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Case Report

Mucormycosis Related to Glucocorticoid Abuse in Suspected Covid 19, Case Report

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Abstract

Background: Mucormycosis is a rare and emerging fungal infection, with a high morbidity and mortality, manifested by a variety of different syndromes in humans, particularly in immunocompromised patients with diabetes mellitus. In the latest reported studies, it has been shown that the incidence of the disease appears to be increasing, despite current treatment options, which often include widespread disfiguring surgical intervention and antifungal therapy, mortality rates from mucormycosis range from 50% to 100%.

Clinical Case: Patient who after management with glucocorticoids in a prolonged manner presented dermatosis located in the left hemiface (left infraorbital region) and ipsilateral maxillary region at the expense of erythematous macula of imprecise edges, irregular shape, with subsequent increase in volume and temperature to the touch, accompanied by ipsilateral maxillary abscess requiring biopsy for refractoriness to treatment reporting in histopathology hyphae of variable diameter and length, not septate compatible with mucormycosis, so management was initiated with liposomal amphotericin as well as 3 surgical debridement's to the maxilla and fatty tissue on the orbit floor.

Conclusions: We are not in a pandemic process with a high incidence of respiratory infections of both upper and lower airway for which some therapeutic guidelines recommend the use of steroids in a specific way however the indications, guidelines and suggested schemes are not adequately respected, observing a significant increase in the use of this pharmacological too land may predispose to predispose to this type of infections that are associated with high mortality and psychological stigmas due to the destructive nature of the disease affecting areas as delicate as facial region.

Keywords: Mucormycosis; Glucocorticoids; Dermatosis; *Rhizopus spp.*; Covid-19; Abscess; Invasion

Background

Mucormycosis is a rare and emerging fungal infection, with ahigh morbidity and mortality[1,] manifested by a variety of different syndromes in humans, particularly in immunocompromised patients and with diabetes mellitus. Rhino orbital-cerebral and pulmonary infections that can become devastating are the most common syndromes caused by these fungi, tissue necrosis is the hallmark of mucormycosis, with the most common etiological agents being *Rhizopus* spp., *Mucor* spp. And *Lichtheimia* (formerly *Absidia and Mycocladus)* spp. Genera of other Mucorales, such as *Rhizomucor, Saksenaea, Cunninghamella,* and *Apophysomyces,* are less common [1]. Mucorales can enter a susceptible host through

inhalation, ingestion of contaminated food, or scraped skin [2], in the latest reported studies it has been shown that The incidence of the disease appears to be increasing. Hematological malignancies are the most common underlying disease in high-income countries and uncontrolled diabetes in developing countries The most frequent clinical presentations of mucormycotic are rhino orbitocerebral (34%), pulmonary, cutaneous and disseminated [1]. The true incidence of invasive zygomycotic is not known, although population studies in the United States have estimated at 1.7 cases per 1,000,000 population/year between 1992 and 1993, which is about 500 cases per year. In initial studies involving a large number of patients, until 2003, the most frequent risk factor was diabetes mellitus (36%), followed by malignant hemopathies (17%) [3], Despite current treatment options, which often include generalized disfiguring surgery and antifungal therapy, mortality rates from Mucor mycosis range from 50% to 100% [4]. Cases of Mucor mycosis are rare, but they are increasing and associated mortality is high in other studies mortality is reported (20 to 100%) in addition There was an increase in incidence during this period and most cases were reported in 2014 (23.7%) [5].

