Journal of Microbiology and Infectious Diseases / JMID
2016; 6 (1): 32-35
doi: 10.5799/ahinjs.02.2016.01.0211

**CASE REPORT**

# Treatment of Mucormycosis with Liposomal Amphotericin B, Posaconazole and Deferasirox: A Case Report

Uğur Önal, Meltem Taşbakan, Tansu Yamazhan, Bilgin Arda, Hüsnü Pullukçu, Sercan Ulusoy, Oğuz Reşat Sipahi

*Ege University-Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Izmir/Turkey*

**ABSTRACT**

In this paper, we present a 69 years old diabetic patient with mucormycosis who was succesfully treated with liposomal amphotericin B (LAMB), posaconazole and deferasirox despite having no adequate surgery. There was no relapse on 6 month post-treatment follow-up. We conclude that combination of antifungal antibiotics with deferasirox may be successful in the salvage therapy of mucormycosis especially in diabetic patients. *J Microbiol Infect Dis 2016;6(1): 32-35*

**Key words:** mucormycosis, treatment, diabetes mellitus, mucorales

# Mukormikozisin Amfoterisin B, Posakonazol ve Deferasiroks ile Tedavisi: Bir Olgu

**ÖZET**

Bu yazıda, 69 yaşında, diyabetik ve yeterli cerrahi tedavi yapılamamasına rağmen lipozomal Amfoterisin B (LAMB), posakonazol ve deferasiroks ile başarılı şekilde tedavi edilen bir mukormikoz olgusunu sunmaktayız. Tedavi sonrasında 6 aylık takipte relaps saptanmamıştır. Sonuç olarak olgumuz özellikle diyabetik hastalarda antifungal antibiyotiklerle birlikte deferasiroks kombinasyonunun mukormikoz kurtarma tedavisinde faydalı olabileceğini düşündürmektedir.

**Anahtar kelimeler:** mukormikozis, tedavi, diyabetes mellitus, mucorales

## CASE

A 69 years old female patient with hypertension and type-2 diabetes mellitus, admitted to another setting with complaints of diplopia, pain, edema and conjuctivitis on the right eye. Steroid treatment was started and she was referred to our hospital because of total ophtalmoplegia on her right eye. Physical examination revealed additional right eye chemosis and edema. Eye movements were restricted in all directions with fix-dilated pupilla and cherry red spots were present in fundus examination. Her laboratory findings were as follows; leucocyte: 12.480/mm$^3$, neutrophile count: 72%, C-reactive protein (CRP): 8.6 mg/dL, random serum glucose level: 306 mg/dL, arterial pH: 7.46, keton level in spot urine: 50 mg/dL and serum creatinine level: 0.77 mg/dL. After the endocrinology consultation, 10 units of crystaline insulin, three times per day and 12 units of insulin glargine were started. Orbital computed tomography revealed linear density enhancements in the soft tissue compartment of right preceptal and buccal areas which were considered as inflammatory process and preorbital cellulitis (Figure 1). The patient was internalized in the ophthalmology clinic with piperacilin-tazobactam (4,5 gr q8h i.v.) plus linezolid (600 mg q12 h i.v.) for preorbital cellulitis. After five days of treatment control magnetic resonance imaging (MRI) results were compatible with fungal infection which infiltrated all of the compartments of right eye, right cavernous sinus and occluding right internal carotid artery (Figure 2). After this MRI result, the patient was transferred to infectious diseases clinic with the diagnosis of mucormycosis. Her vital signs were; temperature 37°C, pulse 77/min, TA: 103/62 mmHg and respiratory rate:18/min. Piperacilin-tazobactam was switched to meropenem (1 gr q8h i.v.). Additionally amphotericin B

