

Is Death Possible as a Complication of a Tooth Extraction? Mucormycosis, a Rare and Lethal Infection

Sergio Augusto Luis Fernandes¹, Mario Utrilla Trinidad^{2*} and Juan Fernandes Andrade³

¹Dentist, Oral Surgery Resident Hospital Universitario Fundación Jiménez Díaz Madrid, Spain

²Doctor in Dentistry, MBA in Healthcare Management, Director of the Master in Management and Direction of Dental Clinics of Psico Dent, Spain

³Plastic Surgeon. Madrid, Spain

*Corresponding Author: Mario Utrilla Trinidad, Doctor in Dentistry, MBA in Healthcare Management, Director of the Master in Management and Direction of Dental Clinics of Psico Dent, Spain.

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Abstract

Objective: The aim of this work is to obtain current knowledge about mucormycosis and its relationship to the maxillofacial region.

Material and Method: A bibliographic review has been carried out based on scientific articles of case reports and bibliographic reviews published in PubMed.

Conclusions: Mucormycosis is an infection caused by *Phycomycetes* fungi which usually affects uncontrolled diabetic patients or with some alteration in the immune system. Being able to cause death in a large percentage of cases.

The route of entry of microorganisms is by inhalation, ingestion or inoculation through a loss of anatomical continuity, these fungi possess tropism through the endothelium of the blood vessels, cause thrombus and consequently hypoxia, acidosis, necrosis and fungal proliferation.

For this reason, the maxillofacial region has a high risk of being affected by mucormycosis as it has a high vascularity and is susceptible to the entry of microorganisms.

Treatment, not always successful, consists of surgical debridement, administration of amphotericin B and hyperbaric oxygen, as well as the treatment of symptomatology or associated diseases.

Keywords: Mucormycosis; Rhinocerebral; Dental Extraction

Introduction

In human history, one of the diseases that humans have faced have been fungal infections, so-called mycosis. As early as 1885 Paltauf first described a strange type of mycosis called, at that time, mycosis mucorin whose name was later changed to what is now known as mucormycosis. This disease became minor until in 1942 Gregory, *et al.* published three articles on death by mucormycosis [1].

The pathology-causing microorganism can be classified as class *Phycomycetes*, order *Mucorales*, family *Mucoraceae* and genus *Rhizopus*, *Mucor*, *Rhizomucor* and *Absida* [1]. They are found in a ubiquitous way and can be commonly found on the ground, manure, plants and decomposing material, not causing illness in most health conditions, although if they generate infection, they could be life threatening [2].

Study Objectives

The objective of this study is to obtain a compendium on current knowledge of mucormycosis and its relationship with the maxillofacial region.

Material and Method

A bibliographic review has been carried out based on scientific articles of case reports and bibliographic reviews published in PubMed between 2001 and 2018.

Results and Discussion

Mucormycosis can be defined as an invasive infection and of possible fatal outcome, caused by fungi of the species *Rhizopus* and *Mucor* [3]. These microorganisms are unvirulent, aerobic and grow after two or five days if incubated in the middle of Sabouraud [4]. It can become a rapidly evolving infection [5] and is usually given in certain groups of patients as they may be diabetic (more than half of cases occur in uncontrolled diabetic patients since in these patients are likely to have a defect in the innate cellular response and lower blood flow [6]), transplant or stem cell recipients as well as patients in which the immune system is compromised [3]. Other risk factors include: patients with renal failure, malignancies such as lymphomas and leukemia, long-term use of corticosteroids, burns and malnutrition [7].

The mortality rate is between 40 and 70% of infections [8]. In rhinocerebral form it is 85% despite the start-up of treatment through surgical debridement, antifungal therapy and treatment of other associated problems [6].

Diagnosis is confirmed by anatomopathological examination with histochemical coloration, in particular periodic-Schiff acid (Pas) and Gomori-Grocott, in which short, thick and unsepted micelly filaments with right-angled branches are seen. Differential diagnosis should be made with aspergillosis in which the filaments would be septed and bound by acute angles [4]. Another reported diagnostic medium is calcofluorfluorescence microscopy [9].