Clinical Presentation

Male of 35 years of age Onset of disease 1 month after being suspected of pneumonia by SARS COV- 2 treated with dexamethasone 8 mg every 6 hours for approximately 15 days debuting with dermatosis of subacute evolution located in the face (left infraorbital region) and ipsilateral maxillary region at the expense of erythematous macula of imprecise edges, irregular shape, with subsequent increase in volume and temperature to the touch, not painful on palpation, respecting the rest of the skin and annexes (Figure 1-3), valued in the first instance as a soft tissue abscess treated by drainage and antibiotic therapy without noticeable improvement, in addition to the development of nephrotoxicity by amphotericin deoxycholate having to interrupt treatment so it was referred to maxillofacial Surgery which performed drainage of maxillary sinus taking culture and biopsy of inflammatory process which is compatible with osteonecrosis of the maxilla associated with deep mycotic infection, without isolating agent in culture media but reporting hyphae in histopathology of variable diameter and length, not septate compatible with Mucormycosis (Figure 6,7). It was reported in previous documented cases there may be unilateral facial edema, proptosis and palatine or palpebral fistula which develops into necrosis [6] to which the mentioned case could evolve, it could even result in ulceration, necrosis and palatal perforation [7]. Upon admission, a tomography scan was performed where data of incipient affection is corroborated at the orbital floor, which is alarming since rhino orbital-cerebral infection usually originates in the paranasal sinuses, with bone destruction and subsequent invasion of the orbit, eye and brain [6]. At the time of presentation at our hospital, the patient's physical examination was significant for left facial edema, without left facial paralysis or anesthesia [8]. During his hospitalization began management with liposomal amphotericin as well as 3 surgical debridement's to maxilla and fatty tissue in orbital floor in which tissue was sent to pathology again corroborating diagnosis of Mucormycosis, later it was kept under surveillance in joint support of multiple specialty's (Figure 4,5).

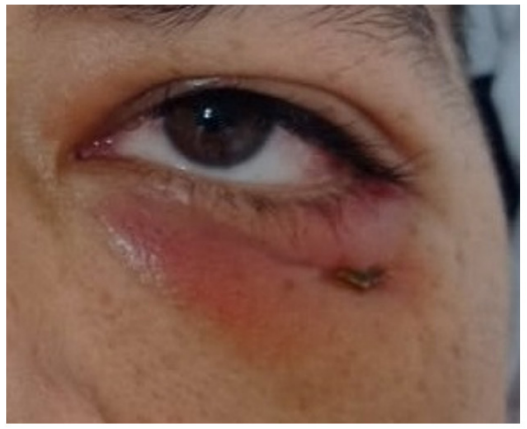

Figure 1: Left infraorbital injury on admission.

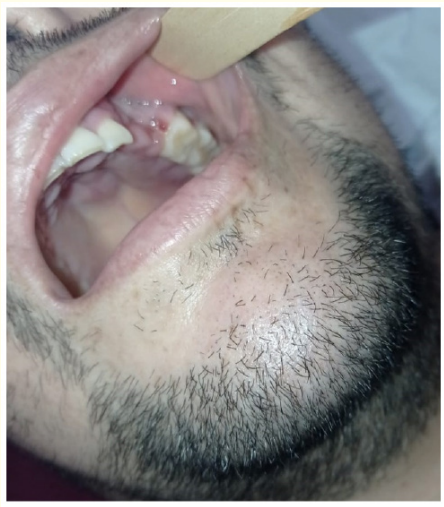

Figure 2: Maxillary injury on admission.

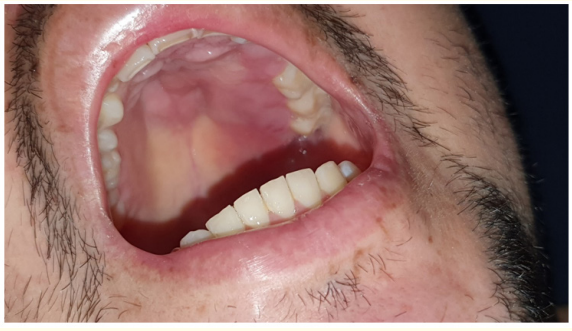

Figure 3: Admission palatal injury.

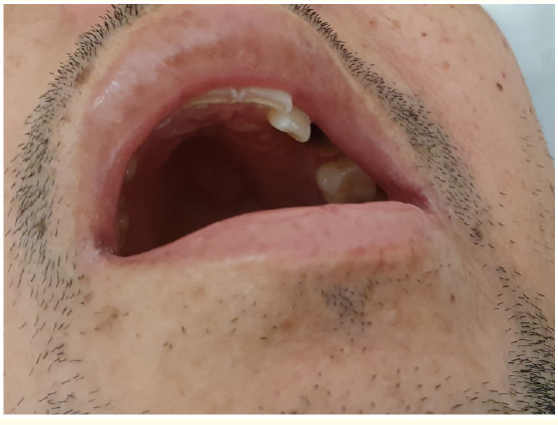

Figure 4: Left maxillary injury at discharge.

