Case Report

Invasive Maxillary Mucormycosis in Post-COVID-19: A Case Report and Review of Literatures

Boosana Kaboosaya[1], Napat Damrongsirirat[1], Saraporn Koosrivinij[2], Atiphan Pimkhaokham[1]

[1]Department of Oral and Maxillofacial Surgery, Chulalongkorn University, Bangkok, Thailand

[2]Oral and Maxillofacial Surgeon, King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Abstract

Patients with COVID-19 are predisposed to opportunistic fungal infections, particularly mucormycosis. This risk is heightened in individuals with specific systemic conditions, such as uncontrolled diabetes mellitus, immunocompromised status, or as a consequence of prescribed medications. Although mucormycosis typically presents acutely in the rhinocerebral region, originating from the upper turbinate and paranasal sinus, reported cases of mucormycosis in the jaws are scarce. This study presents a unique case involving a 60-year-old immunocompetent female with a history of COVID-19. Following discharge, she experienced mobility in the upper anterior teeth accompanied by pus discharge, leading to a diagnosis of maxillary mucormycosis upon histopathological investigation. Notably, the patient exhibited no prior immunocompromised status, emphasizing the need for heightened awareness even in immunocompetent individuals with a history of COVID-19. Globally, there has been an increase in fungal infections following the COVID-19 pandemic, with limited presentations. Prompt identification of maxillary mucormycosis post-SAR-CoV-2 infection is crucial for timely intervention. This study elucidates a case of COVID-19-associated mucormycosis (CAM) in an immunocompetent patient and reviews the existing medical literature on CAM affecting the jaw, thereby contributing to the understanding and management of this emerging issue.

Keywords: COVID-19, Fungal infection, Jaws, Mucormycosis

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Correspondence to:

Boosana Kaboosaya, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Chulalongkorn University 34 Henri-Dunant Road, Wangmai, Patumwan, Bangkok 10330, Thailand. Tel. 02-218-8581 Email: Boosana.k@chula.ac.th

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread worldwide, prompting its classification as a global pandemic by the World Health Organization on March 11, 2020.[1] The clinical presentation of COVID-19 is highly variable, mirroring other pathogens, thus necessitating careful consideration in diagnosis. Prominent symptoms with sensitivities exceeding 50% include cough, sore throat, fever, myalgia or arthralgia, and headache.[2] Notably, approximately one-third of SARS-CoV-2 infections are asymptomatic, while others may progress to severe manifestations such as pneumonia, acute respiratory dis-

tress, and multi-organ failure.[3] Moreover, adding to this complexity, SARS-CoV-2 has been implicated in a spectrum of opportunistic infections, with mucormycosis caused by fungal pathogens emerging as a particularly invasive concern.

Mucormycosis is a rare, life-threatening opportunistic infection caused by fungi commonly known as black fungus. These fungi are widely distributed as decomposers of decaying organic matter in the environment. Transmission primarily occurs through the inhalation of spores,[4] with the rhino-orbital/rhino-cerebral region being the most frequently affected site of infection.[5] Mucormycosis predominantly affects males, with a mean age of approximately 51 years.[6] COVID-19 associated mucormycosis (CAM) has exhibited pronounced incidence in India, with reported cases predominantly observed in individuals undergoing treatment or recovering from SAR-CoV-2 infection, reaching rates approximately 70 times higher than the global data. The overall fatality rate varies between 16.3% and 61.9%, contingent on regional disparities.[4,7] Also, 35% of cases developed mucormycosis during active COVID-19 infections, while 65% manifested post-recovery.[8]

The development of mucormycosis in post-COVID-19 patients can be attributed to various factors. Underlying conditions notably latent diabetes mellitus serve as significant predisposing factors.[6,8-12] The administration of corticosteroids during COVID-19 treatment, aimed at modulating inflammation-mediated lung injury and mitigating the progression of respiratory failure, is identified as a prominent risk factor.[4,8,10-12] Additionally, other contributory risk factors include an immunocompromised host, hematological conditions such as leukemia and lymphoma, and individuals who have undergone solid-organ transplantation.[6] Chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), human immunodeficiency virus (HIV) infection.[5] and iron overload are also associated with an increased predisposition to mucormycosis.

