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Case Report

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Bilateral Blindness Associated with Rhino-Orbital-Cerebral Mucormycosis: A Case Series

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Abstract

Bilateral blindness caused by rhino-orbital-cerebral mucormycosis (ROCM) is a rare but serious complication that presents significant challenges for patients and clinicians. In this case series, we present two cases of mucormycosis-related blindness, including their clinical presentations, diagnostic approaches, management strategies, and outcomes. Our aim is to highlight clinical presentation of mucormycosis and visual impairment to emphasize the importance of early detection and aggressive intervention, to mitigate its potentially severe consequences.

Introduction

Rhino-orbital-cerebral mucormycosis, a rare life-threatening fungal infection due to its potential to cause extensive morbidity and mortality (1). It is caused by members of the Mucorales, the main organisms of these infections in humans are *Rhizopus*, *Mucor*, and *Rhizomucor* (2) . It is generally found in patients who have conditions that affect their immune system as uncontrolled diabetes, hematological malignancies or those who have undergone transplant surgery (1,3). Of the many serious complications, bilateral blindness is particularly devastating, having a huge impact on the quality of life for those affected including the family. There have been only a few reported cases of ROCM affecting both orbits (4–8). By presenting a series of cases in which bilateral blindness was a consequence of mucormycosis, we aim to emphasize the importance for early recognition, multidisciplinary collaboration, and aggressive medical and surgical interventions.

Case Presentation

Case 1

A 54-year-old male presented to the adult emergency department with fever, chills, and a unilateral oppressive headache that had been worsening for two weeks. A week later, he experienced left facial paralysis. Upon admission, he also had gum bleeding, eyelid edema, ophthalmoplegia, and a sudden, progressive, painless bilateral decrease in visual acuity (figure 1a). The patient had a recent diagnosis of untreated type 2 diabetes mellitus, untreated systemic arterial hypertension, and a six-month history of alcoholic hepatic cirrhosis treated with lactulose. Laboratory findings revealed anemia (hb 9.68 g/dl), thrombocytopenia (76,840 platelets), leukocytosis (14.2 thousand), elevated glucose levels (242 mg/dl), as well as altered renal function tests (serum creatinine 1.62 mg/dl, BUN 39.50 mg/dl) and hepatic function (GGT IU/L, total bilirubin 3.89, direct bilirubin 2.50, ALP 170 IU/L, ALT 16 and AST 40). During examination, necrotic tissue was observed in the right nasal cavity (figure 1b). Upon ophthalmological examination, bilateral negative of light perception in visual acuity, ophthalmoplegia, blepharoptosis, eyelid edema, chemosis, fixed and dilated pupils and right eye fundoscopy consistent with CRAO were observed (figure 1c). The left eye showed no alterations. The diagnostic suspicion is invasive mycosis, prompting both imaging and histopathological studies. Imaging, including cranial, orbital, and paranasal sinus CT scans, revealed sinusitis involving the left maxillary, ethmoid, and sphenoid sinuses, as well as orbital cellulitis (figure 1d). The trans-surgical histopathologic report of paranasal sinuses confirmed the presence of mucormycosis (figura 2a-d). The patient underwent bilateral orbital exenteration and extensive debridement of the nose and paranasal sinuses. Therapy with amphotericin B was initiated, with close monitoring of renal function. Post-surgery MRI showed bilateral globe exenteration and invasive sinusitis without intracranial involvement (figure 1e). However, the patient developed a fever 24 hours after surgery. Systemic invasion was ruled out by chest CT and blood cultures, but a week later, the patient's neurological and hemodynamic status deteriorated. Despite efforts, the patient's family opted for no cardiopulmonary resuscitation, and the patient died within 48 hours.

