

Case report**Osteomyelitis of left Maxillary Region due to Mucor Infection**

Ramesh G, Raj A, Pathak S, Mishra S

Abstract: In routine practice, intra-oral exposed bone due to necrosis is generally diagnosed as osteomyelitis. This kind of necrosis can occur due to bacterial osteomyelitis, herpes zoster, trauma, iatrogenic infections, or fungal infections, such as mucormycosis, aspergillosis, etc. In diabetic patients there is a high incidence of mucormycosis caused *Rhizopus arrhizus*, because they produce the enzyme ketoreductase, which allows them to utilize the patient's ketone bodies. Here we present one such case of mucormycosis infection causing osteomyelitis in an extraction socket in a 65 year old male patient with uncontrolled diabetes.

Keywords: Diabetes Mellitus; Fungal; Ketone bodies; Maxilla; Mucormycosis; Osteomyelitis.

INTRODUCTION

Osteomyelitis is an inflammatory bone disease affecting bone marrow. It frequently compromises cortical bone and periosteum. Before the advent of antibiotics, it was a life-threatening disease; in our days, if adequately treated, it can resolve satisfactorily.¹ Although other etiological factors, such as traumatic injuries, radiation, and certain chemical substances, among others, may also produce inflammation of the medullar space, the term "osteomyelitis" is mostly used in the medical literature to describe a true infection of the bone induced by pyogenic microorganisms.²

One of the first reports on osteomyelitis was written in 1832 by British physician Sir Benjamin Brodie, who for the first time described a type of abscess, which in our days is known as the Brodie abscess, and which represents one of the chronic features of osteomyelitis.³

Fungal infection causing osteomyelitis is an increasingly recognized entity both in normal and immunocompromised individuals. Amongst which Mucormycosis is a rare fulminating opportunistic fungal infection caused by a fungus of the order mucorales. Although the fungi and spores of mucorales shows minimal intrinsic pathogenicity towards normal persons, they can initiate aggressive and fulminating infection in the patients whose resistance is lowered by immunocompression, diabetes, malignant disease, burns, trauma and rarely by steroids or in solid organ transplanted patients.⁴ We here report one such case of fungal osteomyelitis in anterior maxillary

region caused due to mucorales in a 65 years old male patient with uncontrolled diabetes.

CASE REPORT

A 65-year-old male patient reported to a private clinic with chief complaint of pain and pus discharge from the maxillary anterior teeth area. Patient also gave a history of extraction of maxillary second premolar two months back following its mobility from a local dentist in rural area. On extra-oral examination there was mild swelling over the nasolabial fold area. On intra-oral examination in the area of the extraction the socket was unhealed and was showing the exposed necrotic grey to brown colored bone with halitosis. The patient was also diabetic since 3 years and was irregular on medication.

There was slight swelling on the palatal surface of the maxilla. A periapical radiograph was taken, which showed radiolucency with thin bony spicules extending close to the floor of maxillary sinus, but not involving it. Based on the history and observations a provisional diagnosis of infective osteomyelitis was made. The area of the socket was curetted, debrided and irrigated and the wound was secondarily closed using an iodoform pack.. The curetted necrotic tissue along with the granulation tissue was sent for histopathological examination. On histopathological examination the decalcified tissue sections revealed acellular basophilic appearing necrotic bone along with highly cellular stroma due to infiltration of mixed inflammatory cells along with proliferated blood capillaries (Fig 1). There were areas of clumps of fungal hyphae (Fig

2&3) which were aseptate, ribbon-like hyphae branching at right angle (Fig 4).

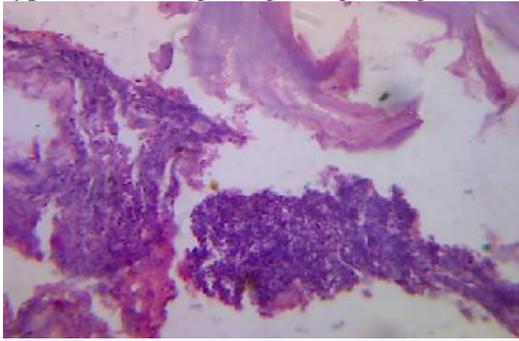


Figure 1: Necrotic bone surrounded by densely inflamed granulation tissue.

