



Zygomycosis: Management in Maxillofacial Surgery, XXI Century National Medical Center (IMSS)

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Abstract

Zygomycosis or mucormycosis is a low incidence disease, with few reports in Maxillofacial Surgery worldwide. It is an infection caused by fungi of the mucoral order, they are generally acquired by the respiratory route since the spores are found in the environment. Most of the patients with mucormycosis are immunocompromised, so they can present with severe symptoms that could have a fatal outcome. Regardless of the location, predisposing factors must be identified and corrected or attenuated to avoid their progress, complication or torpid evolution. A retrospective study performed at the Maxillofacial Surgery (CMF) service of the Dr. Bernardo Sepúlveda Gutiérrez, Specialties Hospital, XXI Century, IMSS is presented. For a period of 6 years (from January 2014 to January 2020). Reporting the results of the management given to patients diagnosed as Mucormycosis by medical-surgical treatment, with amphotericin B and surgical resection by the Maxillofacial Surgery service, XXI Century National Medical Center (IMSS).

Keywords: Zygomycosis; Mucormycosis; Amphotericin B; Margins; Resection

Abbreviations

CMF: Maxillofacial Surgery; IMSS: Mexican Social Security Institute; HIV/AIDS: Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome; *et al.*: And Collaborators; CMN: National Medical Center

Introduction

Paltauf in 1885 described mucormycosis as an acute fungal disease with high mortality, which occurs in patients with systemic compromise (diabetes mellitus, kidney, liver or heart disease, therapy with immunosuppressive agents, chemotherapy or corticosteroids, leukemia, neutropenia, malnutrition, polytraumatism, drug addiction, HIV/AIDS, tuberculosis, extensive burns, etc). Or due to external factors, such as: soils with high nitrogen content, decomposing matter, vegetable waste, manure, fruits, starchy

foods, among others [1-3]. Mucormycosis, zygomycosis, or phycormycosis have a low incidence; It is caused by saprophytic fungi of the zygomycete class, which are opportunistic aerobic fungi [1,2]. It comprises 11 orders and only 2 are of importance medical: Mucorales and Entomophthorales. They are hyaline, cenocytic, are saprophytes of the earth, in vegetable waste and in anemophilous biota [4]. Other common types or genera are: *Rhizopus*, *Absidia*, *Cunninghamella*, *Rhizomucor*, *Syncephalastrum* and *Mucor* as already mentioned [1-3].

Pathogeny

The sources of infection for mucormycosis can be: soils with a high nitrogen content, decomposing matter, vegetable waste, manure, fruits, starchy foods, etc [1-3]. The mucoral order has a high

affinity for the arteries, which favors its affection in immunocompromised patients and uncontrolled diabetics (acidotic condition of the host), which benefits the growth of Mucor and its rapid extension and spread through the tissues [5-8]. Zygomycosis microorganisms have several routes of entry, the most frequent is respiratory: through free spores in the air that implant in the nasal mucosa, beginning mainly in the central-facial region (paranasal sinuses, fossa and nasal septum, and palate) [9,10]. Transcends hematogenous spread from any primary source of infection, because it has tropism for blood vessels [4]. Sometimes it ascends anatomically, which conditions its progressive and rapid extension, due to the contiguity of the nasal septum and orbital floor, including the cranial base, until it converges towards the brain, becoming a neuroinfection. Neurological manifestations can be generalized or focused; when vascular invasion and thrombosis occur, the vessel that is most affected is the internal carotid [11-17].

Clinic

The clinical presentation of zygomycosis is highly variable, requiring early diagnosis and treatment (according to the extent of the disease). There are 5 clinical forms of mucormycosis: rhinocerebral, mucocutaneous, pulmonary, gastrointestinal and disseminated. The rhinocerebral form is the most frequent and has been reported more in uncontrolled diabetic patients [9,10]. The symptoms start as a severe fungal infection (in most cases it will be lethal), some symptoms compatible with acute bacterial rhinosinusitis (headache, runny nose, congestion, pruritus, loss of sensation, discharge of exudate, etc.); with progressive and rapid deterioration (weight loss and cutaneous necrotic areas), with no response to antimicrobial therapy, and pain does not cease with analgesia. These patients generally do not respond to antimicrobial therapy. A definitive diagnosis of zygomycosis must be made by confirmatory biopsy, where they report growth in culture or identification of unseptate hyphae [11]. The overall mortality from zygomycosis is 70 - 80% of the cases reported in the literature. The most significant prognostic factor for survival is 23 - 50% from the suspicion of the clinical diagnosis of mucormycosis. Early diagnosis is reported only in 8% of patients and in 45% late, generally when time has passed since the first signs and symptoms of zygomycosis/mucormycosis, therefore they have already had antimicrobial regimens, analgesia, including some with biopsy and/or previous surgical management, which is sometimes inappropriate or radical. Taking