Timely diagnosis and effective management of aggressive fungal co-infections associated with COVID-19 are imperative to mitigate fatal consequences and reduce mortality rates. However, there is a paucity of literature specifically addressing fungal co-infections in the oral region. This article aims to contribute to the understanding of such infections by presenting our experience with a case of maxillary mucormycosis in a female with a recent history of hospitalization for SARS-CoV-2 infection., The study details both the clinical presentation and histopathological characteristics of the case. Furthermore, the authors conducted a comprehensive review to identify reported cases of mucormycosis affecting the jaws as a consequence of COVID-19, providing valuable insights into the evolving landscape of this rare but serious complication.

Clinical case

A 60-year-old female with a history of hypertension, managed with atenolol (50 mg), was admitted to a cohort ward following the contraction of COVID-19. Her lungs scan showed bilateral reticulonodular infiltrates. Upon admission, she received favipiravir (200 mg), nine tablets every 12 hours on day 1, followed by favipiravir (200 mg), four tablets every 12 hours from day 2 to day 11. Dexamethasone (4 g) was given as two tablets every 12 hours from day 1 to day 10, followed by a shift to prednisolone (5 mg), four tablets every 12 hours from day 11 to day 13. Subsequently, the prednisolone dosage was reduced to two tablets every 12 hours from day 15 to day 18. On day 11, azithromycin (500 mg) was initiated at one tablet per day for a five-day course. Notably, the patient did not require intubation or mechanical ventilation and was discharged after a 19-day hospital stay.

Two months post-hospital discharge, the patient manifested mobility in the upper anterior teeth accompanied by pus discharge. The general dental practitioner conducted scaling and prescribed antibiotics—amoxicillin (500 mg) and metronidazole (400 mg)—to be taken three times a day. Unfortunately, after ten days, there was no improvement, prompting the patient to be referred to our department.

During the clinical examination, the patient complained of significant pain and discomfort, accompanied by mild diffuse swelling on the face. The overlying skin showed slight erythema without warmth (Fig.1A-1D).

Intraoral examination unveiled second- to third-degree mobility of teeth 15 to 25, with probing depths reaching approximately 5-6 mm. Gingival abscesses and fistulas were observed at 12, 14, and 22, although no shallow vestibule or facial space abscess was present (Fig. 2A). Radiographic assessments, including periapical (Fig. 2B-2D) and panoramic images (Fig. 2E), revealed generalized horizontal bone resorption. The initial diagnosis suggested generalized periodontitis, prompting the patient's referral for specialized periodontal treatment.

During a follow-up visit two weeks after the initial encounter, the patient presented with a palatal abscess and significant swelling in the buccal area (Fig. 3A-3B).

An incision and drainage procedure were performed on the hard palate and buccal mucosa (Fig 4A-4B), revealing few positive cocci in the Gram stain. Following this, the patient was prescribed amoxicillin/ clavulanate (1g), to be taken two tablets every 12 hours for a five-day course, and advised to use 0.12 % Chlorhexidine mouthwash.

However, five days later, the periodontist observed a lack of response to the electrical pulp test (EPT) in nearly all the upper teeth, along with an increase in mobility (upgrading from second to third mobility) in teeth 15-25. leading to the suspicion of a non-periodontitis-related cause. Consequently, further investigation using computed tomography (CT) was pursued.

Contrast-enhanced CT unveiled a distinctive radiological profile, showcasing heterogeneous density within the maxillary bone involving the alveolar process. The findings further revealed cortical disruption, extensive bone destruction (Fig. 5A-5B), and there was complete obliteration of the right maxillary sinus, while the left maxillary sinus exhibits partial obliteration (Fig. 5A-5B). Subsequently, the patient underwent a bone and soft tissue biopsy of the anterior maxilla under local anesthesia, revealing necrotic bone across the entire maxilla with minimal discharge.