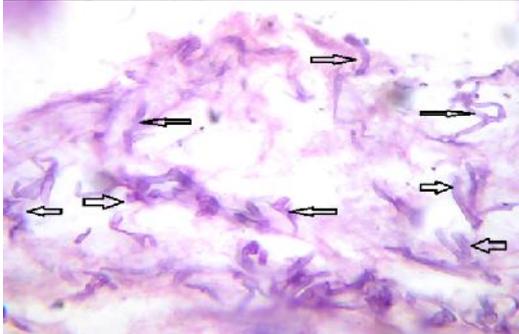


Figure 2&3: The low (circled area) and high power microscopic image showing clumps of hyphae (arrows) within the lesional tissue.

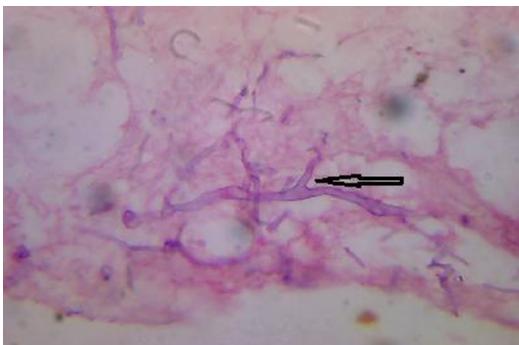


Figure 4: Right angled branching ribbon-like hyphae (arrow).

This morphological feature was reconfirmed by a microbiologist and was finally

diagnosed as osteomyelitis caused due to mucormycotic hyphae. Following the diagnosis the patient was referred to the physician for further medication to control diabetes along with antifungal and was called for regular follow-up. On every follow-up the iodoform gauze was changed after thorough irrigation and dressing was placed. After three weeks of follow-up the socket showed healthy granulation tissue and the wound healed uneventfully within three months of time.

DISCUSSION

Osteomyelitis typically appears during the 5th and 6th decades of life. It is associated to systemic diseases such as diabetes mellitus, auto-immune diseases, agranulocytosis, leukemia, anemia, nutritional deficiencies, syphilis, cancer, chemotherapy and radiotherapy, as well as habits of alcohol or tobacco consumption.⁵ Inflammation has its origin in the bone marrow, and extends to cancellous bone spaces. It then spreads through blood vessels, fibro-elastic tissues, and eventually to the periosteum. When the vascularity of bone tissue is compromised, it induces bone necrosis and sequestration.¹

Among the facial jaw bones, the lower jaw is more frequently affected than the upper jaw. Lower jaw has a singular vascular supply and due to which when there is an intense osteomyelitic infection, there is greater probability to develop bone sequestrations. This is due to a terminal type irrigation which cannot compensate peripheral vascular supply of gums and periodontium. Due to vascular thromboses and endarteritis or sympathetic and parasympathetic vegetative reflexes, a vasoconstriction of these vessels is produced. As a result of odontogenic infection, osteomyelitis can be generated in upper or lower jaws.⁶

The fact being that, in the upper jaw, there is cancellous bone tissue with greater vascular supply, which hinders bacterial colonization, since cellular response is enhanced and has greater blood flow which thus counteracts bone invasion.^{7,8} But in the upper jaw anterior region, vascular supply is juxta-terminal thus favoring bone sequestration, this result to blood being compromised and

eliciting as a consequence oral-nasal communication. The present case also was seen affecting the maxillary anterior region following an extraction.⁹

