

Case report

RHINO-ORBITO-CEREBRAL MUCORMYCOSIS: AN INFECTION STILL FATAL. ABOUT A CASE.

ABSTRACT :

We report a case of a 54-year-old patient, an unbalanced diabetic, who presented rhino-orbito-cerebral mucormycosis with orbital involvement as circumstance of discovery. The aims are to highlight the importance of making an early diagnosis to improve prognosis of this infectious pathology. Early diagnosis requires clinical suspicion of infection in all immunocompromised patients, particularly in diabetics with ketoacidosis and clinical research of typical necrotic plaques on the eyelid, palate or sinus level. Histopathological analysis makes diagnosis. Angiography-MRA and angiography-CT scan remain complementary examinations to assess the extension and guide treatment. The management must be multidisciplinary. Association of intravenous antifungal treatment (especially amphotericin B) and localized or radical surgical debridement is the treatment of choice. Local treatment with amphotericin B increases tissue penetration.

Key words: Mucormycosis; Necrosis; Fungal Infection; Filament; Amphotericin B.

INTRODUCTION :

Mucormycosis is an opportunistic [1] infection caused by saprophytic and ubiquitous fungi that are part of the class Zygomycetes and order Mucorales which includes nine genera, the most frequently isolated during human infections are: Rhizopus, Mucor and Absidia [2]. Multiple locations are possible: rhinocerebral, pulmonary, digestive, cutaneous, disseminated and focal. Rhinocerebral involvement is the most frequent. This impairment occurs preferentially in poorly balanced diabetic patients or in the event of immunosuppression. Mucormycoses can occur in immunocompetent subjects, the evolution is then most often benign [1].

The rhino-orbito-cerebral localization represents approximately 70% of cases. This is the most threatening location and responsible for high mortality [3].

The non-specificity of the clinical manifestations and the rapid progression of the lesions explain the high mortality linked to this infection. Only the anatomopathological and mycological analysis of the biopsies can confirm the diagnosis of mucormycosis. These data contrast with the need for rapid therapeutic management combining surgical debridement, an antifungal (amphotericin B) and strict control of the underlying pathology.

PATIENT AND OBSERVATION:

Patient information:

This is a 54-year-old patient, type 1 diabetic on insulin therapy, poorly balanced, who presented swelling of the inner angle of the left upper eyelid without other signs 10 days before admission, for which he was treated with initial oral antibiotic therapy (amoxicillin-clavulanic acid) for a period of 10 days with worsening of the symptoms. Clinical results:

Initial clinical examination found necrotic plaque in inner angle of the left upper eyelid (Figure 1) with swelling of the entire eyelid, proptosis with ophthalmoplegia, significant chemosis, loss of pupillary reflexes, fundus examination revealed papilledema (figure 2). The patient diagnosed with orbital apex syndrome.

General examination found fever, poor general condition and hyperglycaemia (3g/l). A urine dipstick is done to find acetonuria.



Figure 1: Necrotic area at internal angle and the medial part of the left upper eyelid, very suggestive of the diagnosis.



Figure 2: Severe chemosis of the bulbar conjunctiva associated with ophthalmoplegia.

Diagnostic approach:

A skin sample was taken (necrotic areas) with histopathological analysis and found a Rhizopus-type mycelial filament sensitive only to amphotericin B.

CT scan angiography (Figure 3) and orbito-cerebral angio-MRI were performed and showed infiltration of both maxillary and orbital sinuses and two parenchymal cerebral lesions with cavernous sinus thrombosis.



Figure 3: Orbital CT scan with injection showing grade 2-3 proptosis with sinus filling.

Therapeutic intervention and follow-up:

The patient was put on anti-thrombotics, antifungals amphotericin B at a dose of 1 mg/kg/d intravenously (with difficulty in procuring amphotericin B) with daily monitoring of renal function and glycemic balance, associated with wide surgical debridement of necrotic lesions. Debridement was performed both endonasally and orbitally.

The evolution was marked by therapeutic resistance and the deterioration of the general state and the death of the patient.

DISCUSSION:

Rhino-orbito-cerebral mucormycosis is the most common form of mucormycosis. It is an acute, fatal, opportunistic and rapidly progressive fungal disease. The main genera responsible for human infection are *Rhizopus*, *Rhizomucor*, *Mucor* and *Lichtheimia* [4]. Germs enter by inhalation, percutaneous inoculation or ingestion [5]. The 3-year RetroZygo study in France showed that hematological malignancy was the risk factor in nearly half of the patient population followed by diabetes mellitus (23%) and trauma (18)% [6]. Other known risk factors for mucormycosis are organ transplantation and high-dose of corticosteroids [1].

The diagnosis is not always easy. The location and accessibility of the infectious site condition the diagnosis. The cutaneous and rhino-orbito-cerebral localization are the two most frequent localizations [7]. Diabetic patients more often develop the rhino-orbito-cerebral and pulmonary forms [7].

