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Fungal co infection in COVID 19 - Transmission risk and protective measures in dentistry

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Abstract

Corona virus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been sweeping across the globe. Since the outbreak of COVID-19, worldwide healthcare systems have been severely challenged. The exponential increase in positive cases has increased the demand for medical care. Recently cases of fungal infection have been reported in patients suffering from COVID-19 which include Aspergillosis, candidiasis, mucormycosis and cryptococcosis. Due to the characteristics of dental settings, the risk of cross infection between dental health care personnel (DHCP) and patients can be very high. Awareness of the possibility of fungal co-infection is essential to reduce delays in diagnosis and treatment in order to help prevent severe illness and death from these infections. Therefore, following the protective protocols in the COVID-19 crisis is of utmost importance in a dental setting.

Keywords: COVID-19, Fungal infection, Role of dentist, Dental management,

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been associated with a wide range of opportunistic bacterial and fungal infections. SARS-CoV-2 is responsible for lower respiratory infection and can cause acute respiratory distress syndromes (ARDS)¹. COVID-19 individuals always have immune suppression, with a reduction in CD4+T and CD8+ T cells, in addition to extensive alveolar destruction with significant inflammatory exudation².

Patients who were critically ill, particularly those who were admitted to the intensive care unit (ICU) and required mechanical ventilation, or who were hospitalised for an extended period of time even as long as 50 days, were more likely to develop fungal co-infections³.

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Fungal infections are a common side effect of viral pneumonia, particularly in severy ill individuals. The predominant fungal pathogens for co-infection in persons with COVID-19 have been identified as Aspergillosis and Candida.

Other infrequent opportunistic pathogenic fungus caused lung infections also need to be considered, such as Mucor and Cryptococcus.Several cases of mucormycosis in COVID-19 patients have recently been recorded all over the world, particularly in India. Awareness of the possibility of fungal co-infection is essential to reduce delays in diagnosis and treatment in order to help prevent severe illness and death from these infections.

Discussion

Types of fungal infection related to covid Invasive Aspergillosis (IA)

Invasive pulmonary aspergillosis was first described in 1953. Due to widespread use of chemo therapy and immune suppressive agents, its incidence has increased over the past two decades. It is a complication in immune compromised patients and is encountered frequently in hematopoietic stem cell or solid organ transplant recipients⁴. Aspergillus species could be an important cause of life- threatening infection in COVID-19 patients, especially in those with high risk factors. Continued improvement in diagnostics has revealed that half of the cases of IPA occur in the ICU, in patients who are often non neutropenic⁵. Severe influenza infection is a well-known risk factor for developing IPA in non-neutropenic patients; a syndrome termed influenza-associated aspergillosis (IAA).

Invasive pulmonary aspergillosis (IPA) is a severe disease, and can be found not only in severely immune compromised patients, but also in critically ill patients and those with chronic obstructive pulmonary disease (COPD). Symptoms are nonspecific and usually mimic bronchopneumonia, fever unresponsive to antibiotics, cough, sputum production and dyspnoea. Other symptoms include pleuritic chest pain and hemoptysis, which is mild, but can be severe⁶.

The presence of microbiologic and/or histopathologic evidence is required for the diagnosis of IA, but specimen collection is challenging because lung biopsy might be contraindicated in patients with coagulation disorders or severe respiratory failure. Drugs which ae used for treatment are itraconazole, voriconazole, Amphotericin B and its liposomes and echinococci's

Invasive Candidiasis (IC)

There are increased chances of candidiasis infection in patients with COVID-19 who are to be treated with broad-spectrum antibacterial drugs parenteral nutrition and invasive examinations, or the patients accompanied with prolonged neutropenia and other immune impairment factors⁷. There are now approximately 200 species of Candida, but only a few have been involved in human infection. Blood stream infection by Candida species (candidemia) is the most frequent clinical manifestation of invasive candidiasis, and is a significant cause of morbidity and mortality in hospitalized patients. C. Albicans is the predominant cause of candidemia worldwide Among the confirmed COVID-19 infection, C. albicans infections were attributed to central line source⁸. Culture procedures such as culture of blood or other samples taken under sterile circumstances, which are widely considered gold standards for IC diagnosis, are used to diagnose IC. Nonculture diagnostic procedures such as mannan and anti mannan IgG tests, C. albicans germ tube antibody (CAGTA), BDG, and PCR-based assays are currently being used as adjuncts to cultures in the diagnosis of IC^9 . The patients with confirmed candidemia or invasive candidiasis must be

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treated with echinocandin (caspofungin, micafungin, and anidulafungin), azoles (fluconazole, voriconazole, itraconazole), and Amphotericin B and its liposomes

Invasive Mucormycosis

Also called as Black fungus. After aspergillosis and candidiasis, mucormycosis is the third most common invasive fungal infection¹⁰. Fungi belonging to the class Zygomycetes and order Mucorales often cause devastating angioinvasive fungal infections, primarily in patients with underlying risk factors Mucormycosis (zygomycosis) has high prevalence in India due to high endemicity of diabetes and humid climate, which are conducive to the growth of the fungi COVID-19 patients with trauma, diabetes mellitus, prolonged neutropenia, are more likely to develop mucormycosis. The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background comorbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators. It is known to cause lifethreatening infections, both in immunocompromised individuals and immune competent individuals, in whom the incidence is on the rise¹¹⁻¹⁴. early complete surgical treatment for mucormycosis whenever possible, in addition to systemic antifungal treatment. Amphotericin B lipid complex, liposomal Amphotericin B and Posaconazole oral suspension are treated as the first-line antifungal monotherapy, while isavuconazole is strongly supported as salvage treatment.