**Correspondence:** Ugur Onal, Ege University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Bornova Izmir Turkey Email: ugur.onal@ege.edu.tr
Received: 06 July 2015, Accepted: 06 August 2015

deoxycholate 1 mg/kg was started but due to allergic reactions, it was switched to liposomal amphotericin B (LAMB-5mg/kg/day). Ethmoidal and sphenoidal sinus biopsies were performed endoscopically, by otolaryngology. Sphenoidal sinus biopsy specimens were reported as mucormycosis in the pathologic examination. The patient was consulted to the ophtalmotology, plastic surgery and Ear Nose Throat clinics and Department for debridement. The surgical debridement was not found applicable by the surgical consultants. The dose of LAMB B was increased to 7 mg/kg/day on the 10th day of LAMB. After six days, posaconazole (400 mg/day q12h p.o.) was added due to no clinical improvement and worsening of the patient's headache. Control cranial MRI (Figure 3) showed progression to the cavernous sinus and internal carotid artery and therefore LAMB was increased to 10mg/kg/day and deferasirox was added (20 mg/kg/day p.o.) on the 15th day of treatment. Deferasirox was given to the patient for two weeks. After that, control cranial MRI (Figure 4) results were stable when compared to previous MRI. On the 30th day of LAMB dose was decreased to 7 mg/kg/day and meropenem plus linezolid were stopped. The patient was discharged with posaconazole (800 mg/day in 2 divided doses p.o.) after 47 days of liposomal amphotericin B treatment. There was no relapse on six month follow-up of the patient with posaconazole which was given for three months at all.