as reference the "no return" of the disease; the diagnostic delay is approximately 10 to 12 days and only 44% to 55% survive after the diagnostic delay, compared to the accurate diagnosis that the percentage is 65 - 85% in less than ten days, what has been previously reported by the Author Shazo D., *et al* [13]. The rapid progression and invasion and the implications of patients with mucormycosis put the life of the patient at risk, making early medical and surgical management important, even without histological confirmation [18-20].

Objective of the Study

To show the results of the management given to patients diagnosed with Zygomycosis/ Mucormycosis, in the Maxillofacial Surgery service of the Specialty Hospital, CMN XXI Century, in a period of 6 years (January 2014 - January 2020).

Materials and Methods

A retrospective, descriptive, cross-sectional study was carried out. In a 6-year period, from January 2014 to January 2020, reporting all patients with Mucormycosis diagnosed and treated by the Maxillofacial Surgery service of the Specialty Hospital, CMN XXI Century. The inclusion criteria were those adult patients with a histopathologically confirmed diagnosis of Mucormycosis, patients who had computed tomography and clinical data of zygomycosis and who were treated by the Maxillofacial Surgery service of the Specialty Hospital, CMN XXI Century. The management given by the Maxillofacial Surgery service, the protocol was first performed for patients diagnosed with Mucormycosis, which implies hospital admission, laboratory and cabinet studies, imprinting, biopsy and culture, evaluation preoperative, medical management in conjunction with the Internal Medicine service and interconsultants such as Ophthalmology, Neurosurgery, Otorhinolaryngology and for subsequent rehabilitation with Plastic and Reconstructive Surgery. The surgical management offered by the Maxillofacial Surgery (CMF) service includes: total maxillectomy, hemi-maxillectomy, resection of the facial middle third and surgical exploration. This includes re-interventions and post-surgical control. Among the possible complications, the family member and patient are informed (by informed consent) of the possibility of presenting: hemorrhage (hypovolemic shock), undesirable fractures, infection of the surgical site, possible recurrences, tissue loss, specialized and/or advanced management of Support Vital, deterioration of the general condition of the patient, sequelae and even death. During the post-surgi-

cal period, a reassessment of the structures adjacent to the surgical site was performed to rule out the possibility of recurrence or persistence of the disease. Subsequently, follow-up was carried out using clinical and imaging controls to determine the stability and improvement of the patient.

Results

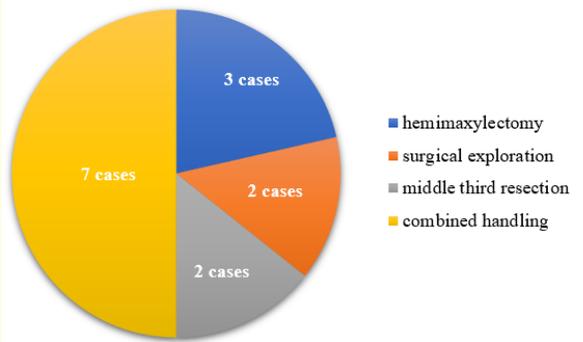
In a period of 6 years, 14 patients with a diagnosis of zygomycosis/mucormycosis presented (Figure 1), treated by the Maxillofacial Surgery service of the Specialty Hospital, CMN XXI Century. Of which 8 were men and 6 women, with an age range of 30 to 74 years. The mean for the age was 49.7142 years, median and mode of 50 years, respectively. The treatment was pharmacological with Amphotericin B with a dose of 1.5 mg/kg/day. Surgical management was depending on the case: total maxillectomy: 3 cases, hemimaxylectomy: 2 patients, surgical exploration: 2 cases, middle third resection, a total of 7 patients with marginal resections (Figure 2) without surgical management by Ophthalmology; the other 7 patients were treated with a combined technique (which included resection with evisceration or enucleation, joint endoscopic surgery with otorhinolaryngology or brain surgery, under management with neurosurgery) (Graph 1). Therefore, it is highlighted that middle third resection is the most frequent treatment of zygomycosis in Maxillofacial Surgery of the CMN XXI Century. Of the total of 14 patients, 3 patients were reconstructed with temporal flap rotation and 4 cases with fistula closure. Only 2 deaths were reported, survival was 85.7142%.



