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Review Article

Post covid-19 fungal infection and its impact on orthodontic practice: A review

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ABSTRACT

As COVID-19 cases are reducing worldwide, the patients recovered from this disease are showing some complications include impact on lungs, kidneys, heart, and cases of a black fungal infection, called mucormycosis. There are a variety of bacterial and fungal co-infections which is associated with poorly controlled diabetes mellitus and other immune impaired condition. The COVID-19 exhibits, a specific pathophysiological feature, which will result in secondary fungal infections. The recent COVID-19 wave showed that many children and young people are testing positive for this disease. There is high chance for some of them can come across an orthodontic clinic. Oral mucormycosis is normally developed from the breathing of spores or through an open contaminated oral wound, affecting mainly immunocompromised patients. Oral mucormycosis is reported in some patient, following tooth extraction. The fungal spore can reach the body when there is a loss of anatomical continuity as can occur after a tooth extraction or in an ulcer. Chance for Post COVID-19 Mucormycosis in orthodontic patients are very rare. However, Orthodontist should take care when doing minor surgical procedure in the patient recovered from severe COVID-19 infection. Orthodontic appliances can increase the number of bacteria and fungus by limiting oral hygiene. Orthodontist should advise patients to the importance of maintaining basic oral hygiene measures, which include simple things like changing the toothbrush once they test negative, oral rinsing and brushing.

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1. Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is caused by the coronavirus disease 2019 (COVID-19) infection, can cause a variety of symptoms, from mild to life-threatening pneumonia. There are a variety of bacterial and fungal co-infections which is associated with poorly controlled diabetes mellitus and other immune impaired condition.¹

Systemic immune alterations in COVID-19 infection and other preexisting immunocompromised condition like a Diabetic Mellitus, previous respiratory pathology or use

of immunosuppressive therapy can result in secondary infections.² A review by Rawson TM³ shown during hospital admission, 8% of patients had secondary bacterial or fungal infections. This may be associated with extensive use of broad-spectrum antibiotics with no underlying evidence of infection (72% of patients).³

The COVID-19 exhibits, a specific pathophysiological feature, which will result in secondary fungal infections, like an extensive pulmonary disease cause an alveolo-interstitial pathology which will increase the chance of invasive fungal infections. And it can be secondary to the immune dysregulation related to COVID-19, with reduced numbers of T lymphocytes, CD4+T, and CD8+T cells, may alter natural immunity.⁴

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The fungal spore enters the body through inhaled dust, results in the nose and paranasal sinus infection. The fungus starts to invade blood vessels, once the infection is established, which results in thrombosis, hypoxia and necrosis. vascularity in the maxillofacial region is high, for this reason there is a high risk of being suffering from mucormycosis and to the entry of microorganisms followed by dental extraction.⁵

As Covid-19 cases are increasing worldwide, many children and young people are testing positive for this disease.⁶ There is high chance for some of them can come across an orthodontic clinic. Orthodontic appliances can increase the number of bacteria and fungus by limiting oral hygiene.⁷ Orthodontist should advise patients to the importance of maintaining basic oral hygiene measures, which include simple things like changing the toothbrush once they test negative, oral rinsing and brushing.

2. Mucormycosis

Mucormycosis is a rare fungal infection caused by mucoromycete, which usually effect the maxillofacial region. These fungi found throughout the environment, particularly in soil and in the rotten organic matter, like leaves, compost pile, or rotting trees. This type of fungus people frequently experiences, when they have rotten fruit or molded bread in their kitchen.⁸

People get mucormycosis, when fungus from then environments enter the body when someone breathes in spores. This type of mucormycosis usually occur in patients, who have chronic diseases or take medicines that lower the body immunity. Mucormycosis also can develop on the skin after the fungus enters the skin through a cut, scrape, burn, or other sort of skin trauma.⁹

3. Etiology

Mucormycosis is a communicable disease caused by a fungus of the class of Zygomycetes and therefore the order of Mucorales. The species most often isolated from patients are Apophysomyces, Cunninghamella, Lichtheimia, Mucor, Rhizopus, Rhizomucor, and Saksenaea.¹⁰