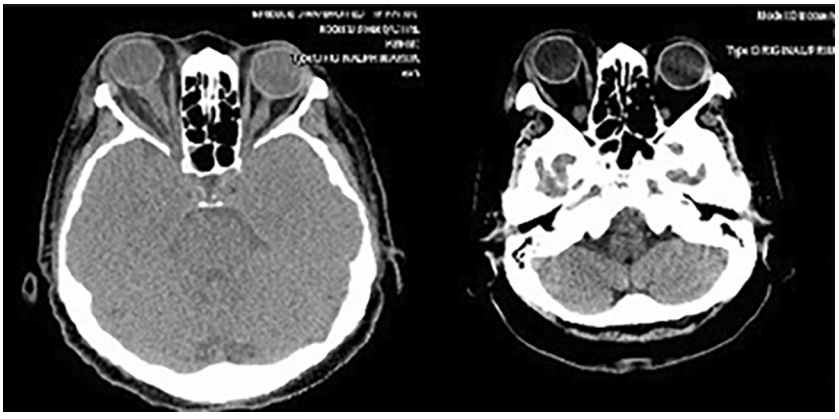

**Figure 1.** Orbital computer tomography.

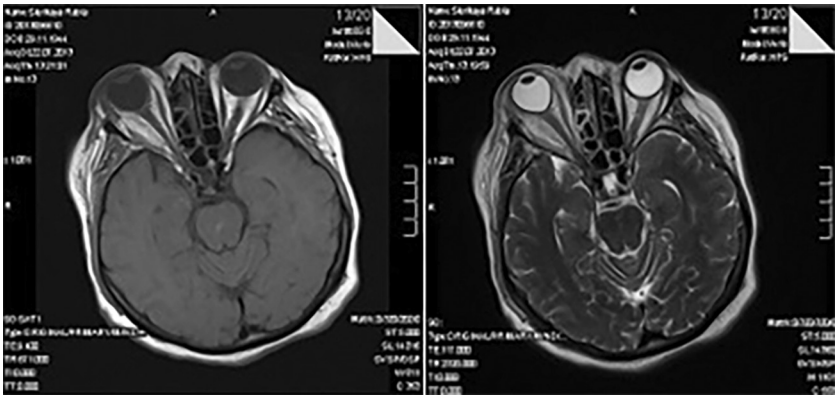

**Figure 2.** Cranial Magnetic Resonance Imaging (T1/2 weighted horizontal sections).

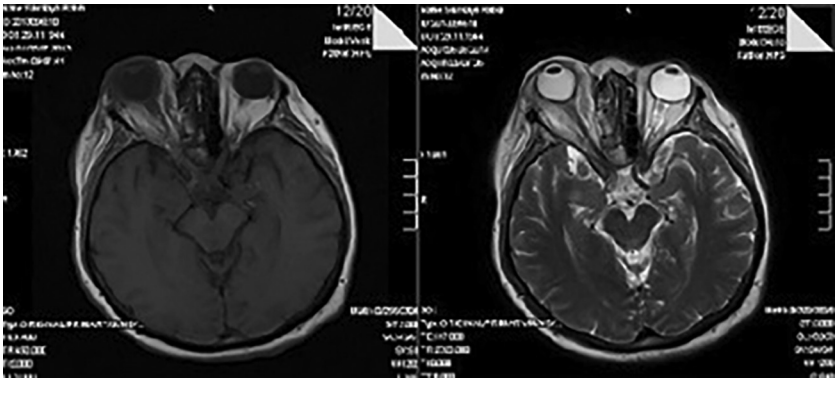

**Figure 3.** Cranial Magnetic Resonance Imaging (T1/2 weighted horizontal sections).

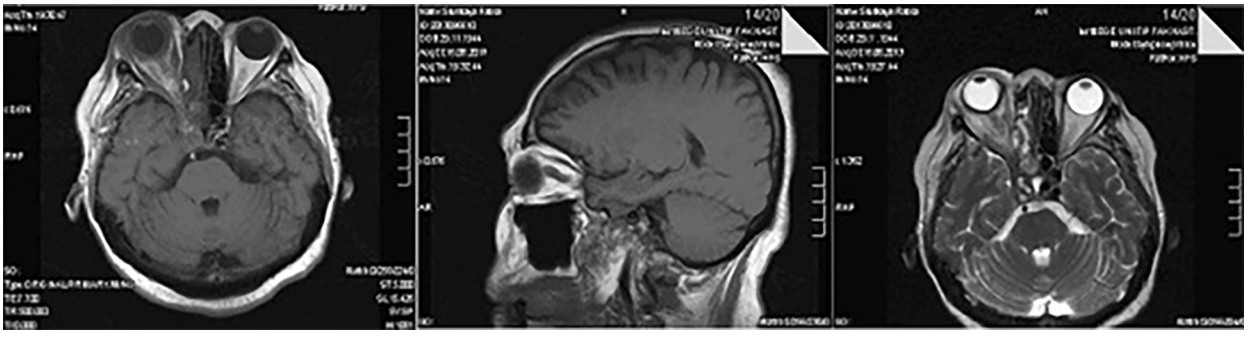

**Figure 4.** Cranial Magnetic Resonance Imaging (T1/2 weighted horizontal and sagittal sections).

## DISCUSSION

Mucormycosis is manifested by a variety of different syndromes in humans such as rhino-orbito-cerebral, pulmonary, renal and disseminated forms particularly in immunosuppressive and diabetic patients. Mucor, Rhizopus, Rhizomucor and Absidia species are classified in the Mucorales order and they are the main pathogens of mucormycosis. Diabetes, hematologic malignancies and immunosuppressive therapies such as long term steroid treatment are the major risk factors for invasive fungal infections and mucormycosis. Disseminated or pulmonary forms are common in patients with immune deficiency while rhinocerebral form is common in diabetes mellitus [1-4]. Management consists of surgical debridement and antifungal therapy. First-line antifungal treatment is considered as an amphotericin derivative, preferably with liposomal amphotericin due to less nephrotoxicity. Oral posaconazole treatment is used for either as a salvage therapy or as step-down therapy. In addition to this, uncontrolled diabetes is an important risk factor for mucormycosis thus control of hyperglycaemia and ketoacidosis is suggested [5]. In our case, the patient was followed up carefully via insulin treatment in the terms of glycemic control.

The possible utility of oral iron chelating agent, deferasirox, as an adjunctive therapy for mucormycosis has been evaluated in small studies, with conflicting results [5,6]. In this report, we presented a 69 years old diabetic patient with mucormycosis which was succesfully treated with liposomal amphotericin B (LAMB), posaconazole and deferasirox.

Despite developments in the antifungal therapy mucormycosis may still cause more than 50% mortality [1]. Prompt diagnosis and antifungal-surgical treatments are important steps in the management [1,5]. The diagnosis of the case was confirmed by the pathological examination of the biopsy. However, mycologic culture did not reveal the pathogen probably since it was performed after the antifungal therapy. Although optimum treatment is considered to be combination of antifungal and surgical therapy, the case could not receive optimum surgical debridement.