Figure 1 *Clinical presentation on first visit; A) frontal view. B) worm's-eye view. C) left side, D) right side*

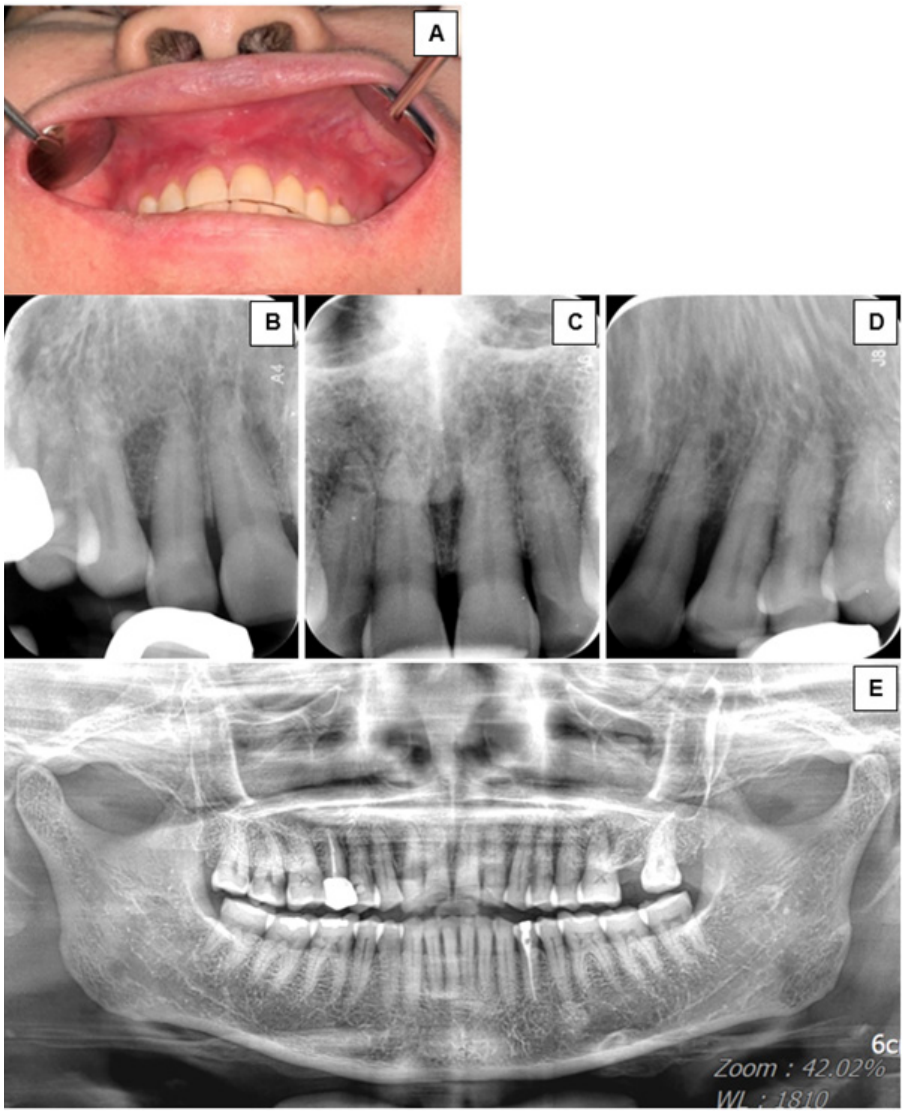

Figure 2 *Clinical presentation on first visit; A) upper vestibular area B) upper right C) middle D) upper left E) panoramic radiograph on first visit*

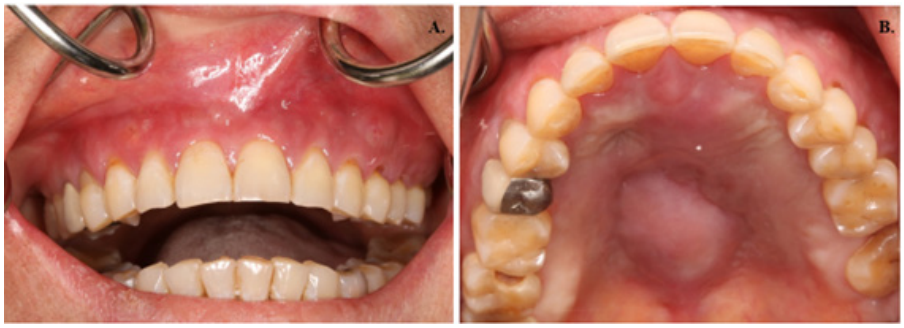

Figure 3 *Clinical presentation on second visit showed multiple draining sinuses A) buccal area, B) palatal area*