They are usually seen in surroundings and aren't harmful to people with innate immunity. In immunocompromised patients like transplant patients, HIV, patients under chronic steroids, leukemia or other cancer patients, they will present with a rapidly progressive necrotizing infection. Similarly, patients with uncontrolled diabetics also are in danger.¹⁰⁻¹²

4. Types of Mucormycosis

4.1. Rhino-orbital mucormycosis (ROCM)

This type of mucormycosis seen in people with uncontrolled diabetes and in those who have had a kidney transplant, which occurs in the sinus then spread to the brain.¹³

4.2. Pulmonary (lung) mucormycosis

This type of mucormycosis found in cancer patients and in those who have had a transplant.⁹

4.3. Gastrointestinal mucormycosis

This type of mucormycosis is more common among young children and premature and low birth weight infants than adults, who have had antibiotics or medications that lower the body immunity.⁵

4.4. Cutaneous (skin) mucormycosis

It is the most common type of mucormycosis. When the patient is suffering from chronic disease, this type of fungus enters the body through an opening within the skin.⁹

4.5. Disseminated mucormycosis

It occurs when the fungus enters the blood to affect another part of the body. Usually it effects on the brain, but can also affect other organs like the spleen, heart, and skin.⁹

5. Epidemiologic Characteristics

Among invasive fungal infections it is estimated that mucormycosis represents 0.7% of them, affecting sinus tissues mainly, but are often found in a skin, pulmonary and digestive form, establishing the rhino cerebral form between 40 and 49% of those fungal infections. Being the third-commonest mycosis after aspergillosis and candida infection.^{14,15}

India, alongside the Covid-19 outbreak, is additionally witnessing a surge within the cases of mucormycosis among coronavirus patients. However, India isn't the sole country facing this problem. Before the outbreak of Covid-19, mucormycosis cases were reported in diabetes mellitus patients.¹⁶ As per March 2021, India accounted for 71 per cent of the entire cases of mucormycosis reported from around the world.¹⁷

According to report from Pakistan media, the country is also facing a surge in cases of ' mucormycosis ' among Covid-19 patients. Like in India, Pakistan suspects the rampant use of steroids for the surge in cases of this rare disease. Russia too, on 17 May, confirmed reports of Black Fungus among COVID-19 patients. Russia, though has ruled out a chance of a person to person the spread of the Fungus and has claimed that the case is in control.¹⁸

6. Oral Manifestation

In reference to dental practice, it can manifest from the beginning with symptoms like facial pain, ear pain or dental pain.¹⁹ On the other hand, the inflow of the fungus may occur at dental consultation when a wound occurs after a tooth extraction or curettage. The disease also can develop

from the beginning as a periodontitis. Generating ulcerative-necrotizing gingivitis and with the possible spread to the bone, producing its necrosis and, therefore, dental mobility when the periodontium is destroyed.²⁰

Other Fungal Infection Associated with COVID-19

6.1. Invasive candidiasis (IC)

Candida infection is seen in severe COVID-19 patients, who have treated with broad-spectrum antibacterial drugs, invasive examinations, or the patients accompanied by prolonged neutropenia and other immunocompromised condition.²¹

Candida auris is an emerging fungus which will cause outbreaks of severe infections in healthcare facilities. Earlier in the United States, candida infection was reported in patients with chronic diseases. However, since the beginning of the COVID-19 pandemic, outbreaks of *C. auris* are reported in COVID-19 units of acute care hospitals. The changes in routine infection control practices during the COVID-19 pandemic, including limited obtainability of gloves and gowns, or reuse of those items, and changes in cleaning and disinfection practices, could be the reason for this outbreak. New *Candida auris* cases are reported, without any links to known cases or healthcare in multiple states, alarming a rise in undetected transmission.⁹

7. Oral Manifestation

Oral manifestation may vary according to types of oral candidiasis. The most frequent type of oral candidiasis is Pseudomembranous candidiasis, which presents white or yellow scrapable plaques on the oral mucosa. The yeast that predisposes keratinocyte desquamation is seen as a white and/or yellow plaque on the oral mucosa. It can be either acute or chronic. The Pseudomembranous type of oral candidiasis is seen in patients with immune dysregulation or immunosuppressive medications.²²

