Rhino-orbital Mucormycosis in a Diabetic Patient: A Case Report

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ABSTRACT

Mucormycosis is a rare opportunistic fungal infection that occurs mainly in immunocompromised patients such as those with diabetes and blood diseases. Uncontrolled underlying immunocompromising conditions predispose patients to rhino-orbital-cerebral mucormycosis, which is life-threatening. We report a 45-year-old man with uncontrolled type 2 diabetes mellitus presenting with a two-week history of left nasal pain, headache, and fever. The biopsy of nasopharynx revealed fungal infection. After a two-week treatment with liposomal amphotericin B, his clinical condition improved. He was discharged and followed-up at our clinic for diabetes treatment without antifungal step-down therapy. At the 3-month follow-up, his HbA1c level had decreased to 5.9% without mucormycosis recurrence. Conventionally, mucormycosis is treated by surgical debridement, but it can also be simply and alternatively treated via medical therapy and the control of underlying immunocompromising conditions, as we have in this case. This case provides the important reference values for clinical alertness, prompt diagnosis, and alternative treatment strategy.


Key words: Mucormycosis, Diabetes mellitus, Amphotericin B

Introduction

Mucormycosis is a rare opportunistic fungal infection caused by members of the family Mucoraceae. Clinically, mucormycosis occurs mainly in immunocompromised patients, such as people with diabetes and...
blood diseases, and can cause infections in various parts of the body.[1-3] The commonly affected parts are rhino-orbital-cerebral regions (44-49%), subcutaneous tissue (10-16%), lung (10-11%), and gastrointestinal regions (2-11%).[1,4] Uncontrolled diabetes and tooth extraction predispose patients to rhino-orbital-cerebral mucormycosis, which is life-threatening.[3] Herein, we describe a case involving a patient with uncontrolled diabetes who presented with nasal pain and was initially diagnosed with suspicious nasopharyngeal carcinoma (NPC). Subsequently, he was referred to our hospital. Without any delay, mucormycosis without central nervous system involvement and malignancy was diagnosed, and the patient was successfully treated with liposomal amphotericin B instead of step-down therapy.

Case Report

A 45-year-old man presented with a two-week history of left nasal pain, throbbing headache, and intermittent fever. He had been diagnosed with type 2 diabetes mellitus but received no therapy. Initially, he had visited another hospital because of persistent symptoms. Head and neck computed tomography (CT) and sinoscopy showed left maxillary sinus mucosal thickening. He was referred to our hospital because of suspected NPC. At presentation, his body mass index (BMI) was 23.6kg/m². We observed no appearance-related abnormalities, jaundice, or defects in vision. Investigations upon admission showed the following: white blood cell count, 10.85×10³/uL (91.2% neutrophil); platelet count, 351×10³/uL; and haemoglobin, sodium, potassium, creatinine, and glycated haemoglobin (HbA1c) levels of 14.7g/dL, 131mmol/L, 4.5mmol/L, 0.9mg/dL, and 16.4%, respectively. Urinalysis showed ketonuria and glycosuria. We prescribed empirical oxacillin for facial soft tissue infection. Magnetic resonance imaging (MRI) and sinoscopy performed two days after admission revealed left para-nasopharyngeal swelling and mucus discharge, with soft tissue obstruction at the sinus opening (Figure 1A, 1B). Biopsy revealed many broad non-septated fungal hyphae branching at 90° and numerous neutrophils and histiocytes within the necrotic debris (Figure 1C). Staining with periodic acid-Schiff and Grocott's methenamine silver was positive. After confirming nasal mucormycosis, we prescribed amphotericin B deoxycholate (AmBd), 1mg/kg/day on the fourth day of admission. However, acute kidney injury and hypokalemia developed after three days of AmBd treatment. Hence, we started administering 8mg/kg/day of liposomal amphotericin B, and his renal function returned to normal. After two weeks of liposomal amphotericin B treatment, follow-up sinus MRI revealed slight improvement in chronic sinusitis and mastoiditis. His clinical condition improved, nasal tenderness disappeared, and sinoscopy showed clinical improvement. Unfortunately, the pathogenic molds could not be cultured successfully. He was discharged and followed up at our clinic for diabetes using injectable insulin treatment without antifungal step-down therapy (posaconazole or isavuconazole). At the 3-month follow-up, his HbA1c levels had decreased to 5.9% without mucormycosis recurrence. Serum creatinine also recovered to 0.74mg/dL. Furthermore, a repeat sinoscopy showed decreased necrotic mucosa and discharge (Figure 2).
Figure 1. Initial magnetic resonance imaging of the left maxillary sinus (a), sinoscopic findings (b), and periodic acid-Schiff-stained biopsy specimen (c).

