

## Rhinoorbitocerebral Mucormycosis in an Immunocompetent Patient: A Case Report

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### Abstract

**Objective:** To report a case of a 48-year-old male diagnosed with mucormycosis immunocompetent Rhinoorbitocerebral is presented, the signs, symptoms and complications that can be seen in the cases despite aggressive treatment protocol is determined.

**Case Report:** Male 48 years old, single, a native of Tumbes, multifarious worker who has been preceded by a psychiatric disorder with irregular unspecified drug treatment.

**Result:** The patient has headache, decreased visual acuity, pain with eye movements with proptosis, chemosis and bilateral palpebral edema. At the time of consultation has AV in MM which ended in NPL, exophthalmos with complete restriction of eye movements, conjunctival chemosis with necrosis, hypoesthesia periocular signs of sites, fundus retinal ischemia shows pallor of the optic nerve and both eyes; necrotic lesions in the palate, soft diffuse induration to Paracervical level is associated parts; microbiological study is indicated mucormycosis and treatment with antibiotics Amphotericin B.

**Conclusion:** Mucormycosis infection in the region rhinoorbitaria is serious and delicate, endangers the life of the patient and often requires mutilating surgery or brain involvement with a lethal outcome as in and patient. Vascular thrombosis resulting in tissue necrosis during mucormycosis justifies the use of anticoagulants; Early medical management based antifungals (amphotericin B) is one of the fundamental pillars in the survival of these patients with the early diagnosis.

**Keywords:** Mucormycosis; Fungal Infections; Encephalitis; Cerebral Rhinoorbital; Orbit

### Introduction

Mucormycosis is an infection considered serious from the Mucoraceae or mucoral family, but the term zygomycetes is commonly used and therefore also called zygomycosis. Within the Mucoraceae or mucoral family there are three subfamilies, *Mucor*, *Rhizopus* and *Absidia*, which are considered the fungi responsible for this fungal infection [1].

Acute, angioinvasive infections are considered, of which 6 clinical forms of presentation have been described which are based on their anatomical location: 1) rhinoorbitocerebral; 2) pulmonary; 3) cutaneous; 4) tummy tuck or gastrointestinal; 5) disseminated, and 6) a miscellaneous of other forms (endocarditis, osteomyelitis, etc). The clinical presentation is closely related to risk factors [1-7].

Rhino-orbito-cerebral mucormycosis is a rare, potentially lethal opportunistic infection that occurs mainly in immunocompromised patients [2]. Davies BD published an increase in cases of post-generalized rhinoorbitocerebral mycosis that occurred in Colorado in 2013,

so it relates the incidence to the immunocompromised state and to environmental exposure [3]. Such infection is rare in healthy individuals. Inhalation of spores provides access to the oral and nasal mucosa of the human. In people without immune compromise, these spores are eliminated by phagocytosis, while in the immunocompromised host there may be germination and hyphae formation with vascular invasion [4]. Immunologically, neutrophils are the main cells responsible for the process of reducing infection by this type of fungi, neutropenia also significantly increases the risk of suffering from rhinoorbital mucormycosis [5]. In this type of fungal infections mortality is high, it is presumed that even with antifungal treatment, mortality reaches even more than 40% in case of any hematopoietic disease related to malignancy, mortality increases by up to 25% as previously described according to some authors.

As for their pathogenesis, these microorganisms can penetrate in several ways, being the most frequent by the respiratory route, where the spores that are free in the air are implanted in the nasal mucosa, the ethmoid sinuses, nostrils being starting places, septum and palate. Other less important routes would be oral, conjunctival or traumas in open wounds, catheters, etc [6].

There are studies in which they emphasize the importance of discarding this entity as soon as possible when it is suspected. The change in a survival rate of 83% to 47% has been described, if the treatment takes more than six days to complete, however, when the diagnosis is made in less than five days, the mortality will decrease significant [8].