Invasive Cryptococcosis

COVID-19 patients with human immunodeficiency virus (HIV) infection accompanied by CD4 + Tlymphocyte count\200 cells/lL, or other immune impaired are susceptible to crypto coccosis which predominantly present as meningoencephalitis¹⁵.

Cryptococcus neoformans is the main causative agent. In immune compromised patients such as those with HIV/AIDS, transplant recipients, and patients with liver cirrhosis and recently covid-19, it can cause devastating meningoencephalitis. Inhalation is the usual route of infection. To diagnose cryptococcosis, specimen from cerebrospinal fluid (CSF) can be mixed with India ink and observed under a microscope that the distinctive structure for Cryptococcus spp. with narrow budding encapsulated yeasts usually can be found. Inhalation is the usual route of infection. Treatment include (i) Induction phase for amphotericin B deoxy cholate and+ flucytosine, followed by fluconazole; alternative options for fluconazole+flucytosine or amphotericin В deoxycholate + fluconazole. (ii) Consolidation phase for fluconazole. (iii) Maintenance (or secondary prophylaxis) phase for fluconazole

Role of dentist

Before entering a dental office

Patients with symptoms of COVID-19 are advised "to avoid non-emergent dental care and advised, "if possible, to delay dental care until the patient has recovered"¹⁶. Management of dental appointments, and active screening of dental staff should be done.

At the dental office

Active patient screening and social distancing in the dental office should be managed. Patient should be educated regarding safety measures which should be taken in COVID-19. Facemask must be worn by everyone present in the dental office. The usage of

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personal protective equipment (PPE) by the dental team and the management of the dental operatory room are the procedures that must be followed in dental offices.

During dental treatment

Extra oral radiographs should be preferred. Avoid aerosol generating procedures by using four handed dentistry. High volume saliva ejectors must be used. During dental operations, cleaning and disinfection measures should be followed.

Post dental treatment

Following standard protocols, handling of laundry and medical waste should be considered after dental treatment.

Hence, before doing clinical procedure screening of patients should be done prior to their dental appointments. The goal of the screening is to identify patients who may be infected with COVID-19 and reduce the risk of infection and exposure to Dental care providers, staff, and to other patients. Many patients who are asymptomatic may be carriers. For this reason, it is suggested that all patients visiting a dental office must be treated with due precautions. ADA recommended obtaining a travel history (to any of the affected countries during the last 14 days) as well as history should be taken whether there is any contact with the diagnosed and suspected cases of COVID-19. Following that, the patient's dental condition and the urgency of their dental treatment needs are assessed. The clinical conditions of dental origin, which require priority care but do not increase the patient's death risk are categorised as URGENT and which increase the patient's death risk are categorised as EMERGENCY. List of emergency and urgent dental care conditions that require immediate treatment and is based on ADA interim guidance are shown in Table 1.

Table 1: List of emergent and urgent dental care adoptedfrom ADA intern guidance (2020).

Dental	Cellulitis, extra or intraoral swelling
Emergency	compromising airways
	Facial trauma
	Uncontrolled bleeding
	Dental pain due to pulpal inflammation
	Pericoronitis
Urgent	Dry socket
Dental	Localized dental abscess (periapical or
Needs	periodontal)
	Tooth fracture causing pain
	Dental trauma, avulsion or luxation
	Suture removal
	Denture repair due to injury to soft
	tissue or prior to medical care
	Soft tissue injury form orthodontic wire/
	appliance
	Dental treatment prior to medical care
	e.g., radiation therapy
	Biopsy of abnormal tissue
	Replacement of lost temporary filling or
	cementation of permanent bridges if the
	temporary prosthesis is broken

Environmental disinfection of the dental clinic is very important because the corona virus can persist on inanimate surfaces like metal, glass, or plastic for up to 9 days, but fortunately, it is very sensitive to the action of disinfectants.

Different disinfectant agents can be used against severe acute respiratory syndrome (SARS), such as ethanol ,2propanol, benzal konium chloride, dodecyl dimethyl ammonium chloride, chlorhexidine digluconate, sodium hypochlorite, hydrogen peroxide, formaldehyde.

Possible risk of Trans mission of COVID-19 in dentistry

In dental practices, COVID-19 transmission is expected *via* droplets and aerosols generated during clinical procedures especially when using drills or ultrasonic devices that cause aerosol release¹⁸.Splatters created during oral surgery procedures, like aerosols, are also contaminated by respiratory pathogens. If dental instruments are not

decontaminated properly, they can lead to virus transmission^{19,20}. As a result, it is recommended that healthcare personnel wear N95 masks during the COVID-19 outbreak²¹. Protective eyewear with side shields or face shields for dentists, protects from aerosols and spatter that transmit infection.

Precaution which should be taken while doing dental Procedure.

All aerosol-generating dental procedures should be done in isolated and adequately ventilated rooms or in a negative pressure room (when available). All staff and dentist must use surgical attire in the dental office, and all personal clothing should be avoided. COVID-19 virus can potentially survive in the environment for several hours/days. Premises and areas potentially contaminated with the virus to be cleaned before their reuse. Remove the majority of bioburden, and disinfect equipment and environmental surfaces.

Conclusion

Dental health care professionals must be aware of the risks of (SARS) - CoV-2 virus transmission in a clinical setting. Also, they must keep themselves updated about any new knowledge on this disease. Therefore, following the protective protocols in the COVID-19 crisis is of utmost importance in a dental setting. As the information on this pandemic is continuously changing, it is vital that dental professionals stay updated on the

emerging research to be able to continue providing dental treatment in a safe environment.

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