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Mucormycosis of Maxilla: A Case Report

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Abstract

Mucormycosis is a very common and dangerous type of fungal infection that comes on quickly and gets worse quickly. It mostly affects the nasal cavity and the paranasal sinuses. It happens when people breathe in fungal spores that are present in the air in moderate quantity. Fungi from the genera *Absidia, Mucor, Rhizomucor* and *Rhizopus* are the main causes of this condition. They belong to the subphylum Mucormycotina. These organisms have a propensity to induce severe disease in individuals who have weakened immune systems. People with immunodeficiency syndromes, especially those with diabetes mellitus, are at a much higher risk. The rhinomaxillary region is the most common place for this infection to happen, which makes it more likely to spread. This report deals with two clinical cases that were handled in our department of Oral and Maxillofacial Surgery (OMFS). Both cases needed a combination of treatments, such as surgery, antibiotics and antifungals. After the infection was successfully treated, the patients were exposed to obturator prostheses. The use of obturators was a big part of the rehabilitation process because they made things work better and made people more comfortable. After treatment, the overall quality of life of the patients got a lot better.

Keywords: Cases, Diabetes Mellitus, Maxilla, Mucormycosis, Surgery.

Introduction

Fungal osteomyelitis is a rare but serious infection that mostly affects the maxilla. It gets worse over time, especially in people with weak immune systems. This condition is very common in people with weak immune systems, especially those between the ages of 10 and 65. This suggests that both younger and older people may be at risk when they have other health problems. It is mainly seen in men, with a reported male-to-female ratio of 2.1:1, which means that men are more likely to be affected or exposed (1). The order Mucorales is responsible for about 44% of reported cases of this condition. Aspergillus species are responsible for almost 2% of infections. India has a much higher rate of fungal osteomyelitis, with rates ranging from 0.02 to 9.5 cases per 1,000 people (2). This number is about seventy times higher than the worldwide average, which strongly suggests that factors related to the region, the environment, the economy, and healthcare may be making this disease more common in the country. These observations suggest that some local conditions and risk factors may be very important in making fungal osteomyelitis more likely to happen.

The disease is especially bad because it has high rates of illness and death, which show how much it hurts people physically, functionally, and mentally. A lot of these bad outcomes can be traced back to late diagnosis, serious underlying medical conditions, and the fact that fungal pathogens are naturally aggressive. In numerous instances, initial symptoms may be subtle or nonspecific, resulting in misdiagnosis or postponed treatment. People with diabetes mellitus, especially those who have diabetic ketoacidosis, are more likely to get fungal osteomyelitis because their immune systems are weaker and their metabolisms are different (3). As the disease gets worse, it often destroys a lot of tissue, which can cause severe facial deformities, constant pain, trouble eating and talking, and a lot of social and emotional distress. In very bad cases, if diagnosis and treatment aren't started right away, the infection could become fatal and even kill the person. This paper talks about two cases like this that we treated in our oral and maxillofacial surgery clinic. In these cases, full management included surgery as well as antifungal and antibiotic therapy. Also, obturator

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prostheses were used to help with recovery and restore oral function, which made the overall results of rehabilitation better (4).

The initial recorded case of mucormycosis, a significant contributor to fungal osteomyelitis, was noted by Friedrich Kuechenmeister in 1855 (5, 6). His early work set the stage for later studies of the clinical and pathological aspects of this infection. The COVID-19 pandemic has shown a worrying link between mucormycosis and SARS-CoV-2 infection, especially in people with uncontrolled diabetes and those who are getting immunosuppressive treatments (7).

