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MODESTUM

Case Report **OPEN ACCESS**

First Reported Cases of COVID-19-Associated Mucormycosis in Tunisia

Rim Khemakhem [1], Ichrak Bougharriou [2*], Nesrine Kallel [1], Anis Bafoun [2], Feten Mahmoudi [2], Samy Kammoun [1]

[1] Pulmonology Department, Hedi Chaker Hospital, University of Sfax, TUNISIA
[2] Covid Oxygen Unit, Military Field Hospital, University of Sfax, TUNISIA
***Corresponding Author:** ichrak.bougharriou@gmail.com

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ABSTRACT

COVID-19 infection is associated with several complications such as mucormycosis. We report, to the best of our knowledge, the first published cases of mucormycosis associated with severe COVID-19 infection in Tunisia. The first case was a diabetic, 68-year-old man, who presented a rhino-orbito-cerebral mucromycosis. The second case was a 37-year-old woman with a chronic renal failure hemodialysis stage and liver disease and who presented a rhino-sinuso-orbital mucormycosis. The diagnosis of mucormycosis was retained in both cases seven days after COVID-19 infection. Antifungal treatment was prescriped. Surgical treatment was not possible. Both cases died. We should think about mucormycosis in patients with COVID-19 infection and emergency medical and surgical treatment must be started to reduce mortality.

Keywords: COVID-19, mucormycosis, Tunisia

INTRODUCTION

Mucormycosis is uncommon and mostly occurs in patients with immunodeficiency. COVID-19-associated mucormycosis (CAM) was reported in many coutries. It is caused primarily by immunosuppression due to COVID-19, corticosteroid therapy and high blood sugar [1]. We report here, to our knowledge, the first published cases of CAM in Tunisia.

CASES REPORTS

Case 1

The first case was a diabetic, 68-year-old man. He had dyspnea and fever, evolving for four days. The SARS-CoV-2 infection was confirmed by naso-pharyngeal swab. A computed tomography (CT) scan of the chest showed multiple ground-glass opacities in 80% of both lungs with peripheral distribution. We prescribed dexamethasone (4 mg twice daily), general supportive care and subcutaneous enoxaparin (0.4 ml twice daily). One week after, he gradually deteriorated with the onset of acute respiratory distress syndrome. A right eyelid edema with ptosis and periorbital and nasal necrosis were noted (**Figure 1**).

C-reactive protein (CRP) was 105 mg/l. CT scan of the orbits and sinuses showed a soft tissue swelling in the right preseptal regions and mild right proptosis (**Figure 2**).

The mycological study of the nasal swab confirmed the diagnosis of mucormycosis. The patient received amphotericin B deoxycholate (1 mg/kg/day). But he continued to deteriorate with neurological symptoms and blindness and surgical treatment was not possible. The patient died a week later.

Case 2

The second case was a 37-year-old woman with a chronic renal failure hemodialysis stage and liver disease. She presented with cough and dyspnea. COVID-19 infection was confirmed by throat swab. She received dexamethasone (4 mg twice daily), subcutaneous enoxaparin (0.4 ml once daily), and oxygen (3 l/min). On the 7th day of hospitalization, the patient presented with edema of the left hemiface, ptosis, nasal, perinasal, and perioral necrosis and fever (**Figure 3**).

A CT scan of the orbits and sinuses showed severe pansinusitis, mucosal opacification of the ostiomeatal units and several abcess. Mucormycosis was confirmed by the mycological sudy of a nasal swab. Surgical treatment was not possible due to the extension of lesions. Amphotericin B deoxycholate (0.5 mg/kg/48hours) was administered. The patient continued to experience worsening and died few weeks later.

DISCUSSION

Mucormycosis is caused by environmental fungi belonging to the class zygomycetes, order mucorales. Contamination is through the inhalation of fungal spores [1]. It has a vascular tropism, inducing thrombosis and host tissue necrosis [2, 3]. It is a rare and fatal opportunistic fungal infection. Risk factors

