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Case Report

Hospital Dentistry Approach to a Patient with Mucormycosis treated with Amphotericin B: Case Report

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Abstract: This study addresses rhino-orbito-cerebral mucormycosis, a serious and opportunistic fungal infection, especially in immunosuppressed patients, such as those with type II diabetes mellitus. The study highlights the importance of a multidisciplinary approach in diagnosing and treating this condition, emphasizing collaboration between medical and dental specialties. Through a clinical case, it demonstrates how early and coordinated intervention can minimize the devastating consequences of the infection, underscoring amphotericin B, especially in its liposomal form, as the preferred treatment and the need for surgical debridement. The study reinforces the vigilance and early recognition of mucormycosis symptoms, particularly in patients with risk factors such as uncontrolled diabetes, illustrating the importance of integration between different medical fields in managing complex diseases.

Keywords: Rhino-orbito-cerebral mucormycosis; Multidisciplinary approach; Type II diabetes mellitus; Amphotericin B.

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1. Introduction

Mucormycosis (*zygomycosis*) is a rare and severe opportunistic fungal infection associated with fungi from the Mucorales order. Popularly known as "black fungus" during the COVID-19 pandemic, it primarily affects patients with compromised immune systems [1, 2]. Mucormycosis poses significant risks, especially to individuals with type II diabetes mellitus, due to the weakening of the immune system. This infection is notably angioinvasive, causing extensive tissue destruction and is often observed in the rhino-orbital/cerebral and pulmonary-sinus regions, resulting from the inhalation of environmental spores. In the presence of abnormal iron levels, these spores can germinate and evade the host's immune response, leading to severe complications [3]. A recent systematic review focused on the oral manifestations of mucormycosis, highlighting the importance of early recognition to improve treatment outcomes and reduce mortality. Common oral manifestations identified include bone exposure, oral ulcers, halitosis, purulent discharge, gingival thickening, and periodontitis. These symptoms underline the aggressive nature of mucormycosis when it invades oral tissues, emphasizing the need for immediate medical intervention.

The clinical manifestations of mucormycosis can vary, including localized cutaneous infections in immunocompromised patients or pulmonary involvement, which can be identified through specific radiological signs. Despite the varied presentations, the

underlying immunological interactions, particularly involving alveolar macrophages and their inability to effectively kill Mucorales spores, play a critical role in disease progression [4]. Case studies further illustrate the diverse manifestations of mucormycosis in the oral cavity, with some cases showing involvement of the maxillary sinus leading to facial swelling, nasal congestion, and, in severe cases, destruction of facial structures. These clinical cases underscore the aggressive nature of mucormycosis and its potential to cause significant morbidity if not diagnosed and treated promptly [5]. The reviewed studies emphasize the critical role of healthcare professionals in recognizing the early signs of oral mucormycosis, crucial for initiating timely and effective treatment. This approach is essential for managing the infection and mitigating its severe consequences.

Here, we present a clinical case of mucormycosis infection in a patient with type II diabetes mellitus, significantly contributing to their vulnerability to mucormycosis, aligning with studies reporting on the prevalence and severity of the disease in diabetic individuals. The suspected diagnosis, subsequent medical interventions, and the challenges encountered in this case reflect the complex interaction between the pathogen and the compromised immune response of the host, highlighting the need for rapid and effective treatment strategies to mitigate the risks associated with this formidable infection.

2. Case Report

A 44-year-old man, diagnosed with type II diabetes mellitus, sought emergency care at the General Hospital of Fortaleza, in Ceará, presenting significant extraoral edema on the left side, accompanied by loss of vision in the left eye and paresthesia in the cranial nerves II, III, IV, V, and VI on the same side. Given this situation, the medical team requested a consultation with the Hospital Dentistry team for the removal of a fixed orthodontic appliance. This procedure was necessary to eliminate potential interferences (artifacts) during a magnetic resonance imaging examination the patient was scheduled to undergo, aiming for a more accurate diagnosis of his condition.