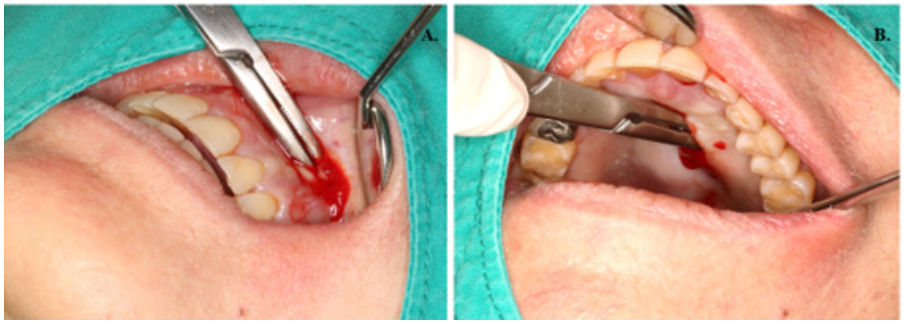

Figure 4 *Incision and drain procedure under local anesthesia A) buccal area, B) palatal area*

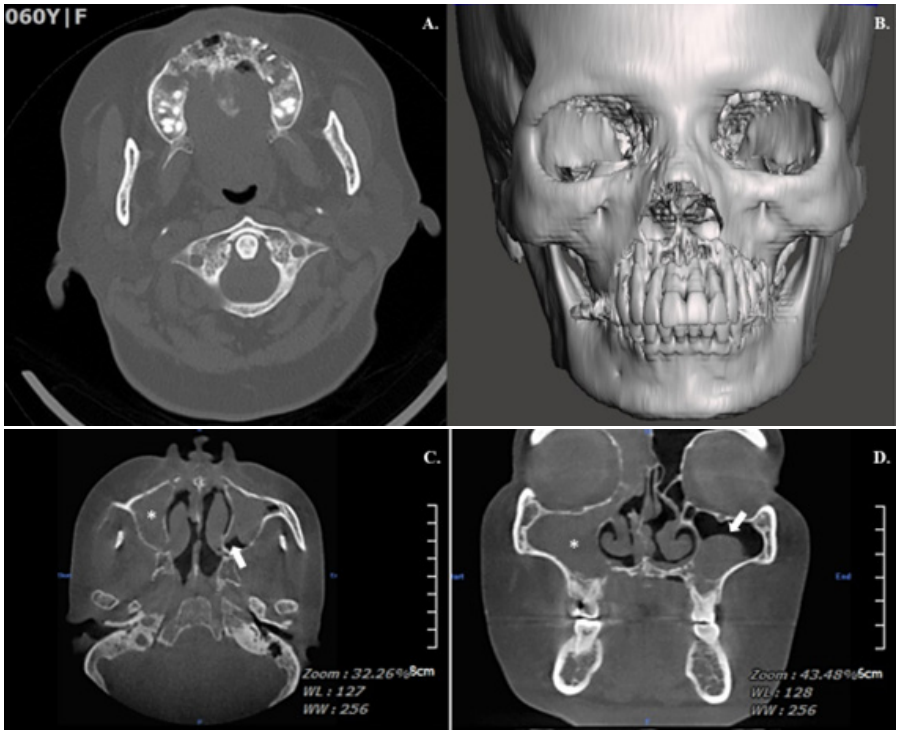

Figure 5 *Computed tomography A) axial view B) 3-dimensions showing areas of bone erosion with multiple air foci and hypodense collection in marrow cavity. C) axial view D) coronal view, presented complete obliteration of the right maxillary sinus (depicted by the white asterisk), partial obliteration of the left maxillary sinus exhibits (indicated by the white arrow).*

A negative acid-fast stain for bacterial infection was observed. However, the culture results demonstrated the presence of numerous Serratia marcescens and Klebsiella pneumonia. Histopathological analysis confirmed the presence of non-septate hyphae in the hard tissue (Fig. 6A-6C), further validated by periodic acid-Schiff (PAS) staining, which highlighted positive fungal non-septate hyphae of relatively large size (Fig. 4D). This distinct histopathological finding strongly supported the diagnosis of a deep fungal infection, specifically indicative of mucormycosis.