The erythematous type can be acute or chronic. Erythematous patches are commonly seen on the palate and dorsum of the tongue and are usually presented as atrophied areas of the oral mucosa. Patient under corticosteroids or broad-spectrum antibiotics may develop Erythematous candidiasis. The chronic hyperplastic type of candidiasis manifests as a white plaque on the commissural region of the oral cavity. The white plaque areas are seen in chronic hyperplastic candidiasis cannot be readily scrapped off.²³

7.1. Invasive aspergillosis (IA)

Invasive Aspergillosis might be a deadly infection in COVID-19 patients, especially seen in those with high risk factors. Bacterial and fungal infections are reported in a severe COVID-19 patient, those who are admitted to Intensive Care Unit.²⁴ “Diagnosis is very difficult

as patients often associates non-specific symptoms and testing typically requires a specimen from deep within the lungs.^{9”} A German study found COVID-19 associated invasive pulmonary aspergillosis (IPA) was found in five (26.3%) of 19 consecutive critically ill patients with moderate to severe ARDS.²⁴

7.2. Clinical features

Primary aspergillosis of oral cavity seen in the palate and posterior region of tongue, which manifests as black or yellow necrotic tissue on an ulcer base. The toxins of aspergillosis hyphae can penetrate into the vessel wall and form thrombosis that results in infarction and necrosis. Aspergillosis organisms show centrifugal linear growth and eventually become ball-shaped masses. On radiographic examination, inorganic phosphate in the middle of the mass is identified as foreign bodies.²³

7.3. Invasive cryptococcosis

The human immunodeficiency virus (HIV) infection patients with less than 200 cells of T-lymphocyte count and other immune disease are vulnerable to cryptococcosis, which manifest as meningoencephalitis.²¹ Using immunosuppressant drugs for COVID-19 patients may results in infections like Cryptococemia, leading to death within 30 days.²⁵

7.4. Clinical features

Cryptococcosis is deep fungal infection with invasive character, seen in the face, neck, and scalp region.²⁶ Oral lesions are very rare, but can see in immunocompromised condition, which manifested as mucosal surface ulceration, nodules, or granuloma formation. Oral ulcerations sometimes look like carcinomatous tissue.²⁷

8. Impact on Orthodontist

The orthodontic brackets effect on good oral hygiene, leading to plaque accumulation and increase in cariogenic microorganisms in saliva like candida and dental plaque of patients.²⁸ Increased number of bacteria and yeasts are associated with the fixed orthodontic appliances.¹⁹ oral mycosis can develop, when there is underlying predisposing factors along with an increased number of fungus in the oral cavity.²⁹

Mouth is the entry for respiratory and digestive systems, it is important to maintain good oral hygiene. Oral mucormycosis is normally developed from the breathing of spores or through an open contaminated oral wound, affecting mainly immunocompromised patients.³⁰ Chance of Post COVID-19 mucormycosis in orthodontic patients are very rare. However, orthodontist should stress about oral hygiene measurements in these patients.

9. Minor Surgical Procedure in Orthodontics

The intake route for fungi can be a loss of anatomical continuity as can occur after a tooth extraction or in an ulcer and therefore the spores can reach the body by inhalation, inoculation or ingestion. These spores usually face the primary line of defense of the organism (mononuclear and polynuclear phagocytes) and in healthy patients don't generate infection, destroying the spores of mucor fungi by oxidative metabolites and defensins.³⁰

However, some cases are reported in immune compromised patients.³¹ Orthodontist should use caution when doing minor surgery in patients, who's recently recovered from COVID-19.

10. Conclusion

Maintaining good oral hygiene, post-COVID-19 recovery is a must for patients to guard themselves from the effect of the disease. Orthodontist should advice to change the toothbrush once they test negative. A COVID-19 recovered patient should have a separate brush holder and they should Clean brush, tongue cleaner regularly using an antiseptic mouthwash.

Chance for Post COVID-19 Mucormycosis in orthodontic patients are very rare. However, Orthodontist should take care when doing minor surgical procedure in the patient recovered from severe COVID-19 infection.

11. Source of Funding

None.

12. Conflict of Interest

The authors declare no conflict of interest.


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