Figure 2. Follow-up left maxillary sinus computed tomography (a) and sinoscopic findings (b).
Discussion

Mucormycosis is a rare opportunistic fungal infection caused by Mucorales. Agents of mucormycosis are ubiquitous fungi in environments commonly found in decaying organic substrates including bread, fruits, vegetable matter, soil, compost piles, and animal excreta. Rhino-orbital-cerebral mucormycosis, the most common spore-inhalation-related mucormycosis, is initially localized to the nasal turbinates and paranasal sinuses following inhalation of spores. It can rapidly progress to the orbit or brain, particularly in patients with diabetic ketoacidosis or profound neutropenia. Infection usually starts with fever, nasal ulceration/necrosis, periorbital/facial swelling, vision defects, eye pain, and sinusitis. Our patient presented classic symptoms, including nasal pain. Rhizopus species predominantly cause rhino-orbital-cerebral mucormycosis. Usually, the molds cannot be cultured. Patients with suspected rhinocerebral mucormycosis need to undergo a thorough examination, including CT scan of the paranasal sinuses and endoscopic examination of nasal turbinates with biopsy of any suspicious lesions or necrotic eschars. Diagnosis is based on direct microbiological exam and histopathological findings. In tissues, Mucorales hyphae can often be distinguished from other more common opportunistic molds such as Aspergillus and Fusarium by their broad (3- to 25-μm diameter), empty, thin-walled, mostly aseptate hyphae. Clinically, mucormycosis is often misdiagnosed as NPC. However, an MRI can be used to accurately diagnose NPC. On T2-weighted images, NPC usually shows intermediate signal intensity higher than muscle signals, with low signal intensity on T1-weighted images. On MRI, mucormycosis lesions tend to be isointense or hypo-intense in all sequences. Treatment includes surgical debridement and elimination of the underlying conditions (hyperglycemia and neutropenia). In rhinosinusitis, surgical debridement of infected tissue is a crucial component of therapy and should be urgently performed to limit the aggressive spread of infection to contiguous structures. Regarding medical treatment of mucormycosis, no prospective studies on the primary treatment of mucormycosis have been performed owing to its rarity and heterogeneous nature. Evidence concerning the activity of existing antifungals has come from small case series, anecdotal case reports, and animal models of infection. The antifungal of choice is AmBd or liposomal amphotericin B. For this case, we did not use step-down therapy with posaconazole or isavuconazole, as both were unavailable in our hospital. Isavuconazole has been reported to have an anti-mucormycosis effect similar to AmBd. Overall mortality due to rhino-orbital-cerebral mucormycosis ranges from 25% to 62%, and the prognosis is better among patients with sinus-confined infection.

In conclusion, successful management of mucormycosis includes prompt control of underlying immunocompromising conditions, like diabetes mellitus in this case, and an immediate initiation of high dose of liposomal amphotericin B treatment. The findings from this case may provide the important reference values for clinical alertness, prompt diagnosis, and alternative treatment strategy.

Conflicts of Interest Statement

The authors declare no conflicts of interest.


侵犯鼻腔眼窩的白黴菌病：
一名糖尿病病例報告
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摘 要

白黴菌病(Mucormycosis)為臨床上罕見的黴菌感染，以侵犯糖尿病和血液病等免疫不全的病人為主。不受控制的免疫不全病症皆易使患者在鼻腔、眼窩及顱內等部位感染到危及生命的白黴菌病。我們報告一位糖尿病控制不佳的45歲男性，出現了兩周的左鼻部疼痛，頭痛及發燒等病史。鼻咽切片顯示為黴菌感染。用liposomal amphotericin B治療兩周後臨床症狀改善即出院，在門診接受積極血糖控制治療且未接受抗黴菌的降壓治療。3個月後HbA1c降到5.9%，且患者的白黴菌病也未曾再復發。通常白黴菌病都須經由反覆的手術清創來完成治療，但也可以如同本個案一般，簡單地或選擇性地通過藥物給予和控制潛在的免疫不全條件來進行治療成效，病人也有良好的預後。本案例為臨床高度警覺、及時診斷與替代治療策略選擇提供了重要的參考價值。

關鍵詞：白黴菌病、糖尿病、Amphotericin B