Case 2

A 38-year-old male presented to the adult emergency department with symptoms consistent with sinusitis and left eyelid edema that had been worsening for three months. He reported receiving unspecified oral antibiotic treatment. His condition aggravated over the past three weeks, with additional right eyelid edema one week later. On admission, he had elevated blood glucose levels (117 mg/dl). Due to suspicion of rhino-orbital mycosis, cranial, orbital, and paranasal sinus magnetic resonance imaging was performed, revealing bilateral predominantly left-sided pansinusitis and orbital cellulitis (figure 3a-b). Trans-surgical KOH cytology of the paranasal sinuses showed thick, hyaline, branched filaments characteristic of a mucoral fungus. Treatment with liposomal amphotericin B and systemic antibiotic therapy was initiated due to suspected bacterial coinfection. Within the initial twenty-four hours, the patient experienced a progressive decrease in visual acuity to

negative perception of light. Left orbital exenteration and extensive debridement of the nose and paranasal sinuses were performed. Histopathological findings confirmed mucormycosis (4a-b). Additional testing revealed HIV, MRI showed post-surgical changes in the left maxillary sinus and orbit, as well as sphenoidal, maxillary, and ethmoidal sinusitis; right orbit showed proptosis, extraocular muscle inflammation, and optic nerve sheath enhancement and meningeal enhancement predominated in the left frontal region (figure 3c). During the first week of in-hospital stay, the patient reported a progressive, painless decrease in visual acuity in the right eye, and in less than 24 hours, the patient presented with negative light perception loss, orbital exenteration was performed (figure 3d). Ultimately, two weeks after surgery patient developed neurological deterioration and hemodynamic instability, leading to death within 48 hours.

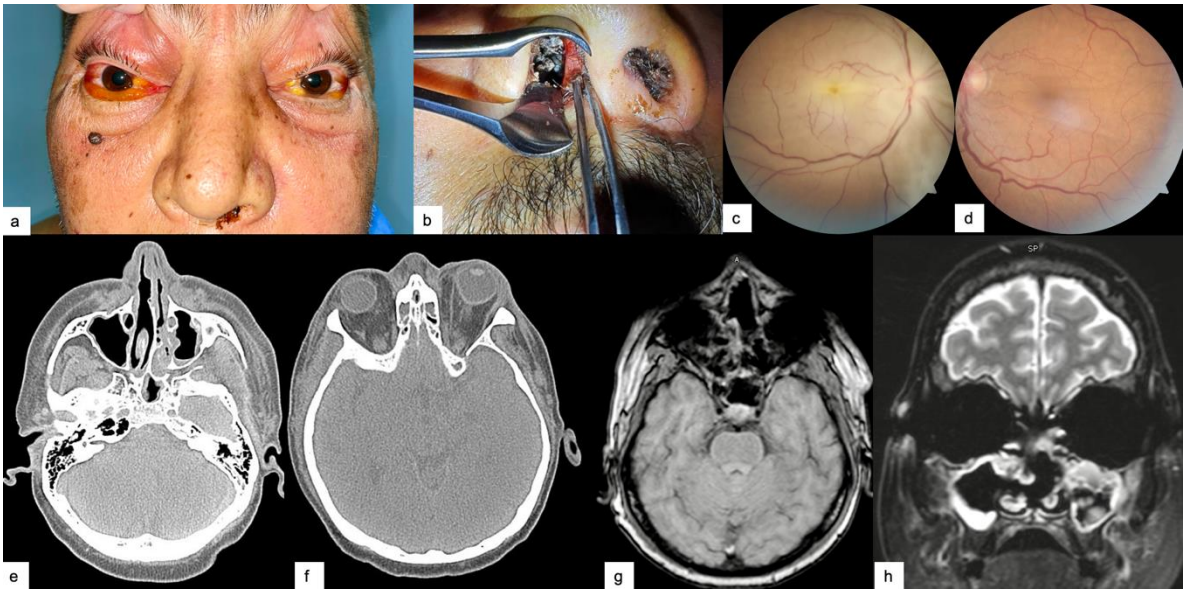

Figure1: (a) Ophthalmoplegia, blepharoptosis, eyelid edema, chemosis and fixed and dilated pupils. (b) Necrotic tissue in the right nasal fossa. (c) CRAO on right eye (d) left eye with no alterations (e) paranasal sinus CT revealed maxillary sinusitis and (f) orbita CT showed bilateral orbital cellulitis. (g,h) Orbita MRI bilateral globe exenteration.