We found different clinical forms, the rhinocerebral being the most frequent. It begins with involvement of the sinuses, nasal mucosa and palate extending to the orbital and periorbital region [7-9]. Once the orbit is affected, the orbital apex syndrome can be seen with: ophthalmoplegia, palpebral ptosis, mydriasis, hypo or hyperesthesia in the distribution of the first branch of the V pair and optic nerve dysfunction. From there, it spreads to the cavernous sinus producing thrombosis, affecting meninges and brain tissue and finally coma and death [10]. Usually the disease begins in the nasal cavity and sinuses, and its progression is by direct extension or hematogenous spread to the palate, pharynx and orbit, with subsequent intracranial dissemination by invasion through the superior orbital fissure, ophthalmic veins, cribriform or carotid lamina [11-13].

As for the diagnosis, it is made through the pathological and microbiological study. In the culture, the colonies are usually filamentous, with brown-blackish color and with exuberant growth in two or three days. The hyphae are usually large, wide and branched, not buried and at right angles. In the anatomy-pathology, the presence of zygomycetes in the biopsied tissues producing vascular invasion is evidenced [11]. Several steps for the management of this infection are systematically described, including an early diagnosis, the treatment of the underlying disease, a good antifungal therapy and timely surgical treatment, a special mention is made later.

As for therapeutics, there is no worldwide accepted treatment protocol, but despite this, it is based on 3 fundamental pillars: the treatment of the underlying disease, systemic antifungal therapy and surgery [12]. The mainstay of the treatment of rhino-orbito-cerebral mucormycosis is surgical debridement, medical therapy with early amphotericin B and reversing the ketoacidotic or immunosuppression status of the host. The extent and time required to perform surgical debridement to maximize results has never been defined [13]. Orbital exenteration seems to improve survival in patients with ophthalmoplegia. However, there is much controversy in the literature regarding the indications for performing this procedure and its influence on the progression of the disease [14].

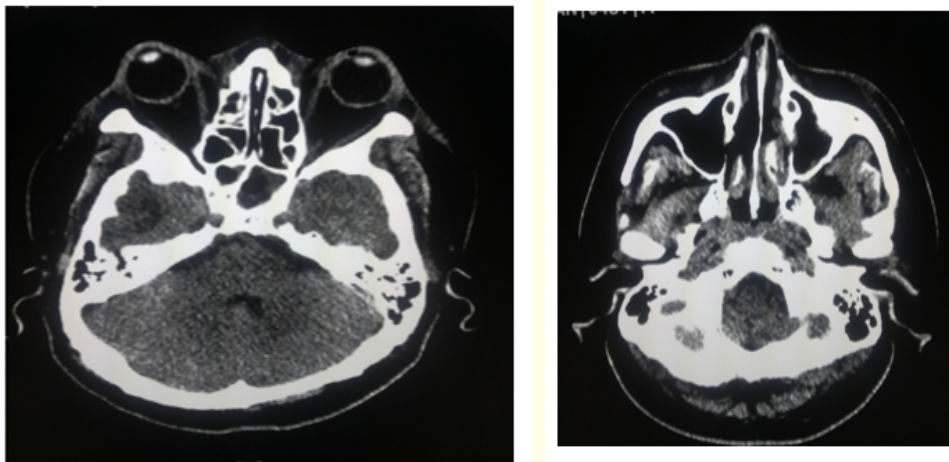
### Objective of the Study

The objective of this work is to describe a form of aggressive clinical presentation, treatment and evolution in patients with rhinoorbitocerebral mucormycosis, as well as determine the extent of particularly aggressive infection and its intracranial condition.