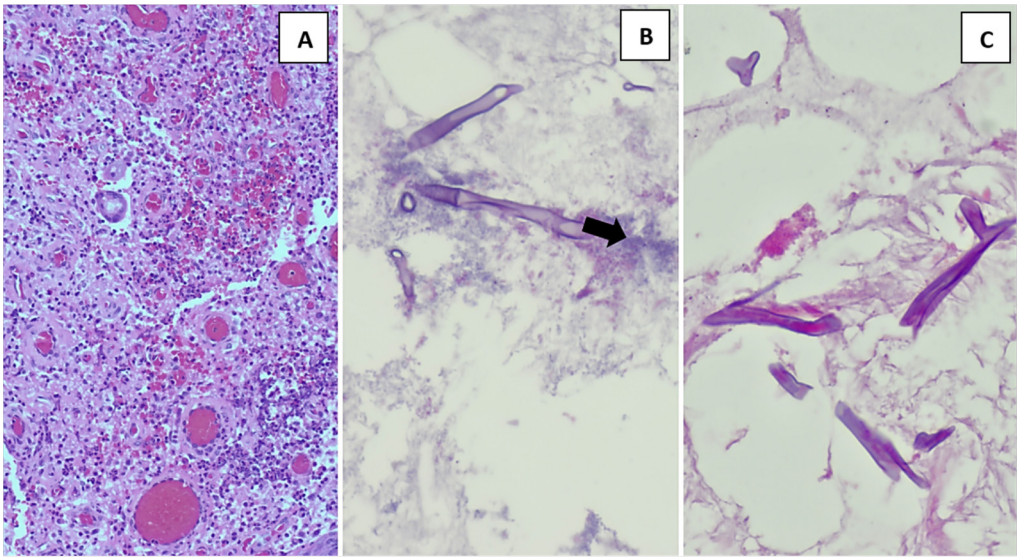

Figure 6 *Histopathology of biopsy: A) Haematoxylin and Eosin (H&E) at 20x magnification. B) H&E image at 100x magnification showing the large, non-septate, right-angle fungal hyphae (black arrow). C) Periodic Acid Schiff (PAS) images at 100x magnification showing broad, non-septate fungal hyphae*