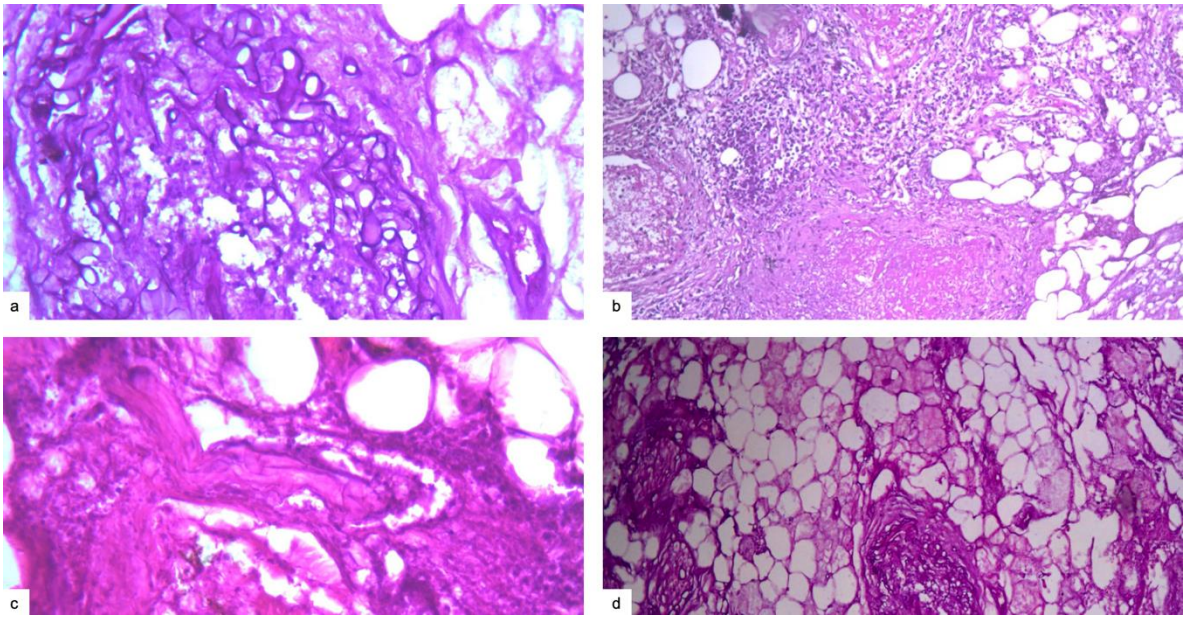

Figure 2: (a, b) Thick, and irregular hyphae consistent with mucormycosis.(c, d) Fibroadipose tissue with blood vessels occluded by masses of fungal hyphae and multiple areas of necrosis.