### Case Report

A 48-year-old male patient, single, originating and resident of multi-worker worker Tumbes, who as an antecedent presents an unspecified psychiatric disorder with unspecified irregular pharmacological treatment who, from 10 days prior to the consultation, begins with moderate-intensity dental pain of right side to which increase in face and neck volume is added, in turn a sensation of thermal rise

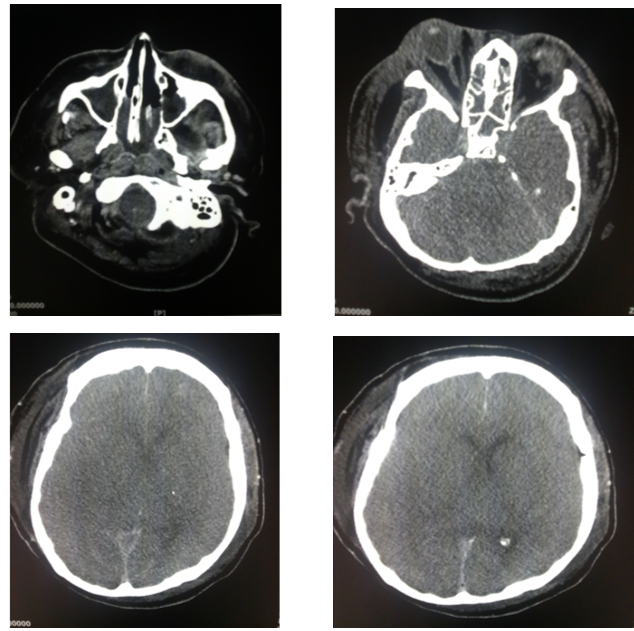
with values of 38°C; 3 days prior to the consultation, he presented with a headache with a predominance of the left and an inability to open the mouth, conjunctival redness was evidenced with a progressive decrease in bilateral vision and poor mucopurulent secretion in fornix; After two days the discomfort became persistent and ocular proptosis and bilateral eyelid edema with chemosis, pain and bilateral amaurosis are added, so it enters the Emergency Service of our Hospital, the day of evaluation by the Ophthalmology Service disorder is appreciated of the sensory which increases as the days go by as do the eye symptoms. Upon physical examination of AV (visual acuity) in MM (hand movement) which ended in NPL (no perception of light) both eyes, exophthalmos with total restriction of eye movements, chemosis with conjunctival necrosis which begins in the left eye and as the days go by it is generalized in both eyes, the anterior segment shows corneal edema, periocular hypoaesthesia with signs of phlogosis, fundus shows retinal ischemia and paleness of the optic nerve both eyes; Necrotic lesions at the palate level, diffuse induration of soft tissues at the paracervical level to the posterior left predominance, which becomes progressive from admission to the hospital, is associated with the physical examination. Given the characteristics of the condition and the clinical context of the patient, ICU was admitted with Meropenem, Vancomycin, Clindamycin and Amphotericin B treatment, however the evolution was unfavorable. In the CT scan, thickening of the mucosal type of the frontal, maxillary, anterior and posterior paranasal sinuses, sphenoid is being compatible with pansinusitis is observed, at the level of the right mastoid cells a focal area of sclerosis associated with the presence of content is observed inflammatory hypodense compatible with a picture of right mastoiditis.



**Figure 1 and 2:** CT axial section where there is evidence of paranasal sinuses.

At 3 days post-training, he presented severe respiratory distress, which is why he intubated and placed in mechanical ventilation, there is a marked increase in edema in the face, which has an indurated area on palpation in the region of the left posterior neck and in conjunction with the laboratory analysis is concluded in a severe sepsis at an osteodermal focus with severe bilateral ocular involvement, hyponatremia, hypocalcemia; in the therapeutic itraconazole is added; Subsequently, a sample of palate lesion is received, showing yeasts and hyphae in large quantities. CT scan shows signs of severe endocranial hypertension, biparietal ischemia to the right predominance, IV ventricle is not observed and with Glasgow 3 points.

Patient does not respond to treatment, there is evidence of necrosis of the ocular surface both eyes and periorbital with signs of paracervical crushing; Pathologic result of palate and sinus lesions compatible with Mucormycosis. A few days later, the patient dies due to multiorgan dysfunction.



**Figure 3 and 4:** CT scan where progression is evidenced.



**Figure 5:** Patient in context of orbital mucormycosis in the left eye, evident proptosis, chemosis, limitation in all the ductions.