Diabetes mellitus is a long-term metabolic disorder that causes blood sugar levels to stay high because the body doesn't make enough insulin, the insulin doesn't work properly, or both. If this condition isn't treated, it can cause a lot of problems throughout the body, such as damage to blood vessels, neuropathy, and problems with the immune system (8). These changes make the body more likely to get opportunistic infections like fungal osteomyelitis. There are many clinical forms of the disease, such as rhino-cerebral, pulmonary, gastrointestinal, disseminated, cutaneous, and other types. The rhino-cerebral or rhinomaxillary form is the most common of these, especially in people with poorly controlled diabetes mellitus (9). Most of the time, the infection starts in the nasal or palatal mucosa and then moves to the paranasal sinuses. As the disease gets worse, it may spread to nearby blood vessels, such as the angular, lacrimal, and ethmoidal vessels, which makes it easier for it to spread quickly.

Invasive fungi, like *Rhizopus oryzae*, take advantage of the host's weakened immune system, especially in people with diabetic ketoacidosis. In these people, transferrin's ability to bind to iron is lower, which makes more free iron available. This encourages fungal growth and virulence. Fungal osteomyelitis often starts out looking like less serious infections, with symptoms like low-grade fever, headache, facial pain, facial swelling, and general malaise. If not treated, the disease could spread to the lungs, the back of the eyes, and the central nervous system. This widespread involvement often leads to death because of hematogenous spread and failure of multiple organs (10).

The goal of this case report is to look more closely at the pathophysiology, diagnostic problems, treatment options, and clinical outcomes of fungal osteomyelitis, with a focus on mucormycosis. It underscores the essential significance of prompt identification and intervention, along with the imperative of a multidisciplinary management approach. This kind of approach involves working together with surgeons, doctors, microbiologists, and rehabilitation specialists, as well as giving the right antifungal therapy, surgical debridement, and other treatments. It is possible to lower the risk of long-term complications, improve functional recovery, and raise survival rates through comprehensive and integrated care for this serious condition.

Methodology

Mucorales moulds are delicate and tend to disintegrate during collection of specimens leading to low culture sensitivity. As a result, the positive cultured on Sabouraud agar of only the microscopically positive specimen is only in the range of one-third. Contamination as opposed to infection often occurs in isolation of non-sterile sites, thus making specificity difficult. The use of tissue-based diagnosis is based on the identification of the typical wide (311m diameter), thin-walled, ribbon-shaped, highly aseptate hyphae that branch at right angles. Nucleic acid detection by polymerase chain reaction can help to diagnose mucormycosis earlier.

Radiologic imaging, which is not specific enough to make a definitive diagnosis, still provides an opportunity to quantify the anatomic involvement (11). Modern diagnostic modalities are gadolinium-enhanced magnetic resonance imaging (MRI) and contrast-enhanced computer tomography (CT). Bone scintigraphy, a specialised radiologic procedure, allows an assessment of skeletal involvement, and is more sensitive than CT in identifying physiological remodelling and erosion which could be mistaken as osteomyelitis. CT can also be used to determine mucosal thickness, air-fluid levels and erosion of bone. It is assumed that aggressive osteomyelitic activity occurs in the zygoma and maxilla when bone loss is observed; such observation is quite predictive of an invasive fungal infection in severely-immunocompromised patients. Extraorbital muscular hypertrophy often is the first sign of involvement in orbital imaging, either on CT or MRI.

A 38 years old male patient reported to the oral and maxillofacial surgery with one month of left cheek pain and purulent discharge in the mouth. On intraoral examination, there were several sinu tracts that were draining over the left buccal mucosa, mid-palatal area, and the anterior one-third of the hard palate. Dental mobility was grade II in teeth 23, 24, 25, and 26 as well as grade III in tooth 27. Later clinical examination revealed facial imbalance, left infra orbital edema and focal paresthesia. The medical history of the patient revealed diabetes mellitus that was diagnosed about one and a half months ago; the patient did not have any history of COVID-19 infection. A computed-tomograph scan revealed resorption of left maxillary bones but with the left maxillary sinuosity also involved. To obtain more diagnostic evidence, an incisional biopsy was done which showed histopathologic evidence of fungal osteomyelitis. In the case of surgery, local anaesthesia was provided and a crestal incision was done to carry out the sequestrectomy of the left maxilla. The necrotic bony defect was exposed by a full-thickness mucoperiosteal flap, the whole bony part was moved and abraded with osteotome, and the uneven edges were smoothened. The infected maxillary sinas happened then intensive irrigated and the hole stuffed with iodoform and paraffin ribbon gauze, the incision of release was sutured using 3-0 silk sutures. Six weeks of systemic antifungal therapy was ordered and patient was advised to come after fifteen days to change the dressing (Figure 2 A-F).