Fungi have been one of the causative infectious agents for humans earlier than bacteria.¹⁰ Amongst which Mucormycosis incorporates a variety of infections caused by *zygomycetes*; a class of fungi that produce branching ribbon-like hyphae and reproduce sexually by formation of zygospores. These organisms have been isolated from fruits, soil, feces, and also been cultured from the oral cavity, nasal passages, throat of healthy disease-free individuals. *Mucorales* a subtype of *zygomycetes* is angiotropic, causing tissue necrosis, and are associated with disseminated and often fatal infections, especially in immunocompromised hosts.¹¹

Ulceration in the mucosa or an extraction wound in the mouth can be a port of entry for mucormycosis in the maxillofacial region, particularly when the host is immunocompromised and causing osteomyelitis in the extraction socket region. Diabetes mellitus one such disease causing immunocompromised state alters the normal immunological response of body to any infection in several ways.¹¹

India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the “diabetes capital of the world”.¹² Unfortunately the poor diabetic subjects delay taking treatment leading to increased risk of complications.¹³ The low socioeconomic status and unavailability of aseptic and atraumatic conditions for surgery at remote areas is common most explained reason for osteomyelitis after tooth extraction whereas, the use of antibiotic in modern era has improved this condition especially in rural areas.¹⁴

Our case also presented a state of exposed, necrotic bone in the region of extraction on the maxillary alveolar area following an extraction performed by a local dentist that lead to infection caused by mucorales a common infection in uncontrolled diabetic patients. This explains that a dental practitioner in Indian scenario should not

neglect the case history especially of diabetes before performing an extraction in a rural center since it may jeopardize the bone causing complications.¹⁵

Invasive mucormycosis is characterized by the rapid development of tissue necrosis resulting from incursion of blood vessels, ensuing thrombosis. Hyperglycemia stimulates fungal proliferation, and the diabetic reduction in chemotaxis and phagocytic efficiency permit these otherwise innocuous organisms to thrive in acid-rich environment. In the diabetic ketoacidotic patient there is a high incidence of mucormycosis caused by *Rhizopus oryzae* because they produce the enzyme ketoreductase, which allows them to utilize the patient’s ketone bodies.¹¹ It has been established that diabetic ketoacidosis momentarily disrupts the ability of transferrin to bind iron and this alteration eliminates a significant host defense mechanism and permits the growth of *Rhizopus oryzae*.¹⁶

Mucormycosis can be successfully managed by early diagnosis, reversal of underlying predisposing factors, prompt and ideally broad surgical debridement of infected tissue and rapid administration of systemic antifungal therapy.¹⁴ The mortality rate in recent times has been reduced due to better diagnosis and management of the usual comorbidities. The control of underlying predisposing illness and aggressive surgical debridement, along with prompt parenteral administration of amphotericin B remains the essential treatment for better recover.¹⁷

Though amphotericin B formulations have remained the basis of treatment for mucormycosis, recent studies have demonstrated that posaconazole, an extended-spectrum triazole agent, has in vitro activity against *zygomycetes* and may represent a therapeutic option for patients with serious invasive fungal infections.^{18,19} According to Pandey et al. (2011)¹⁷ however clinical data on the use of this medication for mucormycosis are limited and Posaconazole cannot be used for treatment of such cases here in India, as the drug is not available in India.

CONCLUSION: Fungal infections of the jaws are usually seen in both immunocompromised and immunocompetent individuals, so clinicians should be aware that osteomyelitis caused due to infections that is unresponsive to usual management is highly suggestive of mycoses of the jaws. Any individual with underlying immunocompromised status with suspected osteomyelitis of the jawbones should be investigated for fungal infections also. The effective case history taken prior to extraction would prevent the patient from all complications. It should be noted that the uncontrolled diabetic state is always a relative contraindication for extraction and the patient's blood sugar level should be in controlled state before extraction. Aggressive surgical management in the form of ideal broad surgical debridement should be initiated promptly and as early as possible since most antifungal agents have poor penetration ability at the diseased site. Invasion of tissue by the hyphae must be seen microscopically to establish the diagnosis and to avoid the high morbidity and mortality associated with this destructive disease.

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