**Figure 6:** Conjunctival and soft tissue necrosis in the paracervical region.

## Discussion

We present a case of rhinoorbitocerebral mucormycosis in which one of the main pillars is its short-term diagnosis and aggressive treatment since it has a large lethality rate as the literature supports us, so in cases where rhinoorbital mucormycosis is suspected, A protocol must be initiated to diagnose this pathology immediately. As the infection evolves, several clinical signs become evident, such as periorbital cellulitis, facial edema and ocular involvement with conjunctival necrosis. These data may already be talking about a severe infection that is becoming widespread. It is considered as data of serious infection that could have involvement of the central nervous system since in our case the patient has a sensory disorder and a very marked decrease in Glasgow with respiratory compromise. According to Seiff, *et al.* the pterygopalatine fossa, through the sphenopalatine foramen, is the main reservoir for *Mucor* and acts as a conduit for the spread of infection to other sites [14].

Regarding the diagnostic protocol, it is important to highlight the history of diseases to provide the patient's immunocompromise data, subsequently the most commonly used are images, with CT being the most common where evidence of sinusitis; However, we must emphasize the fact that frank disease does not show frank disease or data compatible with mucormycosis, does not rule out the diagnosis.

In this case, the diagnosis of said infection is not made at first, as this type of infection is uncommon in patients without immune compromise and without evidence of neutropenia.

Therapeutics should always be aimed at treating the causative microorganism in this case in the first instance would be Amphotericin B as a choice, however we must consider its nephrotoxicity; Recently, liposomal formulas of amphotericin B are used, since the drug can remain longer in systemic circulation without being eliminated, and in turn be less nephrotoxic. It is said that if both drugs are compared, the fat-soluble amphotericin offers a survival rate of up to 67% compared to its non-fat soluble presentation, which offers 39% [5]. Drugs of the azole family such as itraconazole, parconazole, ketoconazole, fluconazole have not been shown to have reliable activity against *Mucor*, however they are considered second-choice medications in case the polyenes are not well accepted by the patient. Conservative treatment ranges from non-exenteration to focal debridement of affected tissue, in turn instilling liposoluble amphotericin B through catheters in the region [15]. Whereas *Mucor* generally grows in acidic environments, and a repetitive process of invasion, arterial occlusion, hypoxia, local acidosis, necrosis and significant proliferation begins; The functionality of the use of the hyperbaric chamber has been investigated,



as there are studies that show that the higher the oxygen tension, the greater the recruitment of leukocytes. This can be used as therapy attached to surgical debridement and amphotericin B [8].

Vascular thrombosis resulting in tissue necrosis during mucormycosis justifies the use of anticoagulants, although a controlled study would be required to determine their usefulness [16].

### Conclusion

Mucormycosis infection in the rhinoorbital region is serious and delicate, as it endangers the patient's life and often requires mutilating surgery (exenteration), however the decision regarding surgical management is difficult and highly debated, depending on the evolution and the underlying disease of the patient. It is preferable to use the most conservative surgical alternatives, such as focused debridement and instillation of amphotericin B by means of a catheter in the affected region in cases where the poor evolution is evident; Everything will depend on the location of the infected tissue, the severity of the infection, the experience of the surgeon, the type of patient and if you have the necessary resources to perform this procedure, unfortunately in our case there was no time to perform the surgical management

We emphasize that early medical management based on antifungals (amphotericin B) is one of the fundamental pillars in the survival of these patients. In our institution we do not have liposomal amphotericin, despite being the antifungal of choice because it is more effective and less nephrotoxic than traditional amphotericin. We consider that early diagnosis with the establishment of amphotericin B and the surgical debridement of necrotic lesions when feasible, is of vital importance for a favorable evolution. If the brain CT does not show injuries then we will assess the possibility of more aggressive surgeries in order to eradicate the disease. The prognosis continues to be disastrous and the disease is usually fatal when there is cerebral involvement as it happened in our patient.

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