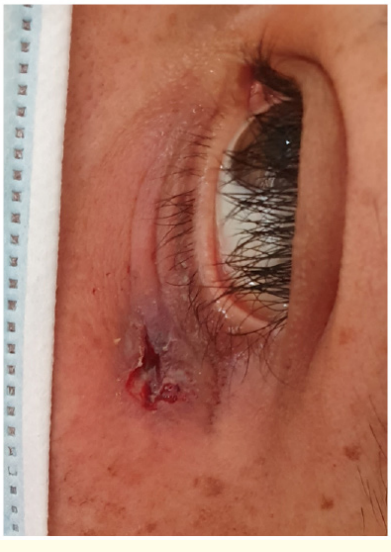

Figure 5: Left infraorbital injury at discharge.

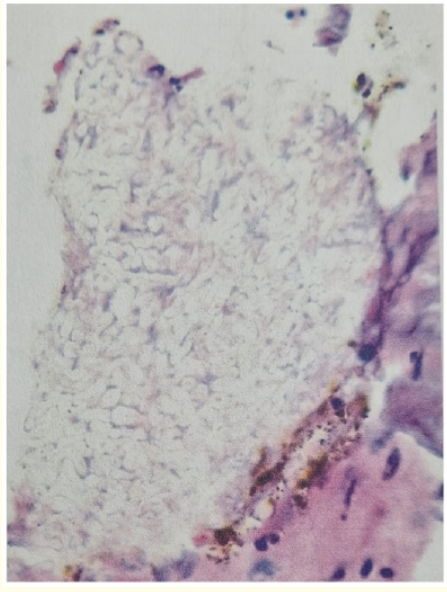

Figure 6: Right maxillary sinus histopathology.

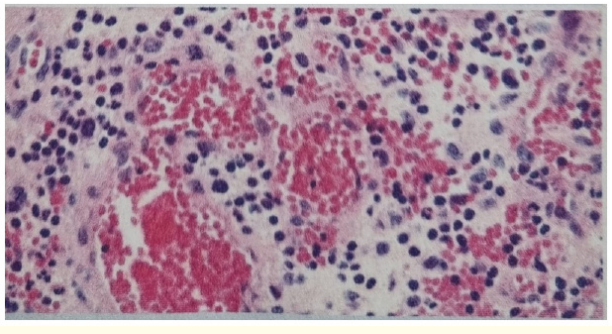

Figure 7: Left maxillary sinus histopathology.

Discussion

It should be noted that the prerequisites for the diagnosis of Mucormycosis are a high index of suspicion, recognition of host factors and rapid evaluation of clinical manifestations, however, the clinical approach to diagnosis lacks sensitivity and specificity. So microscopy (direct and histopathological) and culture are the pillars of the diagnosis, it is striking that despite multiple sampling during procedures it was never possible to isolate a specific etiological agent. Tissue histopathology is dominated by inflammation that can be neutrophilic or granulomatous; Inflammation seems to be absent in some cases, particularly in immunosuppressed pa-

