológica. **Conclusão**: O uso de anfotericina B desoxicolato pode resultar em efeitos adversos. Nestas situações a formulação lipídica da anfotericina B é geralmente a droga de escolha.

Palavras-chave: Mucormicose. Anfotericina B; Formulação Lipossomal; Tratamento Farmacológico.

INTRODUCTION

Mucormycosis is an infection caused by the ubiquitous saprophyte fungi belonging to the class Zygomycetes and the order Mucorales[1,2]. It is a worldwide occurrence, with rapid and aggressive progression, especially in immunocompromised patients such as those with bone marrow transplants, hematological diseases, and diabetes, intravenous drug users, and even those without apparent immunosuppression3,4. Mucormycosis is an opportunistic infection that affects immunosuppressed patients with impaired phagocytosis2,5. It is believed that the main mode of transmission of Mucorales occurs through inhalation of spores present in the environment[3-5].

In immunocompromised patients, diabetes mellitus is the main underlying pathology associated with mucormycosis[3]. In these patients, the most commonly involved areas are the breasts and the face, with or without impairment of orbit or brain tissue[3,5]. The management usually includes metabolic support, antifungal therapy, and surgical debridement of all necrotic tissue[1,5]. Herein, we report the case of a 57-year-old woman diagnosed with rhino-orbital mucormycosis presenting with decreased renal function with amphotericin B deoxycholate, amphotericin B lipid-complex, and itraconazole therapy and otorhinolaryngological surgery.

CASE REPORT

A 57-year-old woman presented with a 3-month history of intense headache, facial pain, and edema in the right periorbital region. She also presented with post-nasal discharge, hemorrhagic and purulent rhinorrhea, ipsilateral nasal erythema, and otalgia. After 1 month, the case evolved with worsening edema and pain, as well as amaurosis in the right eye. In this period, she reported anorexia and weight loss of 16

Correspondence: Luis Arthur Brasil Gadelha Farias. Address: Juazeiro do Norte St, number 333, Ed. Rui Castelo Branco, aptoº 102, Meireles, CEP: 60165-110. Fortaleza, Ceará, Brasil. Email: luisarthurbrasilk@hotmail.com
Conflict of interest: The authors declare that there is no conflict of interest.
Received: 2020 Sep 26; Revised: 2021 May 7; Accepted: 2021 May 12

kg. She had a previous history of systemic arterial hypertension and decompensated diabetes. On physical examination right-sided edema and ipsilateral amaurosis was noted. The patient had no other complaints or findings.

Results of blood and white blood cell counts, platelets, liver, and renal function tests were unremarkable. Anti-human immunodeficiency virus (HIV) 1 and 2, anti-HCV, HBsAg, Anti-HBs, and VDRL test results were all negative. Chest radiography performed during admission was normal. She was initially treated symptomatically and an MRI of the orbits and sinuses was performed. MRI revealed aggressive and aggressive right maxillo-ethmoidal inflammatory sinusopathy, with inflammatory processes extending into the orbital canal and the infero-medial canal corresponding to involvement of extrinsic musculature with presence of amorphous tissue (Figure 1). The process extends into the palate and masticator space, with a localized abscess and into the middle cranial fossa with probable abscess and perilesional edema. There was no cavernous sinus thrombosis.

Zygomycosis was suspected and remained the most likely diagnosis. Other differential diagnoses included malignancy, autoimmune disorders, and other bacterial/fungal infections. Maxillary sinusotomy, anterior and posterior right ethmoidectomy, sphenoidotomy, turbinectomy and septoplasty were performed. The histopathological material of the maxillary region revealed mucosal fragments lined by respiratory epithelium, upon which mucus containing numerous large hyphae were found, ribbonlike and with branches, generally a right angle (90°) compatible with zygomycosis. There was also a representation of mature bone tissue, with no particularities.

Before the histopathological result, empiric treatment with amphotericin B deoxycholate had been initiated for 5 days (accumulated dose of 250 mg), with progressive deterioration of renal function (Table 1). Then, amphotericin B lipid-complex (ABLC) was initiated. The patient received 20 days of treatment with ABLC at a 5 mg/kg/day dose (cumulative dose of 6 g), with a significant improvement of renal function, but new rise in serum creatinine up to 2.5 mg/dL (Table 1). Dialysis was not needed. After 20 days, ABLC was discontinued, and oral itraconazole was initiated (delay due to lack of posaconazole in the institution). The patient was discharged with a creatinine of 1.7 mg/dL. The underlying disease was controlled with fixed and mobile subcutaneous insulin administration. The patient had continued success with this therapy. Findings of post-treatment MRI of the orbits and sinuses (Figure 2) and fiberoptic nasolaryngoscopy were normal, without any indication for further surgical therapy.