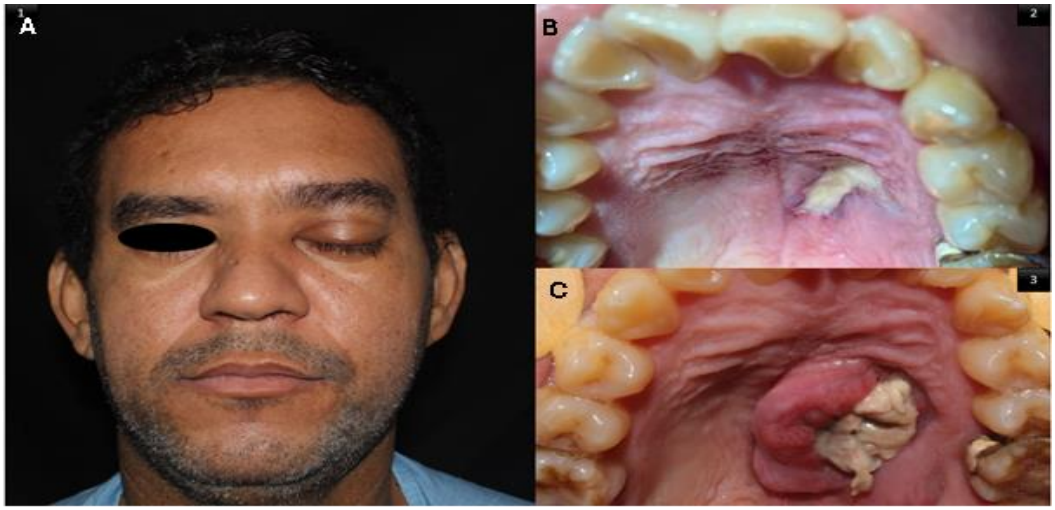
The patient was evaluated in his bed within the unit where he was admitted. During the clinical examination, partially present dentition, and a lesion on the hard palate, located in the same region as the observed extraoral edema (Figure 1), were identified. After the evaluation, the orthodontic appliance was removed. The patient could not specify the duration since the lesion appeared. Throughout the consultation, the affected area was carefully palpated, and the patient denied experiencing pain upon touch. Attempts at drainage were made, but no purulent secretion was released. Given these findings, the medical team suspected mucormycosis and recommended starting treatment with amphotericin B.

In line with the diagnostic hypothesis, the patient was evaluated by the otorhinolaryngology team, which, during the clinical examination, identified signs of a fungal infection and agreed with the need to start antifungal treatment. On the first day of his hospitalization, an incisional biopsy of the affected area was performed using local anesthesia with 2% mepivacaine. Based on the clinical findings, the decision was made to empirically start antifungal therapy with amphotericin B, administering 50 mg of the medication diluted in 10 mL of a specific diluent, followed by a dilution in 5% glucose solution, to be infused intravenously every 24 hours. This approach was adopted while waiting for the results of the histopathological analysis.

The outcome of the first biopsy indicated a mild lymphoplasmacytic inflammatory process and fibrosis, without the detection of fungi. Despite this negative result for the presence of fungi, the administration of amphotericin B was maintained, given the correspondence between the clinical signs and symptoms presented by the patient and the characteristics associated with mucormycosis described in the medical literature. The patient remained under the integrated care of the otorhinolaryngology, ophthalmology, and dentistry teams. During the treatment, the patient developed acute renal failure attributed to the use of amphotericin B deoxycholate, leading to the substitution of this

drug with the liposomal version of amphotericin, aiming to minimize risks and adverse effects. A left maxillary antrostomy and debridement were performed by the otorhinolaryngology team, as the patient presented with pansinusitis, and the histopathological result of the specimens collected during this debridement was positive for mucormycosis, thereby diagnosing the patient with rhino-orbito-cerebral mucormycosis.

Figure 1. A. Extraoral appearance of the patient. B. Initial appearance of the lesion on the palate after removal of the appliance. C. Appearance of the lesion on the palate before the approach in the surgical center.