Elevated serum iron level which was shown by clinical and animal trials is a risk factor for mucormycosis. Deferasirox is a novel iron chelator, which is proposed to be a non-antifungal therapeutic candidate for the salvage therapy of mucormycosis. Ibrahim et al. [6] reported that 28 of 29 clinical Mucorales isolates were inhibited in vitro by the deferasirox iron chelation and when this iron chelator, deferasirox, was administered to diabetic ketoacidotic or neutropenic mice, a significant improvement of survival rates and host inflammatory response plus reduced fungal tissue burden with combination of LAMB were observed. However, in clinical practice there are success and failure reports related to deferasirox in mucormycosis. Spellberg et al., compared LAMB + deferasirox with LAMB+placebo in a small randomized controlled trial [7]. Eleven patients in the deferasirox arm and nine patients in the placebo arm were compared in terms of survival but deferasirox combination did not reveal any significant advantage. Only four patients (36%) completed the two weeks of treatment in the deferasirox arm, whereas seven patients (78%) in the placebo arm. On the other hand malignancy, corticosteroid treatment and neutropenia in the deferasirox arm were more likely than the placebo group and were less likely to receive non-study antifungal agent at the same time. Because of these population imbalances, a strong recommendation about using the deferasirox as an adjunctive treatment for mucormycosis is difficult to assess. In the presented case deferasirox was started as the latest salvage thera-

py option and the result was survival in combination with LAMB and posaconasole.

Histopathological examination of the tissue samples is one of the major diagnostic tools in mucormycosis as in our case. Characteristic histopathological findings are infarcts (94%), angioinvasion (100%), perineural invasion (90%) and hyphal branches varying from 45 to 90 degrees (95%) [8]. Rüping et al reported a total number of 41 mucormycosis patients that 26 (63.4%) were diagnosed via histopathology [9].

To our knowledge this is the first case of mucormycosis from Turkey related to deferasirox usage in the treatment of mucormycosis. In high risk groups, mucormycosis should be kept in mind for early diagnosis and combination of high dose LAMB and posaconasole as well as deferasirox may be successful in the salvage treatment especially in cases in whom adequate surgical debridement cannot be performed.

**Declaration of Conflicting Interests:** No conflict of interest of any author exists.

**Financial Disclosure:** The authors declared no financial support.

## REFERENCES

1. Zeka AN, Taşbakan M, Pullukçu H, et al. Evaluation of zygomycosis cases by pooled analysis method reported from Turkey. Mikrobiyol Bul 2013;47:708-716.
2. Roden MM, Zaoutis TE, Buchanan WL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis 2005; 41:634-653.
3. Aslan M, Öz Y, Akay MO, Akşit F. Evaluation of febrile neutropenia in hematologic malignancy patients. Mediterr J Infect Microb Antimicrob 2014; 3:20.
4. Özden M, Denk A, Demirdağ K, Elkıran T. Investigation of Febrile Neutropenic Cases and Risk Factors. Mediterr J Infect Microb Antimicrob 2014;2:3.
5. Cornely OA, Arikan-Akdagli S, Dannaoui E, et al. ESCMID and ECMM Joint Clinical Guidelines for the Diagnosis and Management of Mucormycosis 2013. Clin Microbiol Infec 2014; 20 Suppl. 3:5-26.
6. Ibrahim AS, Gebermariam T, Fu Y, et al. The iron chelator deferasirox protects mice from mucormycosis through iron starvation. J Clin Invest 2007;117: 2649-2657.
7. Spellberg B, Ibrahim AS, Chin-Hong PV, et al. The Deferasirox–AmBisome Therapy for Mucormycosis (DEFEAT Mucor) study: a randomized, double-blinded, placebo-controlled trial. J Antimicrob Chemother 2012;67:715-722.
8. Frater JL, Hall GS, Procop GW. Histologic features of zygomycosis: emphasis on perineural invasion and fungal morphology. Arch Pathol Lab Med 2001; 125: 375-378.
9. Rüping MJ, Heinz WJ, Kindo AJ, et al. Forty-one recent cases of invasive zygomycosis from a global clinical registry. J Antimicrob Chemother 2010; 65:296-302.