Figure 1. Right maxillo-ethmoidal inflammatory sinusopathy, with inflammatory processes extending into the orbital canal and the infero-medial canal.

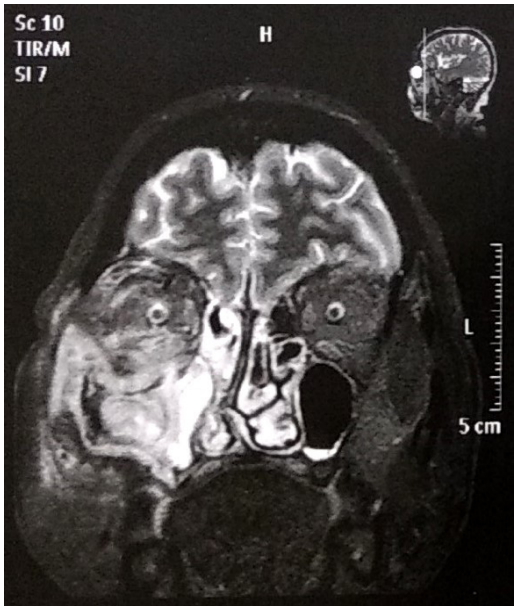

Figure 2. Post-treatment MRI of the orbits and sinuses showing the cicatricial aspect after surgery.

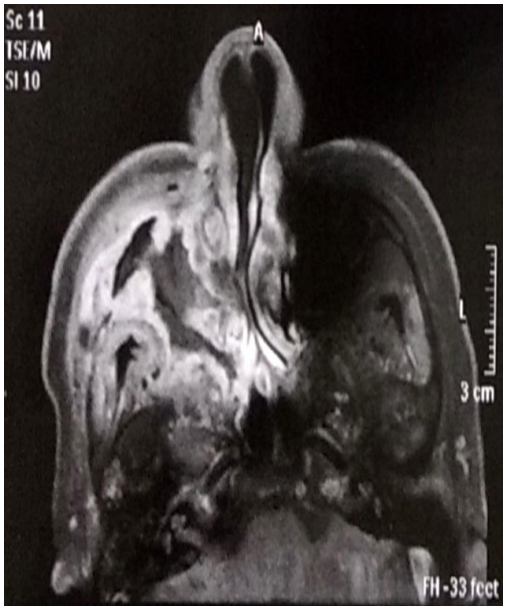

Table 1. Renal function during hospital stay.

Examinations	Pre-admission	Admission	After 5-day amphotericin B deoxycholate regimen	Start ABLC	End ABLC	Discharge
Date	12/06/17	10/08/17	06/09/17	11/09/17	02/10/17	09/10/17
Creatinine (mg/dL)	0.8	1.2	3.7	1.9	2.5	1.7
Urea (mg/dL)	13	42	116	82	100	71
ClCr (mL/min/1.73m²) CKD-EPI	82.1	50.3	12.9	28.9	20.7	33

DISCUSSION

Mucormycosis presents with challenges in diagnosis and prompt treatment. The histopathological analysis may be essential to making a diagnosis. A systemic evaluation through endoscopy of the ear, nose, and throat is important for response to treatment[4]. Cultures of certain regions, such as those in the reported case, may help to identify the infectious etiology with considerable sensitivity,[5]. Visualization of hyphae by microscopy in clinical samples is highly suggestive of disease[1,4]. The hyphae usually are hyaline or ribbonlike with structures of 5-25 µm, with branches/invasions - generally with right angles[1,4,5]. When hyphae are fragmented, the diagnosis is compromised. A culture may be necessary for confirmation[1,4]. When cultures are negative, molecular screening may confirm the histopathological diagnosis; however, there is no standardized test yet[4].

Recognizing the risk groups and intervening early with antifungal therapy, mainly with amphotericin B, may delay the progression of this devastating infection. The therapeutic management is based on administration of antifungal agents, surgical debridement, and baseline condition control[4,5]. Antifungal therapy should be continued until there are no signs of disease progression[5]. ABLCs are the drug of choice. The triazole posaconazole is a promising second-line drug when there is intolerance to the first line and is used for maintenance treatment[4].

ABLC at a 5 mg/kg/day dose appears to be safe and effective for systemic fungal infections in children and adults who have not tolerated amphotericin B deoxycholate. This dose is effective against a wide range of invasive fungal infections (disseminated candidiasis, disseminated aspergillosis, cryptococcal meningitis, disseminated cryptococcosis in HIV-positive patients, fusariosis and coccidioidomycosis, zygomycosis and blastomycosis). ABLC has superior efficacy to amphotericin B deoxycholate (reduced risk of death by 28%) and greater tolerability than the conventional formulation (reduced risk of nephrotoxicity by 58%). ABLC has similar efficacy to liposomal amphotericin B (L-amphotericin) as well as a reduced risk of nephrotoxicity in the same order of magnitude compared to conventional amphotericin B6. ABLC was also shown to be 72% effective in treating invasive fungal infections in general[7].