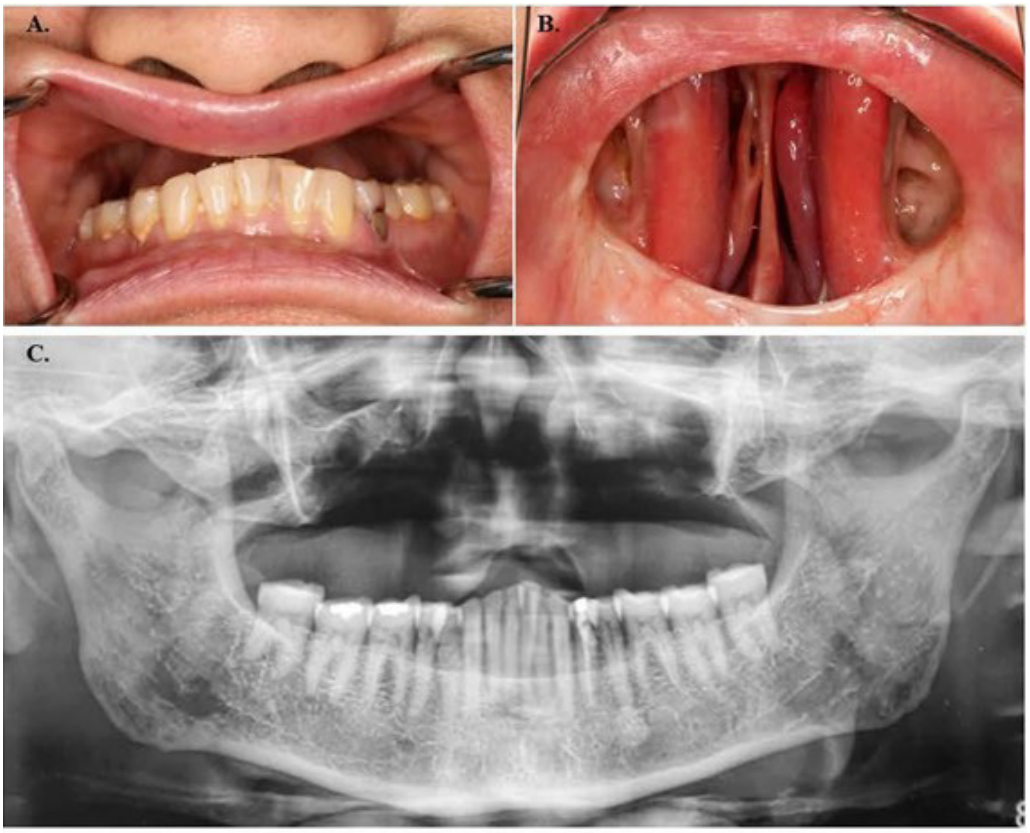

Figure 7 *A.-B.) clinical presentation, C.) panoramic radiograph at 8th months post-maxillectomy*

Following the laboratory report, the serum chemistry of the patient exhibited glucose levels at 87 mg/dL, sodium at 137 mEq/L, potassium at 4.5 mEq/L, chloride at 99 mEq/L, total CO_2 at 25 mEq/L, and a morning cortisol level of 14.7 ug/dl. Due to limitations at the initial medical facility, the patient was referred to a tertiary care teaching hospital. Diagnostic sinonasal endoscopy revealed destruction of the nasal septum at the posterior bony part, along with darkened discoloration of the mucosa from the right nasal floor to the septum, not extending to the inferior meatus. Subsequently, an urgent maxillectomy and surgical debridement were performed, with concurrent administration of ceftriaxone (2 g) intravenously once daily and systemic antifungal treatment. The antifungal regimen consisted of amphotericin B administered intravenously as a 60-mg dose in 5% dextrose in water (500 ml) infused over a six-hour period. Premedication immediately before amphotericin B administration included chlorpheniramine 10 mg intravenously and paracetamol 500 mg orally, along with a 500-ml intravenous drip of normal saline over six hours.

The wound healed by secondary intention, resulting in oro-antral communication. During a follow-up visit four months after discharge, the patient remained asymptomatic with no signs of infection (Fig. 7A-7C).

Materials and Methods

A comprehensive literature search was conducted using the PubMed interface of MEDLINE, Web of Science, and Scopus to identify English language case reports, case series, and observational studies related to oral mucormycosis. The search strategy involved the use of the terms "[COVID-19] OR [SARS-CoV-2] OR [SARS-CoV2] OR [2019-nCoV] AND [Mucormycosis] OR [Mucorales] OR [Black fungus]" within the publication timeline of December 1, 2019, to April 30, 2022. Additionally, the authors manually reviewed references in pertinent articles. This review specifically focused on CAM cases involving jaws with active or recent SAR-CoV-2 infection. Cases with concurrent sino-maxillary involvement were excluded, as the pathogenesis may differ from isolated maxillary and mandibular region involvement.

Results

Following a meticulous screening process, fourteen articles were identified encompassing 90 cases that manifested mucormycosis of the jaws as a result of COVID-19. A comprehensive overview of patient characteristics and oral manifestations, highlighting predisposing conditions, is presented in Table 1.[13-28]

The age range of the affected individuals spanned from 29 to 77 years, with males constituting 74.44% of the entire patient cohort. The onset of symptoms after COVID-19 detection varied, ranging from one day to 159 days. Notably, diabetes mellitus emerged as a prevalent underlying condition in almost all the cases reviewed, with 24 cases reported in the maxillary area, one case in the mandibular region, and one article (Suresh *et al.*[25]) failing to specify the exact affected area. Additionally, a notable occurrence of mandibular mucormycosis was identified in a young, previously healthy adult post-COVID-19 infection. Twenty-one articles noted a potential association between steroid administration during COVID-19 and the occurrence of mucormycosis, albeit employing varying descriptions. Specifically, 13 articles reported steroid use during coronavirus treatment, while eight articles mentioned steroid use during COVID-19 treatment. Clinical symptoms predominantly manifested in the maxilla. While some articles lacked specific details regarding the fungal agent causing osteonecrosis, non-septate right-angle branched fungal hyphae emerged as the most encountered pathogen.