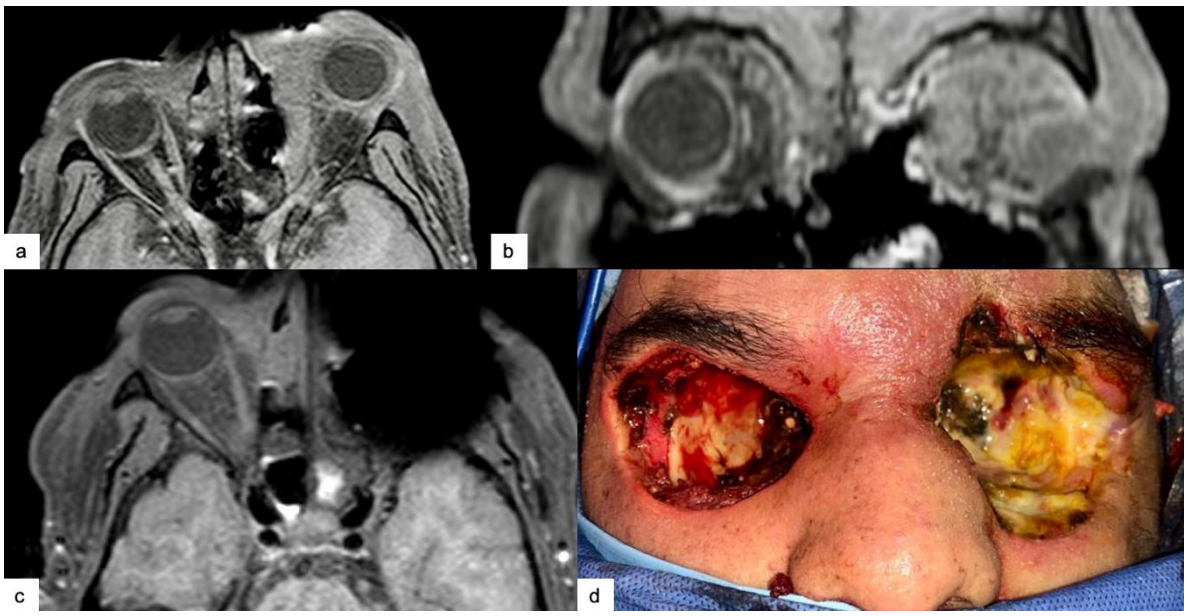

Figure 3: (a,b) Orbita MRI revealed orbital cellulitis predominantly left-sided. (c) Orbita MRI showed left globe exenteration and right orbit showed proptosis, extraocular muscle inflammation. (d) bilateral exenteration was performed.

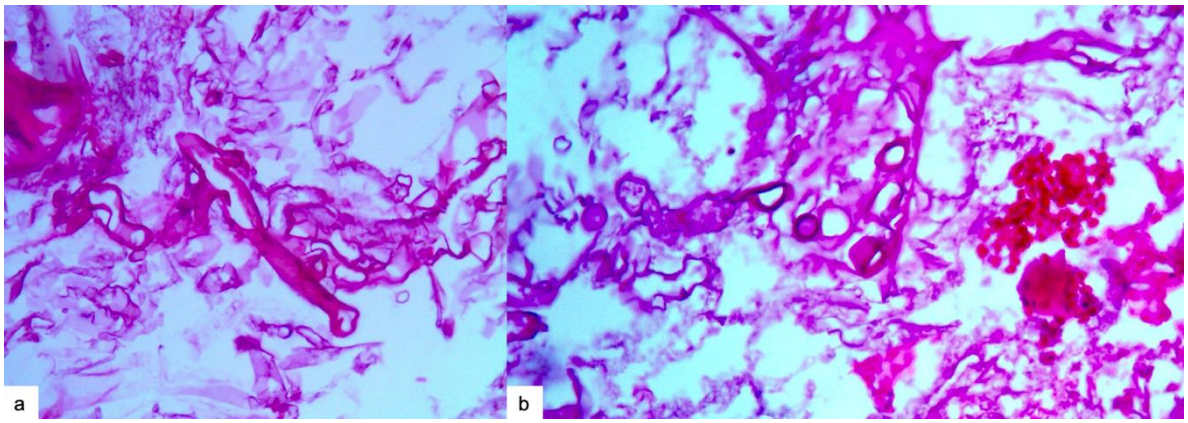

Figure 4: (a) PAS staining enhancing the red-purple outline of the irregular and thick hyphae. (b) Hyphae within the vascular wall, obliterating the vessel; on the right side, extravasated erythrocytes and areas of necrosis.