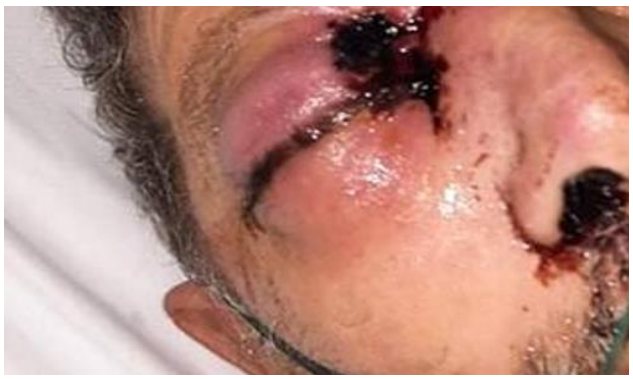

Figure 1. Right eyelid edema with ptosis & periorbital & nasal necrosis

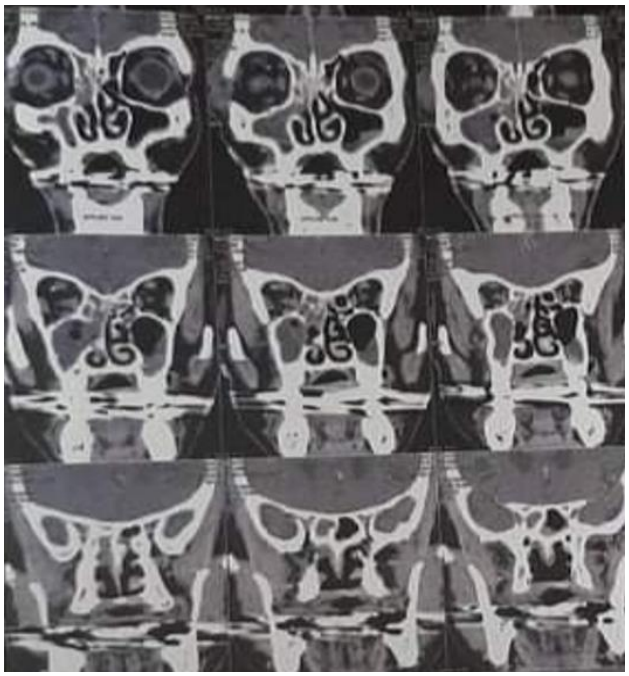

Figure 2. CT scan of the orbits & sinuses: a soft tissue swelling was noted in right preseptal regions with mild right proptosis

include diabetes (especially uncontrolled or with ketoacidosis), cancer, organ or stem cell transplantation, immunosuppressive or deferoxamine or corticosteroid use, immunocompromised individuals, hemochromatosis, neutropenia, severe burn, and post traumatic open wound [3,4].

The COVID-19 infection is a new predisposing factor. CAM was described in 100 patients, in a recent systematic review. The majority of patients are from India (68.68%) [4]. No COVID-19 related case is previously published from Tunisia. Mucormycosis essentially occurs in severe or critical COVID-19 infection, but also in mild or moderate one [5]. It occurs during COVID-19 infection (53%) or in post-COVID-19 disease (47%) [4]. Mucormycosis occurs on average 15 days after COVID-19 infection [5]. CAM is mainly due to corticosteroid use, high blood sugar, prolonged antibiotic therapy, and mechanical ventilation.

Several other factors are reported: elevated serum ferritin and iron, endothelitis, humid climate, tissue hypoxia, dissemination of spores through water humidifying oxygen, viral-induced lymphopenia, phagocyte dysfunction, and high inflammatory cytokines levels such as interleukin-6 [4-7]. In a

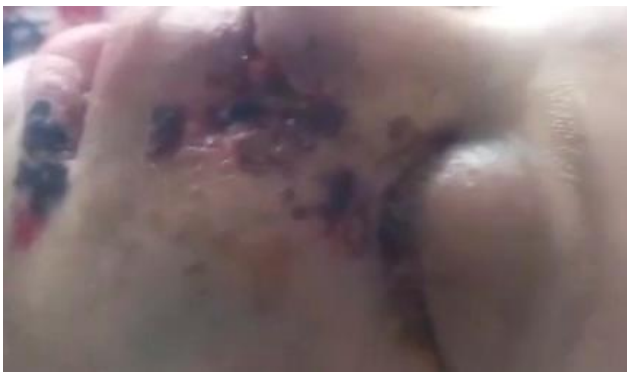

Figure 3. Edema of the left hemiface, ptosis, nasal, perinasal, & perioral necrosis

recent review [4], different clinical forms of CAM are reported. The most frequent one are rhino-orbital (50%), rhino-sinusal (17%), and rhino-orbito-cerebral (15%).

The main clinical manifestations of these forms are: fever, nasal secretions, nasal or palatine eschar, unilateral facial edema, orbital symptoms (exophtalmos, ptosis, diplopia, and blindness), and neurological symptoms (headache, localising signs, and seizures) [2,8]. MRI or CT scan evaluate the sinus, orbital, endocranial, and vascular extension [8]. The diagnosis of mucormycosis is confirmed by mycological study or anatomopathological examination of the local sample [8, 9]. Rhino-orbito-cerebral mucormycosis is classified as possible (only clinical signs), probable (clinical signs with diagnostic nasal endoscopy findings or MRI or CT scan), and proven (clinical and radiological signs with mycological confirmation) [8].

Mucormycosis's treatment is based on antifungal therapy, surgical debridement of necrotic tissues, glycemic control, and reversal of immunosuppression if it's possible [8,10]. The first-line indicated antifungal treatment is liposomal amphotericin B. If not available, we can use amphotericin B deoxycholate or amphotericin B lipid complex [8,10]. Posaconazole and isavuconazole can also be used [2]. It was shown that despite adequate medical and surgical treatment, mortality remains high (34%) [5].

Herein, we presented two cases of proven mucormycosis associated with severe COVID-19 infection. Clinical forms were rhino-orbito-cerebral and rhino-sinuso-orbital. The first patient was old and diabetic and the second presented a chronic renal failure hemodialysis stage and liver disease. The signs of CAM were noted after one week of admission for COVID-19 infection and treatment with steroids. The two patients received amphotericin B deoxycholate (liposomal amphotericin B, posaconazole, and isavuconazole were not available in Tunisia). Surgical treatment was not possible in the two cases and outcomes were not favorable.

CONCLUSIONS

We must think about mucormycosis as a complication of COVID-19 infection. Diagnosis and treatment must be urgents to improve the prognosis. We may be able to reduce the incidence of CAM by optimizing the use of corticosteroids.

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