Mucormycosis can affect immunocompetent subjects but mainly affects immunocompromised patients, in particular poorly balanced diabetics in 60 to 80% of cases [9-10]. Acidosis constitutes a risk factor, it increases the free iron necessary for fungal proliferation and pullulation by reducing the binding of iron to transferrin [9-10]. Ketoacidosis also decreases the response of phagocytes and their lysis capacities [11]. Contamination can be by direct inoculation of traumatic origin [11]. Rhino-orbito-cerebral infection begins with infection of the palate or sinuses, progresses to the orbit and then intracranial if an early diagnosis has not been made [7].

Clinical signs in the early stages are nonspecific and include fever, lethargy, headache, orbital pain, orbital cellulitis, sinusitis and epistaxis. Paresthesias, corneal anesthesia, facial paralysis, sometimes blackish rhinorrhea can also be reported in the later stages [7 ;10]. Facial symptoms include pain and numbness [1]. Any cellulitis beginning at the internal angle in an immunocompromised, diabetic or ketoacidosis subject should suggest mucormycosis, especially if there are necrotic lesions. Orbital infection spreads to the intracranial cavity via the orbital apex. Intracranial involvement may manifest as altered consciousness, gait disturbance and/or convulsions [1]. Rhinocerebral mucormycosis is a fearsome cause of cavernous sinus thrombosis, responsible for high mortality.

Confirmation of the clinical form requires the association of symptoms compatible with histological invasion of the tissues. The diagnosis is easier in rhino-orbital and cutaneous-mucous involvement versus pulmonary involvement where the diagnosis is post-mortem in more than half of the cases [11].

The results of the biological assessment are non-specific and can show hyperglycaemia and/or ketoacidosis [1]. The blood count makes it possible to look for neutropenia [1]. The diagnosis of mucormycosis is based on evidence of the fungus. Biopsy and anatomopathological examination of the necrotic material can find mycelial filaments which are wide, non-septate with ramifications at right angles [12-13]. Imaging assess the lesions, plan surgical debridement and monitor progress under treatment. The lesion assessment is necessary to search asymptomatic localizations. In cases of rhino-orbital lesions, a CT scan can objectify an invasion of the tissues, the sinuses, the bone invasion without specificity in the diagnosis, especially in the early forms. When intracranial involvement is suspected, magnetic resonance imaging with injection is the gold standard to look for complication such as cavernous sinus thrombosis. Fungal tissue usually appears hypointense on T2 and may show peripheral enhancement.

The management requires early diagnosis which allow an early and adequate treatment, a localized debridement with less risk of complications. Correction of predisposing factors with management of glycemic imbalance and ketoacidosis is mandatory. High-dose of liposomal amphotericin B is the treatment of choice with

good tolerance and less resistance. 5 mg/kg dose showed the same efficacy as the higher doses [11; 14].

Surgery combined with the use of antifungal drugs is always better than antifungal treatment alone. The main reason to perform an orbital exenteration is to prevent intracranial extension. This is a surgical emergency [15].

Early aggressive surgical debridement of infected tissue is the mainstay of successful treatment of mucormycosis [15-16]. The principle consists of resection of all infected tissue and necrotic areas [16]. Orbital exenteration may be necessary to improve the vital prognosis, particularly in cases of negative light perception and ophthalmoplegia [16] ; this can be done even after intracranial spread. It is a surgery which makes it possible to control the infection at the expense of a permanent mutilation [16].

Prior to amphotericin B discovery, the only management modality for rhino-orbital mucormycosis was radical surgery including debridement of the sinuses and nasal cavity, as well as orbital exenteration. With antifungal treatment, limited resection can be done. The tissues are usually found in the superomedial quadrant or the medial part of the orbit or along the [15] infraorbital fissure. An incision in the crease of the eyelid for the superomedial and medial location and a lower transconjunctival incision for the lower orbit, followed by an opening of the periorbital to reach the suborbital fissure to reach the focus of infection. Any clinically involved fungal tissue or necrotic tissue is removed. A 0.1% w/w lipid-based amphotericin B gel can be injected at the debridement site with a 5 cc syringe and 1.5 inch [15] 18-G needle.

Local treatment with amphotericin B reduces kidney toxicity and increases tissue penetration. Retrobulbar injection of amphotericin B can also be used to avoid [15] exenteration.

CONCLUSION :

Rhino-orbito-cerebral mucormycosis is a rare and threatening condition, it mainly affect immunocompromised subjects. Keys to successful multidisciplinary treatment include clinical suspicion of the diagnosis, correction of underlying medical conditions such as ketoacidosis, and aggressive medical and surgical intervention.

Legend of figures:

Figure 1: Necrotic area at internal angle and the medial part of the left upper eyelid, very suggestive of the diagnosis.

Figure 2: Severe chemosis of the bulbar conjunctiva associated with ophthalmoplegia.

Figure 3: Orbital CT scan with injection showing grade 2-3 proptosis with sinus filling.

Patient perspective: Amphotericin B treatment is not readily available in our hospitals and surgery (debridement) remains major surgery. Management is multidisciplinary and glycemic control in an infectious context is difficult.

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