Discussion

Bilateral blindness as a result of orbital mucormycosis is a devastating outcome. Epidemiological data exposes its low prevalence and reveal that is primarily associated with immunocompromised states associated with immunocompromised states, such as uncontrolled diabetes, hematologic malignancies, solid organ transplantation and immunosuppressive therapies (2,3). This type of fungi can be found in soil, oral cavity, nasal passages, and feces of healthy individuals. Infection can occur when spores enter the respiratory tract via inhalation, the skin through direct inoculation to areas of trauma, or when they are ingested through the gastrointestinal tract. Once inside, the spores germinate into hyphae, resulting in angioinvasion which may result in arteritis, vessel thrombosis, tissue ischemia, and necrosis, often accompanied by bone erosion. This can potentially lead to hematogenous dissemination, multiorgan involvement, and the fungi can enter the mucosa of the paranasal sinuses, penetrate the orbital and skull bones, and cause cerebral and orbital infections. The growth of this fungus increases in environments high in glucose, iron, and acidity (9,10).

Individuals can present in varied clinical forms, including rhino-orbital-cerebral, pulmonary, cutaneous, and gastrointestinal presentations. In orbital mucormycosis, patients may present orbital cellulitis, proptosis, pain, ophthalmoplegia, orbital apex syndrome and cavernous sinus thrombosis (1,10,11). The symptoms usually progress rapidly over days without proper treatment, underscoring the need for prompt intervention. It has been reported that Rhino-orbital-cerebral mucormycosis has a mortality rate ranging from 25% to 62% (3,12).

Diagnosis of orbital mucormycosis can be challenging due to its rarity. Early detection is vital to begin rapid and effective treatment; however, the initial symptoms are often nonspecific and lead to delayed diagnosis. Radiological imaging, such as CT and MRI, can identify distinct findings, such as soft tissue involvement, bony erosion, sinusitis and thickening of extraocular muscles (13). However, they are generally insufficient for a precise diagnosis but they can help to

determine the extent of infection and guide surgical debridement (14). Definitive diagnosis requires proving fungal etiology with culture growth and histopathological examinations from specimens of involved sites revealing wide, ribbon-like, non-septate hyphae invading tissues (15). A high level of suspicion is necessary, particularly in immunocompromised individuals (16).

The management ROCM requires a multidisciplinary approach involving various specialists for a early diagnosis, addressing underlying risk factors, performing surgical debridement when indicated and initiating prompt antifungal therapy. Early administration of aggressive antifungal therapy, typically involving amphotericin B, is critical to stop the infection's progression and seems to have no impact on the results of tissue diagnosis or cultures. Amphotericin B is considered the first-line therapy for Mucorales infections due to its high in vitro activity (14,15,17). Surgical intervention aims to control the source and reduce tissue necrosis, aggressive debridement can improve survival rates by facilitating better delivery of antifungal agents with procedures like orbital exenteration and sinus debridement. In more severe cases, more extensive resections and multiple debridements may be necessary (18). Bilateral exenteration, is rarely performed in cases of bilateral orbital mucormycosis due to its poor prognosis. However, there have been reported cases of successful survival specially in patients with fever (19). Effective coordination between medical and surgical interventions is crucial to increase the effectiveness of antifungal treatment (20).

In conclusion, the occurrence of bilateral blindness induced by orbital mucormycosis serves as a reminder of the rarity and severity of this clinical presentation. In the cases we presented, bilateral exenteration was the chosen intervention due to the absence of cerebral and systemic involvement upon presentation. The delay in referral for prompt diagnosis and effective treatment may explain the high mortality rate in both cases. This highlights the critical need for increased clinical suspicion among vulnerable populations and immediate referral to specialized centers where a multidisciplinary approach can be employed. These centers utilize radiological imaging, culture growth assessment, and histopathological analysis to initiate treatment without delay, potentially improving outcomes for affected individuals.

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