It was essential to remove the infected tissue from the palate (Figure 2), so a surgical debridement was scheduled in a surgical environment (Figure 3). Anticipating the outcome of the procedure, which included the possibility of communication between the oral and nasal cavities due to the involvement of the palatine bone, an impression of the upper arch was made. Based on this impression, a temporary palatal obturator was fabricated. The purpose of this device was to prevent the entry of food into the nasal cavity, thus ensuring proper functionality and quality of life for the patient during the post-surgical recovery period.

Due to the growth of the lesion, the established surgical plan involved the debridement of the palate and the left maxillary sinus. The operation was performed under general anesthesia and lasted about 2 hours. At the end of the procedure, a temporary prosthesis was installed. The material removed during the surgery was sent to the hospital's pathology laboratory for histopathological analysis, aiming to obtain a diagnostic confirmation. The histopathological results revealed coagulative necrosis associated with a predominantly neutrophilic inflammatory infiltrate and the presence of thick, septate hyphae that branched at right angles, characteristics suggestive of mucormycosis. The identification of spores from the zygomycetes group, as described in the histopathological examination, is typical of this fungal group, which includes genera such as *Absidia, Cunninghamella, Mucor*, and *Rhizopus* (Figure 4).

In the context of a multidisciplinary treatment at a surgical center, the patient in question underwent multiple interventions to address a complex condition. Initially, in addition to the primary surgical approach, the patient underwent an additional surgical debridement procedure performed by the Otorhinolaryngology team. During this procedure, the surgical site was carefully irrigated with amphotericin, an antifungal, to prevent infections. Simultaneously, the Ophthalmology team conducted an endoscopic decompression of the orbit, a delicate procedure aimed at relieving pressure in the affected area.

Figure 2. Axial CT scan showing the infected area of the palate on the left side.

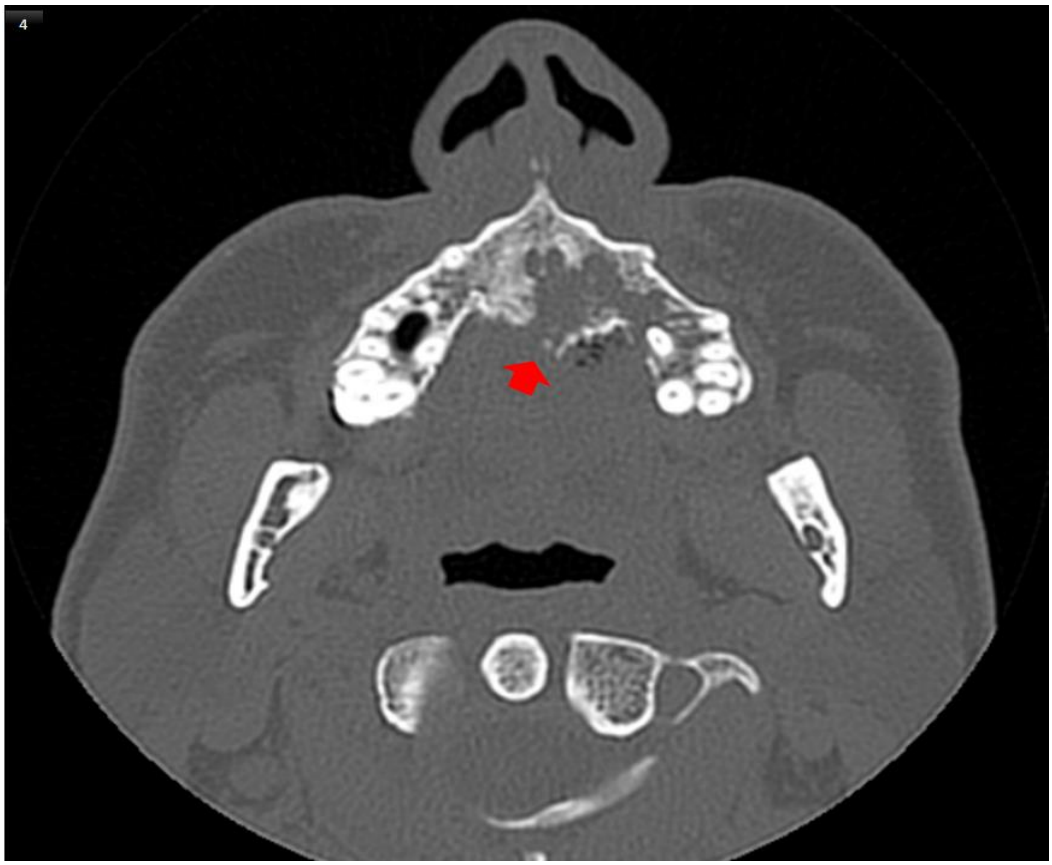
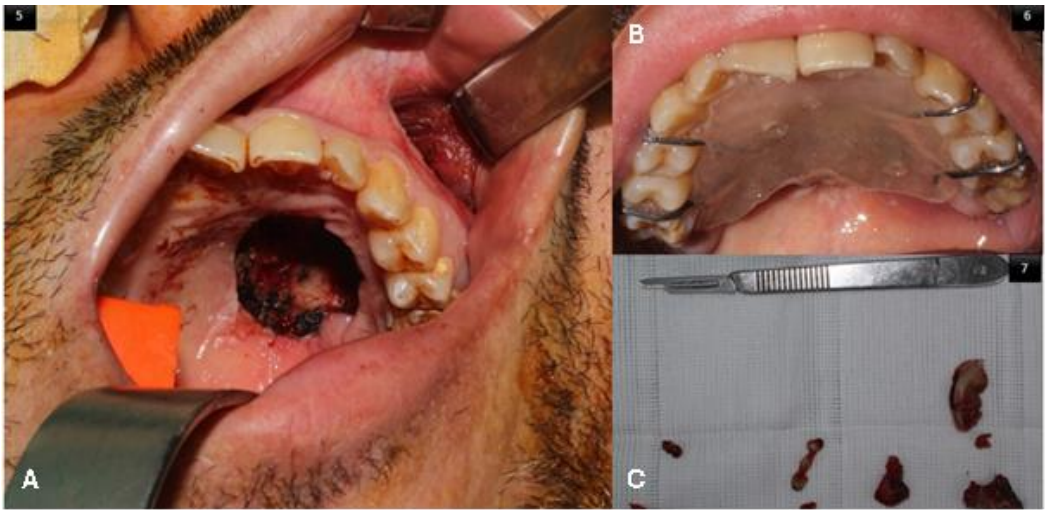