Table 1 *Characteristics of studies included in the review*

Author, year/ location	Study design	Number of case (oral/ total)	Onset of symptom after COVID-19 detection	Gender	Age (years)	Clinical characteristic at the time of presentation	Risk factors	Histopathologic features	Remark
Ahmed *et al.* 2021[13]/ Egypt	Case series	21/21	14 days	M=11 F=10	58±12 (mean)	-Palatal lesion	N/A	N/A	-
Mendhe *et al.* 2021[14]/ India	Case report	1/1		M	31	-Pain and swelling at right maxilla with multiple draining sinuses	N/A	N/A	-No information of COVID-19 infection
Ambereen *et al.* 2021[15]/ India	Case report	1/1	20 days	M	39	-Numbness at left lower lip -Pain and pus discharge at left posterior mandibular teeth	-Steroid use during COVID-19 treatment	-Broad non-septate right-angle branched fungal hyphae	-
Jawanda *et al.* 2021[17]/ India	Case report	1/1	120 days	M	70	-Pain at right maxilla	- Diabetes mellitus - Steroid use during COVID-19 treatment	-Broad non-septate right-angle branched fungal hyphae (mixed infections (Mucormycosis; black fungus, Actinomycosis; yellow fungus, and Candidiasis; white fungus)	-
Pathak *et al.* 2021[18]/ India	Case report	1/1	60 days	M	65	-Necrotic ulceration at hard palate	- Diabetes mellitus - Hypertension	-Numerous large non-septate righ angle branched fungal hyphae	-
Pauli *et al.* 2021[19]/ Brazil	Case report	1/1	8 days	F	50	-Painful bone-exposed ulcer at hard plate	- Diabetes mellitus	- Large non-septate right-angle branched fungal hyphae	-
Venugopal&Marya 2021[21]/ Cambodia	Case report	1/1	8 days	F	53	-Painless lesion at palate	-Diabetes mellitus	-Large non-septate with thin walls and branched hyphae	-
Krishna *et al.* 2021[22]/ India	Case reports	2/2	N/A	M	34	-Pain and swelling at right maxilla	- Diabetes mellitus - Hypertension	-Fungal osteomyelitis (not specific)	-
			N/A	M	50	-Swelling at right malar region	- Uncontrolled diabetes mellitus	-Non-septate right-angle branched fungal hyphae	-
Guptal&Dosi. 2021[23]/ India	Case reports	2/2	30 days	M	58	-Teeth pain and mobility at right maxilla	-Steroid use during COVID-19 treatment	N/A	-
			N/A	M	60	-Teeth pain and mobility at right maxilla	- Diabetes mellitus -Steroid use during COVID-19 treatment	N/A	-