Results

By microscopic examination the stratified squamous epithelium exhibited parakeratinisation and the underlying collagenous connective tissue was in a loosely organized architecture. Branching, thick, septate hyphae were observed, and scattered throughout the connective tissue, and mingled with chronic inflammatory infiltrates. The use of hyphae identification by histological stains, such as haematoxylin and eosin, periodic acid eosin, and Grocotts methenamine silver (GMS), are regularly utilized in identifying the status of septation of hyphae, and GMS is most benefits especially in defining septation status. Figure 1 shows loosely arranged collagenous fibrous connective tissue with parakeratinized stratified squamous epithelium. Septate, broad, and branching hyphae were observed scattered all over the connective tissue and mixed with the chronic inflammatory cells.

Figure 2A shows the patient's frontal facial profile, demonstrating facial asymmetry and left infraorbital swelling at presentation and 2B illustrates the CT scan findings, revealing destruction of the left maxillary bone with involvement of the maxillary sinus. Intraoperatively, a full-thickness mucoperiosteal flap was raised to expose the necrotic area (Figure 2C), followed by removal of the sequestrated maxillary bone (Figure 2D). The excised necrotic bone specimen is shown in Figure 2E. Figure 2F depicts the postoperative clinical appearance following surgical debridement.

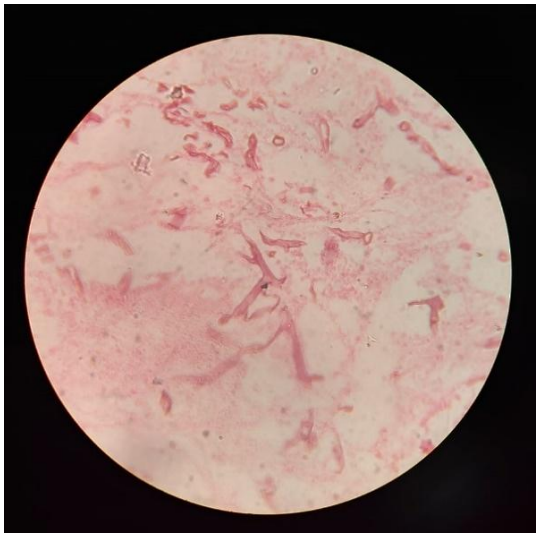

Figure 1: Microscopic Observation of Collagenous Fibrous Connective Tissue and Parakeratinized Stratified Squamous Epithelium Along with Septate, Broad, Branching Hyphae