tients [1], in the present case at the time of diagnosis treatment with amphotericin B deoxycholate was initiated. After the start of treatment, the patient began with acute kidney injury requiring suspension of the same, for this reason as an initial treatment, amphotericin B in its liposomal form is preferable for its lower toxicity and better tolerance, in addition to greater efficacy, to other formulations of amphotericin B, and constitutes the recommendation of the different guidelines [3]. Infusion-related adverse events, including fever and chills, occur in 30% to 72% of patients treated with amphotericin deoxycholate. Nephrotoxicity is also common and occurs in up to 53% of patients during treatment [9]. So once the kidney lesion subsides, management with liposomal amphotericin b is restarted. Cutaneous and soft tissue Mucormycosis are the most common forms of mucormycosis in immunocompetent patients, primarily after a skin break due to traumatic injury (e.g., natural disasters, car accidents, improvised explosive devices in theaters of war or iatrogenic sources), surgery, or burns. Abscesses, skin inflammation, necrosis, dry ulcers and bedsores are characteristic presentations [6]. In a 35-year Mexican retrospective study that has 214 documented cases, the three primary clinical forms were: rhino orbito-cerebral Mucor mycosis (75.9%), cutaneous (8.41%) and pulmonary (7.47%), predominating edema and areas of necrosis to dermatological exploration reaching destructive areas, consistent with the case described which had soft tissue affection and predominantly orbits edema, the pure cutaneous form is rare, manifested by purpuric and necrotic zones under covered areas. In a registry of 214 proven cases of Mucormycosis over 35 years in a third-level hospital in Mexico, the majority of cases were male patients with a median age of 45 years [10], being an age close to this range our patient in addition to being male. Seasonal variations also affect the incidence of Mucormycosis, with most infections occurring from August to November, [1] in other analyses and the peak incidence has been reported from September to November (autumn season; 39.4%), according to Lebanese and Israeli reports and studies from the Middle East., while in European studies, most cases occurred in autumn and winter [5] as in the case of the patient who debuted during the month of November, the current guidelines recommend antifungal treatment, surgical debridement and correction of risk factors [2] requiring that the surgical debridement must be extensive, involving all necrotic areas for rhino-oculo-cerebral infection, and repeated surgical procedures are recommended to achieve local control and improve the result, so during their hospitalization 3 interventions were performed with debridement by joint management of maxillofacial, ophthalmology and otolaryngology [2]. Successful treatment of mucormycosis depends on timely diagnosis and reversal of predisposing factors. Surgical debridement prior to spread of infection to distal organs and tissues has been shown to improve clinical outcomes [11] in terms of pharmacological measures Amphotericin B, Posaconazole and is ravuconazole are the most potent agents in vitro. So far, there is not enough evidence that identifying Mucormycosis at the gender and/or species level helps guide antifungal treatment [12]. A review of 170 cases of sinus Mucor mycosis showed that surgical debridement combined with amphotericin b deoxycholate increased survival from 50% to 70% 11 so this was the antifungal indicated at the beginning of the picture however it had to be discontinued due to the complication already mentioned, analyzing the context of the patient a factor that could have contributed to the development of the infection could have been associated with diabetes since despite not knowing with a diagnosis of diabetes mellitus upon admission presented central plasma glycemia within pathological ranges, taking as a antecedent a Mexican registry 418 identified cases, of which 72% were diabetic patients and a mortality rate of 51% was obtained [13], rhino-orbito-cerebral Mucor mycosis typically develops in patients with diabetes, while these patients very rarely develop lung infection, 6 however in glycosylated hemoglobin analysis it is within normal parameters so that in addition to that could also be attributed causality or predisposition to the fact that the patient recently has a history of indiscriminate use of steroids, it should be noted that despite being well established an increased risk of infection, controversy persists regarding the dose and duration of corticosteroids needed to substantially increase risk. Steroids antagonize macrophage differentiation, as well as suppress the production of macrophages of interleukin 1, interleukin 6, tumor necrosis factor, pro-inflammatory prostaglandins, and leukotrienes. Glucocorticoids also suppress the tumoricidal and microbicidal activities of activated macrophages, so it is suspected to be the main factor associated with the development of infection [14]. It is striking that despite the multiple cultures performed during the procedures we have 3 histopathology reports agreeing with the diagnosis of Mucormycosis however in no culture managed to isolate the specific etiological agent, taking into account that recently or this new species of *Apophysomyces, A. mexicanus,* has been reported in Mexico [15].

Conclusion

Due to the rarity of the disease, it is almost impossible to conduct large, randomized clinical trials, in addition most of the avail-

able data on epidemiology, diagnosis and treatment come from case reports and case series [1], so it is of great relevance to share this clinical experience both for the area of dermatology and multiple specialties that are involved both in the diagnosis and treatment of this entity. Pathological a factor that could be decisive and it is worth noting that we are in a pandemic process with a high incidence of respiratory infections of both upper and lower airway for which some therapeutic guidelines recommend the use of steroids in a specific way however the indications are not adequately respected, adequate guidelines and schemes observing a significant increase in the use of this pharmacological tool and may predispose to this type of infections that are associated with high mortality and the key to success lies in the diagnosis and early antifungal treatment, associated in most cases with a wide surgical flanging, 3 may have important implications on the quality of life of the patient due to the psychological stigma that can cause very extensive procedures.

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