Figure 3. A. Intraoperative view after the removal of infected tissue. B. Patient using a temporary obturator plate in the immediate postoperative period. C. Lesional fragments removed during debridement that were sent for histopathological analysis.



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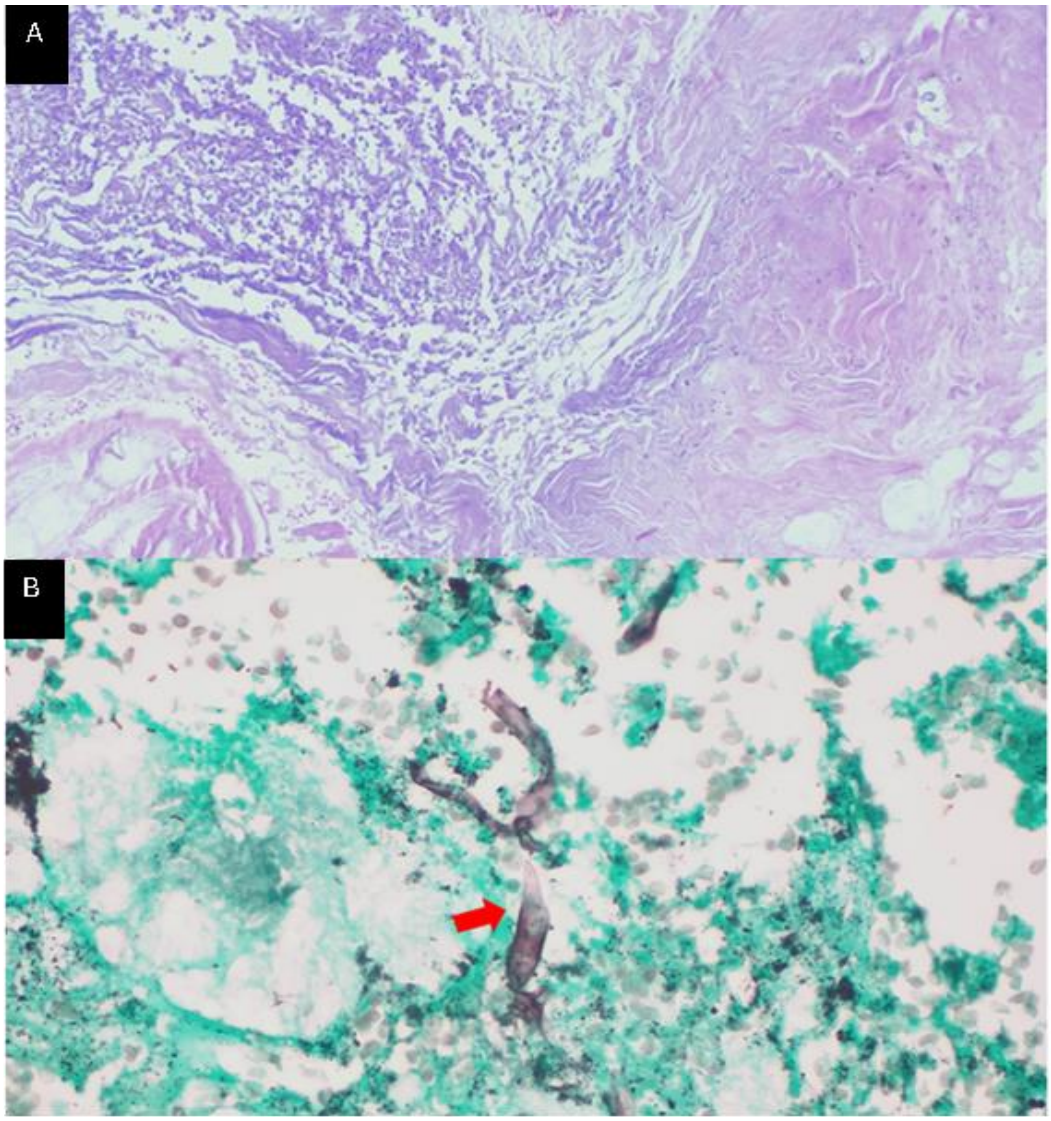
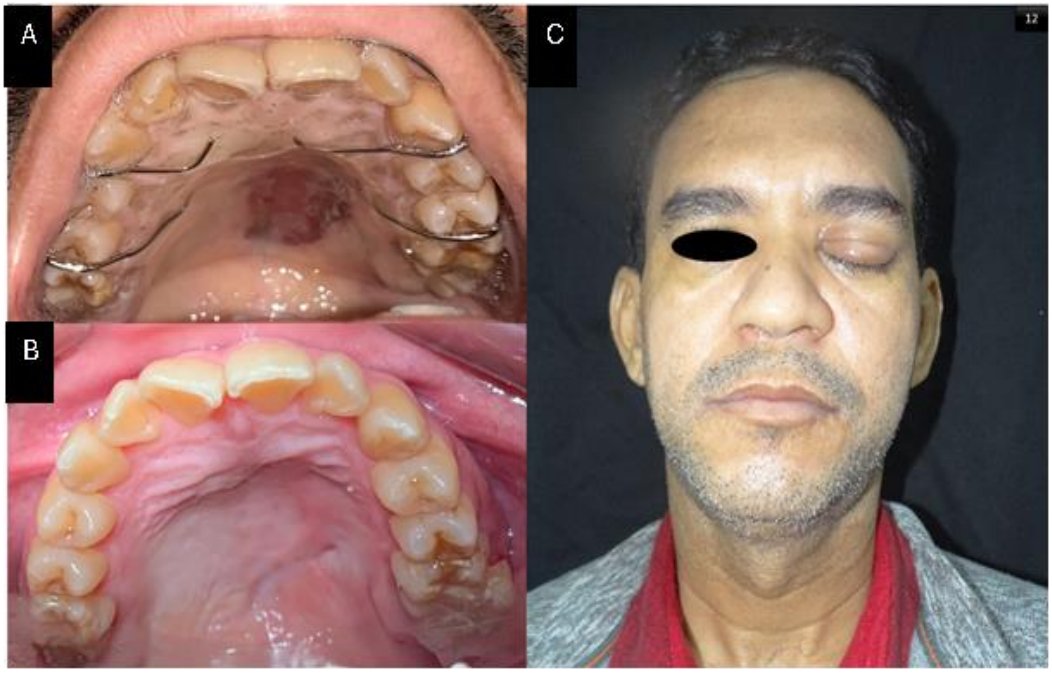
During this intervention, a specific drain was installed to allow daily administration of intraocular amphotericin, aiming to maximize the effectiveness of the treatment in the ocular region. After the palatine region, which had been damaged, healed, a molding procedure was carried out using condensation silicone. This step was crucial for the creation of a definitive palatal obturator, an essential device that allowed the patient a significant improvement in quality of life, enabling the transition from a thickened to a soft diet. The patient's glycemic control was carefully managed through the administration of NPH and regular insulin, crucial for the stability of his health condition. During hospitalization, the patient also received a regimen of antibiotics, which included meropenem, piperacillin with tazobactam, metronidazole, ceftriaxone, and oxacillin, administered concurrently with amphotericin, to combat and prevent infections.