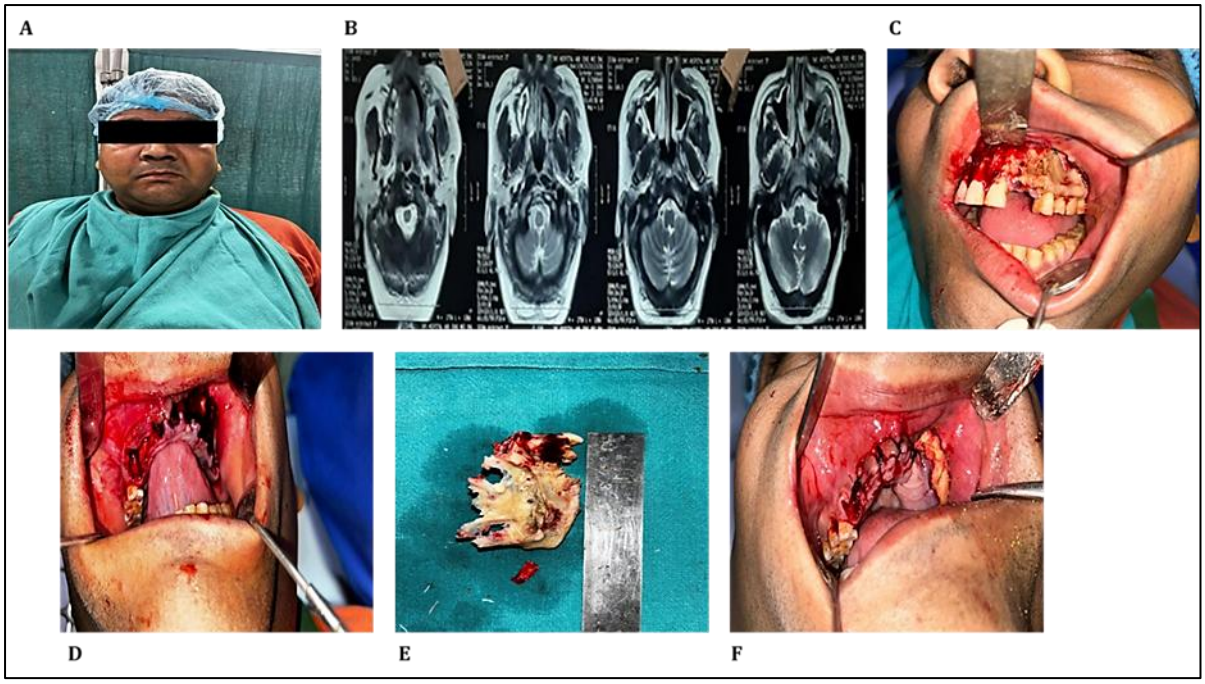

Figure 2: (A) Patient's Front Profile, (B) CT Showing Destruction of Bone with the Involvement of Maxillary Sinus, (C) Flap Raised After Incision, (D) Entire Chunk of Bone Removed, (E) Specimen of Bone, (F) Post-Operation

Discussion

Mucormycosis is highly invasive fungal infection which has a rapid progression; when not treated it can spread to other critical organs thus resulting in death. It has been proven that early surgical debridement and proper antifungal therapy is the keystone in the management. Nevertheless, antifungal drugs have a specific profile of adverse effects, and they should be tailored to the needs of each patient. The most commonly used antifungal in the treatment of mucormycosis include amphotericin 8 and posaconazole (12, 13).

Amphotericin B (AMB) can be considered the first-line treatment option in mucormycosis. AMB lipid preparations have the advantage of having a greater therapeutic index compared to traditional deoxycholate preparations. The most recent recommendations are to use liposomal amphotericin B (LAMB) at 5 mg/kg/day (14). There were no significant differences in response rates or mortality difference between the patients taking the recommended dose and the historical controls (5 mg kg/day -1). On the contrary, the braised LAMB exposure was linked to the electrolyte imbalance and aggravated nephrotoxicity. Though no better efficacy has been found in higher doses (>5 mg/kg/day/kg -1), higher doses can be considered in individual patients under close observation (15).

Traditionally, posaconazole existed only as an oral suspension that had to be ingested in three or four portions per day with food (preferably, a high-fat meal) or an acidic carbonated drink to maximize absorption. Its application in the critically ill patients who might not be able to take food orally or might have nausea due to the dietary restrictions linked with the suspension makes it a difficult treatment choice, and thus, inadequate absorption often led to treatment failures (16). As a way of overcoming these pharmacokinetic shortcomings an intravenous formulation and a gastro-resistant tablet were later created. The tablet has better bioavailability, allows one dose per day, eliminates dietary limitations, and is not dependent on gastric motility or pH, hence causing less inter-patient variability and having more reproducible plasma concentration (17). Therapeutic drug monitoring is still suggested in the tablet despite the improved pharmacokinetics. The IV formulation of β -cyclodextrin has good pharmacokinetic properties and is used in the uncommon situations when the oral route of administration is not possible. The question on how the tablet and IV preparations will be best

used in the management of mucormycosis still remains open. Nowadays, posaconazole suspension is used as 400 mg twice a day with meals or 200 mg four times with no meals, and it is perceived as the salvage treatment of mucormycosis (18).