A study comparing ABLC and L-amphotericin in murine pulmonary mucormycosis concluded that the drugs have different pharmacokinetics. ABLC achieved higher concentrations in the lung parenchyma when administered at 5 mg/kg/day than 10 mg/kg/day. When administered at a dose of 10 mg/kg/day, both reached similar concentrations[8]. A multicenter American study enrolled 3,514 patients who received at least 4 doses of ABLC for documented (70%) or suspected (29%) fungal infection, with an average dose of 4.4 mg/kg/day, averaging 12 days of treatment. The underlying diseases were leukemia (38%), allogeneic bone marrow transplantation (21%), solid organ transplantation (21%), solid organ tumor (10%), lymphoma (8%), graft versus host disease (5%), acquired immunodeficiency syndrome (AIDS) (4%) and autologous bone marrow transplantation (4%). Overall, ABLC was well tolerated by the majority of patients: only 13% of patients had creatinine elevation of at least double the baseline creatinine level. Of these, only 3% reached dialysis or renal transplant[7].

From this study, 64 patients had mucormycosis as a mycological diagnosis, in addition to the underlying disease. Most received 4-5 mg/kg day for an average of 16 days, similar to our case. Of the 64 patients, 16 (100%) had previous renal disease and 14 (88%) received their entire treatment with ABLC without significant worsening of renal function or need for hemodialysis, and three patients had renal function altered by previous antifungal (amphotericin B deoxycholate) treatment and tolerated subsequent ABLC therapy[7].

In the presented case, the patient had the infectious focus treated surgicallyby otorhinolaryngology, and had amphotericin B deoxycholate followed by ABLC administered for a total of 25 days. The recommended doses of ABLC are 5-7.5 mg/kg/day4. Mucormycosis is a relatively rare condition requiring a high index of suspicion and rapid treatment, both surgically and clinically. Amphotericin B lipid complex has been shown to be a safe and effective drug for treating orthomycosis-affected mucormycosis in a patient with diabetes mellitus as underlying disease. More studies will be necessary to understand other therapies such as itraconazole and its derivatives.

ACKNOWLEDGEMENTS

We thank the patient who agreed to participate in the study.

FINANCIAL SUPPORT

None.

REFERENCES

1. Manesh A, Rupali P, Sullivan MO, Mohanraj P, Rupa V, George B, et al. Mucormycosis-A clinicoepidemiological review of cases over 10 years. Mycoses. 2019;62(4):391-8.

2. Afroze SN, Korlepara R, Rao GV, Madala J. Mucormycosis in a diabetic patient: a case report with an insight into its pathophysiology. Contemp Clin Dent. 2017;8(4):662-6.

3. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis. 2005;41(5):634-53.

4. Skiada A, Lanternier F, Groll AH, Pagano L, Zimmerli S, Herbrecht R, et al. Diagnosis and treatment of mucormycosis in patients with hematological malignancies: guidelines from the 3rd European Conference on Infections in Leukemia (ECIL 3). Haematologica. 2013;98(4)492-504.

5. Gutiérrez-Delgado EM, Trevino-González JL, Montemayor-Alatorre A, Cecenas-

Falcón LA, Riz Holguín E, et al. Chronic rhino-orbito-cerebral mucormycosis: A case report and review of the literature. Ann Med Surg. 2016;(6)87-91.

6. Martino R. Efficacy, safety and cost-effectiveness of Amphotericin B Lipid Complex (ABLC): a review of the literature. Curr Med Res Opin. 2004;20(4)485-504.

7. Chandrasekar P. The experience is CLEAR. Int J Antimicrob Agents. 2006;27 Suppl 1:31-5.

8. Lewis RE, Albert ND, Liao G, Hou J, Prince RA, Kontoyiannis DP. Comparative pharmacodynamics of amphotericin B lipid complex and liposomal amphotericin B in a murine model of pulmonary mucormycosis. Antimicrob Agents Chemother. 2010;54(3):1298-304.

Como citar este artigo/ How to cite this article:
Monteiro IGL, Farias LABG, Araújo RMO, Pontes LB. Rhino-orbital mucormycosis in a diabetes patient with renal impairment after amphotericin b deoxycholate: the role of amphotericin B lipid-complex treatment. J Health Biol Sci. 2021; 9(1):1-4.