Figure 4. A. Histological slide showing an area of coagulative and liquefactive necrosis - Hematoxylin and eosin staining. Magnification x 200. B. Histological slide showing thick fungal structure with septation and dichotomization at right angles – Grocott staining. Magnification x 400.



Currently, the patient continues to receive outpatient follow-up in the specialties of Hospital Dentistry, Otorhinolaryngology, and Ophthalmology at the General Hospital of Fortaleza (HGF). Despite the success of various interventions, the ophthalmological damage incurred was unfortunately irreversible. During an outpatient dental follow-up, approximately 8 months after the surgery, it was observed that the patient had complete and spontaneous closure of the oro-nasal communication, indicating a positive progression in the recovery process (Figure 5).

Figure 5. A. Occlusal view of the definitive obturator device installed during hospitalization. B. Intraoral aspect 8 months postoperatively. Note the complete and spontaneous closure of the communication. C. Extraoral aspect 8 months postoperatively.



3. Discussion

Mucormycosis, known for its aggressiveness and vascular invasion, has an increasing incidence rate, mainly attributed to the rising number of individuals with immunosuppression. This fungal infection is notable for its high morbidity and mortality, often associated with conditions like diabetes mellitus, hematological malignancies, and solid organ transplantation. The rhino-orbital-cerebral form is the most prevalent clinical manifestation, often starting in the paranasal sinuses and potentially progressing to serious complications, including vision loss and brain invasion [6].

Diagnosing mucormycosis requires a multimodal approach, including radiological evaluation to determine the disease's extent and biopsy for histopathological analysis, revealing the hyphae characteristics associated with this infection. Treatment is challenging, necessitating early diagnosis, surgical debridement, and intravenous antifungal administration, with amphotericin B being the frontline therapy. Mucormycosis is not limited to the rhino-orbital-cerebral form; its pulmonary, cutaneous, and gastrointestinal variants present distinct symptoms crucial for accurate disease diagnosis and management [7]. Effective management involves a multidisciplinary team and a deep understanding of its various clinical manifestations and therapeutic options.

This case report emphasizes diabetes mellitus as a significant comorbidity in patients, highlighted in Jeong et al.'s meta-analysis [8], which found this condition in 40% of cases, surpassing hematological cancers and post-transplant conditions. Notably, in India, diabetes is the main risk factor for mucormycosis, unlike North America and Europe, where other conditions are more prevalent. The interplay between diabetes and

mucormycosis, particularly in glycemic mismanagement, underscores the importance of careful diabetes management in patients susceptible to this aggressive infection [9].