Isavuconazole, the active metabolite of isavuconazonium sulfate (a prodrug of isavuconazole), is a new broad-spectrum triazole. In the United States and Europe, it has been shown to be used as a treatment of mucormycosis in situations where amphotericin B is not possible. The dosing schedule suggested included a loading dose of 200 mg thrice daily during 2 days which was followed by a maintenance dose of 200 mg once daily; the drug was given both intravenously and orally (19). Isavuconazole has a few pharmacokinetic and pharmacodynamic and safety benefits over other azoles: linear drug kinetics that prevent the need of therapeutic drug monitoring, less drug-drug interaction; decreased hepatotoxicity and other toxic responses (cutaneous and ocular toxicity); no nephrotoxic cyclodextrin contained in the IV formulation, no adjustment in dose in patients with renal, hepatic, or obesity; and superior oral bioavailability regardless of food intake (20, 21).

Conclusion

Given the increasing incidence of mucormycosis, our center's experience indicates that surgical debridement combined with antifungal therapy remains the most effective and dependable standard practice, especially when commenced early in the disease process, as prompt intervention significantly mitigates the risk of additional tissue damage and systemic complications. The delay in treatment is often due to the involvement of nearby vital organs, like the orbit, nasal cavity, and cranial structures. This makes the overall management process much more difficult and complicated, which means that multidisciplinary coordination and careful clinical decision-making are even more important, and it ultimately has a negative effect on the prognosis. Also, late diagnosis and not being able to get specialized care may also cause treatment delays, especially in places with few resources. There is no universally accepted time limit for therapy, as the length of treatment depends on the severity of the disease, how well the patient responds, and any other health problems they may have. As a result, therapy can continue until radiologic remission, stabilization and equilibration of laboratory values, and complete disappearance of clinical manifestations and symptoms are achieved and maintained over time. To check how well the treatment is working and stop it from coming back, it is important to keep an eye on it with imaging studies, lab tests, and clinical assessments. After the wound has healed properly and the tissue has been remodelled, it can be determined that the insertion of an interim prosthesis after the placement of a tooth-bearing obturator can be scheduled to achieve two main goals: preventing food debris from getting stuck in the surgical site and restoring effective chewing function, while also improving speech, facial symmetry, and mental health. This all-encompassing rehabilitation strategy ultimately empowers patients to restore their confidence and resume a typical life without considerable functional impairments or aesthetic detriment.

Abbreviations

AMB: Amphotericin B, CT: Computed Tomography, LAMB: Liposomal Amphotericin B, MRI: Magnetic Resonance Imaging, SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2.

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Author Contributions

Manisha Solanki: conceptualization, writing of the manuscript, Vinod Mehra: literature review, data analysis, writing of the manuscript, Harish Vaishnav: surgical treatment, supervision, writing of the manuscript, Shweta Nehe: case documentation, review of the manuscript, Azaram Khan: histopathological analysis, manuscript editing, Darshan Chauhan: radiological imaging analysis, manuscript editing.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

Declaration of Artificial Intelligence (AI) Assistance

The authors confirm that the research, writing, and analysis were conducted by the listed authors. AI assistance was not involved in any part of the writing or review process.

Ethics Approval

The case report was conducted following ethical guidelines and informed consent was obtained from the patients included in the study. The study did not involve experimental procedures and was based on the clinical management of real cases.

Informed consent

Informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

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