Figure 1: Left half of the face affected by zygomycosis (yellow arrows).



Figure 2: Surgical resection in the left half of the face with left orbital exenteration due to zygomycosis.



Graph 1: Zygomycosis treatment.

Discussion

This research work adheres to the management of patients with Mucormycosis reported in the literature. Since the analysis carried out by various authors on patients with surgical management for zygomycosis, for example the study by Serrano-Higueta., *et al.* Regarding the value of the medical-surgical as well as the clinical-radiographic correlation, it has been of importance for this study. Therefore, early surgical management has guaranteed a better prognosis for patients treated in The Maxillofacial Surgery (CMF) service of the Specialties Hospital of the XXI Century National Medical Center, where it is also reported to be one of the main receiving centers nationwide for this disease [1,5]. Regarding the clinic, similarities were found with the study carried out by Zavaleta Martínez., *et al.* they report the clinical characteristics of zygomycosis

in the case of a treaty in Aguascalientes, Mexico; they are similar with some of the cases in our study, such as: acute sinusitis with fever, nasal congestion and sometimes purulent nasal discharge and headache, affection to the palate (Figure 3), orbit and extension to the skull with cerebral affection [21]. Another author who mentions more severe clinical characteristics is Castrejón-Pérez who mentions they present an ulcerative lesion with necrotic edges with extension to orbit [22], which also coincided with some patients in the sample of this study. Roden M., *et al.* report one of the largest samples of patients with mucormycosis in a retrospective study in the period from 1885 - 2005 of 929 patients, it is a very long period since it is said to be more than one hundred years old [23]. The present study was carried out in a span of 6 years, having 14 patients in total treated by the Maxillofacial Surgery (CMF) service; It is a representative sample compared to other studies that report one to three cases in retrospective studies. On the other hand, like the study by Kauffman C and Malani A [24]. Most of the patients we reported in this study were diabetics and that surgical treatment should preferably be carried out within the first 24 hours of admission.

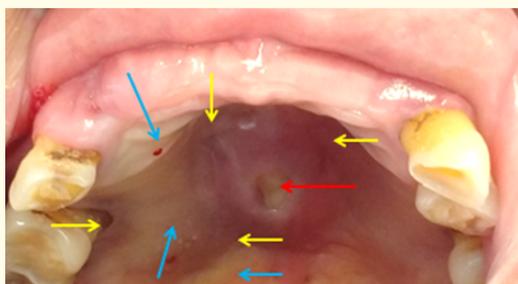


Figure 3: Early-stage zygomycosis: palate with denuded area (red arrow) ischemia (blue arrow) purplish areas and periodontal necrosis (yellow arrows).

Conclusion

Zygomycosis/mucormycosis is a severe fungal infection of rapid progress and extension that occurs frequently in immunocompromised patients, affects the oral cavity, nasal can even reach the skull, which can compromise the life of the patient. In Mexico there are few current studies that report the results of case series or research studies on the management of patients diagnosed with zygomycosis. This study was carried out in one of the most important

Medical Centers in the country. More than three quarters of the patients treated by Maxillofacial Surgery (CMF) service of the Specialties Hospital of the XXI Century National Medical Center, had an adequate prognosis and had no recurrence, in addition, as a result, there was a high percentage of survival of the patients, being almost 86%. It is necessary and essential to know the management of mucormycosis in order to offer the patient a better prognosis and treatment, as well as to contemplate during surgery the maintenance of free edges, which will avoid the extension and progression of the disease, which is why it is necessary to Being radical in the intervention, in addition to this form, the need for re-interventions and the risk that it generally entails for the patient will be reduced.

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Conflict of Interest

Neither the authors nor any member has a financial or interest relationship (currently or in the last 12 months) with any entity producing, marketing, reselling or distributing health care products or services consumed by, or used in, the patients.

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