In the mucormycosis context, early diagnosis is crucial to prevent severe complications like angioinvasion, direct tissue damage, and progression to critical sites like the eyes and brain, reducing the need for extensive surgical resections and improving clinical outcomes [10]. Moreover, identifying host risk factors, such as diabetic ketoacidosis and prolonged corticosteroid use, plays a significant role in assessing the risk of invasive mucormycosis. The diagnostic approach should include careful clinical evaluation, early use of computed tomography (CT) and magnetic resonance imaging (MRI), and histological, microbiological, and molecular detection advancements [10]. A zebrafish model study demonstrated how mucormycosis induces apoptosis in infected macrophages, offering insights into pathogen-host interaction and potentially informing diagnostic and treatment strategies [11].

The discussion case also emphasizes the critical importance of Amphotericin B as the cornerstone of mucormycosis treatment, although its nephrotoxic potential necessitates considering alternatives like liposomal amphotericin B. Liposomal amphotericin B is recommended as a first-line therapy for mucormycosis due to its enhanced safety profile compared to the conventional formulation. Studies have shown that high-dose liposomal amphotericin B is effective in treating this fungal infection, significantly reducing mortality and the need for disfiguring surgical interventions [12]. Moreover, the surgical approach is crucial and should be conducted wherever possible, in parallel with antifungal treatment. In cases of renal failure, alternative medications like posaconazole or isavuconazole can be effective. Combining pharmacological, surgical, and rehabilitative treatments, such as implementing a palatal obturator, reflects the need for a multidisciplinary strategy to improve therapeutic outcomes and quality of life for patients affected by mucormycosis, especially those with significant comorbidities like diabetes mellitus [13].

Surgical intervention and proper management of underlying conditions are equally vital for a positive therapeutic outcome. Additionally, the case illustrates the implementation of a palatal obturator in post-surgical management, highlighting its multiple benefits in patient recovery and quality of life, including improved hygiene, swallowing, surgical site protection, and the restoration of crucial anatomical and physiological functions. This multidisciplinary approach, encompassing pharmacological, surgical, and rehabilitative treatment, reflects the care complexity needed for patients with mucormycosis, especially those with significant comorbidities like diabetes mellitus [14].

In summary, mucormycosis emerges as a fungal infection with severe consequences, with an increasing incidence that underscores the importance of meticulous clinical vigilance and management. The frequent association with comorbidities, particularly diabetes mellitus, and the need for a comprehensive therapeutic strategy, encompassing both medical and surgical treatments, emphasize the management complexity of this disease. Early and accurate diagnosis, coupled with effective treatment, is crucial for improving clinical outcomes in patients with mucormycosis, highlighting the need for a well-coordinated multidisciplinary team. This case report not only illustrates the significant impact of mucormycosis on patient health but also underscores the importance of awareness, timely diagnosis, and an integrated treatment approach to optimize recovery and quality of life for those affected by this challenging infection.

4. Conclusion

Mucormycosis, a severe and opportunistic fungal infection, presents significant challenges in the medical context, particularly in immunosuppressed patients, such as those with type II diabetes mellitus. This study emphasized the importance of a multidisciplinary approach in diagnosing and treating rhino-orbito-cerebral mucormycosis, highlighting the crucial interaction between medical and dental

specialties. Through a detailed clinical case, we observed how the early and coordinated intervention of specialists in dentistry, otorhinolaryngology, and ophthalmology could result in more effective disease management, minimizing the potentially devastating consequences of this infection. The case also underscored the vital role of amphotericin B, particularly its liposomal form, as the preferred treatment, along with the need for surgical debridement to control the infection's spread.

This study reinforces the need for vigilance and early symptom recognition of mucormycosis, particularly in patients with significant risk factors like uncontrolled diabetes. Interdisciplinary collaboration was crucial for therapeutic success, illustrating the importance of integration among different medical fields in managing complex diseases.

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Research Ethics Committee Approval: We declare that the patient approved the study by signing an informed consent form and the study followed the ethical guidelines established by the Declaration of Helsinki.

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Conflicts of Interest: None.

Supplementary Materials: None.

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