Among invasive fungal infections it is estimated that mucormycosis represents 0.7% of them, affecting sinus tissues mainly, but can be found in a skin, pulmonary and digestive form, establishing the rhinocerebral form between 40 and 49% of these fungal infections [4]. The incidence of this disease shows an increase with a prevalence of almost 1.7 cases out of 1,000.00 of the population in the United States. 580 cases per year in that country [3]. Being the third most common fungal infection after aspergillosis and candida infection [1].

The intake route for fungi can be a loss of anatomical continuity as can occur after a tooth extraction or in a ulcer and the spores can reach the body by inhalation, inoculation or ingestion. These spores usually face the first line of defense of the organism (mononuclear and polynuclear phagocytes) and in healthy patients do not generate infection, destroying the spores of *mucoral* fungi by oxidative metabolites and dephensins [7].

Once the infection is established, vascular invasion by the fungi occurs thus producing thrombosis which leads to hypoxia, acidosis and growth of fungi in the tissues and, therefore, necrosis [3]. It has been identified *in vivo* the GRP78 protein as the receptor located in the endothelium that interacts with the mucormycosis-causing spore in angiogenic invasion [8]. If the spores are inhaled the upper airways are affected giving sinus and nasal manifestations, the infection can spread through the blood vessels to the base of the skull with the consequent passage to the nervous system and thus causing the rhino-orbit-brain form or the rest of the body thus causing the potential death [7].

On the other hand, sometimes patients without diabetes and without apparent commitment of the immune system may suffer from this infection and this is probably due to possible fungal infection in epithelials and blood vessels previously affected by direct trauma, infection prior to or the action of cytotoxic agents [7].

In relation to dental practice it is known that mucormycosis can manifest from the beginning with symptoms such as facial pain, ear pain, sinus pain or dental pain so patients can go to the dentist in the first place [10]. On the other hand, the inflow of the fungus may occur at dental consultation when a wound occurs after a tooth extraction or curettage [2,10]. The disease can also develop from the beginning as a periodontal disease. Generating ulcerative-necrotizing gingivitis and with possible spread to the bone, producing its necrosis and, therefore, dental mobility when the periodonto is destroyed [2].

As regards the treatment of mucormycosis, symptomatic treatment should be instituted and, on the other hand, medical treatment using amphotericin B and hyperbaric oxygen and surgical treatment should be instituted by removing the tissues infected and necrotic

[1,11]. As a second treatment line, the use of posaconazole has been described, in cases where amphotericin B cannot be used due to its adverse effects [7].

In a study by Saeed Nezafati, *et al.* seven cases of mucormycosis after maxillary tooth extraction were reported between 2007 and 2017. This ailment can be observed in this area due to the high vascularity of the maxilla that allows the rapid expansion of the fungus especially in diabetic patients with altered immune response [3].

In 2006 Abdulaziz a Bakathir published an article on two cases of mucormycosis after tooth extraction in patients with associated risk factors, type II diabetes and leukemia [12]. In a study by Jone Kim., *et al.* in 2001 a case of death by mucormycosis occurs in a diabetic patient after a tooth extraction, occurring death twelve days after dental intervention [11]. As for mucormycosis as a periodontal disease Nancy E., *et al.* in 2010, they report a case of a leukemia patient with mucormycosis in the periodontium which was successfully treated [9].



Figure 1: Mucormycosis in facial region.



Figure 2: Mucormycosis in facial region.



Figure 3: Mucormycosis in facial region.



Figure 4: Surgical resection of mucormycosis in facial region.



Figure 5: Relapse of Mucormycosis in facial region.

Conclusion

Mucormycosis is an infection caused by *Phycomycetes* fungi which usually affects uncontrolled diabetic patients or with some alteration in the immune system and may cause death in a large percentage of cases.

The route of entry of microorganisms is by inhalation, ingestion or inoculation through a loss of anatomical continuity, these fungi possess tropism through the endothelium of the blood vessels, cause thrombus and consequently hypoxia, acidosis, necrosis and fungal proliferation.

For this reason, the maxillofacial region has a high risk of being affected by mucormycosis as it has a high vascularity and is susceptible to the entry of microorganisms.

Treatment, not always successful, consists of surgical debridement, administration of amphotericin B and hyperbaric oxygen, as well as the treatment of symptomatology or associated diseases.

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