Table 1 *Characteristics of studies included in the review (cont.)*

Author, year/ location	Study design	Number of case (oral/ total)	Onset of symptom after COVID-19 detection	Gender	Age (years)	Clinical characteristic at the time of presentation	Risk factors	Histopathologic features	Remark
Ahmed *et al.* 2021[24]/ Egypt	Case series	14/14	14-30 days	M	45	-Anterior maxillary bone exposure	- Post COVID-19 diabetes mellitus	N/A	-
				M	35	-Right posterior palatal bone exposure	- Post COVID-19 diabetes mellitus	N/A	-
				M	65	-Right and left maxillary bone	- Diabetes mellitus	N/A	-
				M	48	-Right and left maxillary bone exposure	- Diabetes mellitus	N/A	-
				M	76	-Right maxilla bone exposure	- Diabetes mellitus	N/A	-
				F	55	-Left palatal bone exposure	- Diabetes mellitus	N/A	-
				F	61	-Left palatal bone + alveolar bone exposure	- Diabetes mellitus	N/A	-
				M	45	Alveolar + anterior palatal bone exposure	- Post COVID-19 diabetes mellitus	N/A	-
				M	52	-Anterior palatal bone exposure	- Diabetes mellitus	N/A	-
				F	53	-Necrosis of premaxilla	- Diabetes mellitus	N/A	-
				M	29	-Premaxilla + left palatal and alveolar bone exposure	- Post COVID-19 diabetes mellitus	N/A	-
				M	77	-Right and left palatal bone exposure	- Diabetes mellitus	N/A	-
				F	49	-Anterior and right palatal + alveolar bone exposure	- Post COVID-19 diabetes mellitus	N/A	-
				M	69	-Right palatal bone exposure	- Diabetes mellitus	N/A	-
Suresh *et al.* 2022[25]/ India	Observa-tional study	39	1-159 days (mean=53.38)	M=32 F=7	50.69	-Teeth pain (n=32) -Teeth mobility (n=38) -Gingival swelling (n=27) -Sinus opening with pus discharge (n=27) -Ulceration or blackish discoloration of hard plate (n=12)	- Diabetes mellitus (n=32) - Steroid use during COVID-19 treatment (n=21)	-Mucorale spp. (n=33) -Aspergillus fumigatus (n=2) -Curvulria lunata (n=2) - Mucorale spp.+Candida albicans (n=1) - Mucorale spp.+ Aspergillus fumigatus (n=1)	

Table 1 *Characteristics of studies included in the review (cont.)*

Author, year/ location	Study design	Number of case (oral/ total)	Onset of symptom after COVID-19 detection	Gender	Age (years)	Clinical characteristic at the time of presentation	Risk factors	Histopathologic features	Remark
Ingle *et al.* 2022[26]/ India	Case report	1/1	25 days	M	74	-Teeth mobility at left maxilla	-Uncontrolled diabetes mellitus -Steroid use during COVID-19 treatment	-Numerous non-septate hyphae with and without branching in the granulation and necrotic tissues	-Superimposed with ameloblastoma
Chugh *et al.* 2022[27]/ India	Case series	3/4	60 days	M	64	-Pain at posterior right mandible and numbness at right lower lip	-Diabetes mellitus -Steroid use during COVID-19 treatment	-Non-septate hyaline ribbon like right angled branching fungal hyphae	-
			60 days	M	35	-Pain, paresthesia and teeth mobility at left mandible	-Steroid use during COVID-19 treatment	-Fungal hyphae (not specific)	-
			60 days	M	35	-Multiple sinuses with pus discharge at labial gingiva of left maxilla with mobility of dentoalveolar complex	-Steroid use during COVID-19 treatment	-Broad non-septate right-angle branched fungal hyphae and thin septate acute-angle branched fungal hyphae	- Possibility of mixed mucor and aspergillus infection
Fakhar *et al.* 2022[28]/ Iran	Case reports	2/2	30 days	M	35	-Teeth mobility at right maxilla	- Uncontrolled diabetes mellitus	-Broad septate fungal hyphae	-
			30 days	M	40	-Teeth mobility at right maxilla	- Diabetes mellitus	-Broad ribbon-like branched fungal hyphae	-

Discussion

COVID-19 is a new disease that was first documented in December 2019 in China. Previous articles have reported a potential increased risk of developing invasive fungal infection (mucormycosis) in COVID-19 patients.[4,7,10,11,29] A prospective cohort evaluation of 135 COVID-19 patients stated that the fungal infection incidence was 26.7%. The mortality rates in COVID-19-associated patients with and without fungal disease were 53% and 31%, respectively.[30] According to this review, fungal infection of the jaws related to SARS-CoV-2 infection has a male predisposition. The previous article mentioned that the incidence of mucormycosis was not gender-dependent.[31] Nonetheless, the notably higher number of males affected by mucormycosis-related COVID-19 may be attributed to the higher incidence of COVID-19 cases identified in males.[6,9]

Mucormycosis, an angio-invasive fungal infection, causes thrombi formation, reduces blood supply, and leads to blood vessel necrosis.[33] COVID-19 appears to increase susceptibility to mucormycosis, as seen in autopsies by Auckermann *et al.*[34], where COVID-19 induced endothelialitis, microvascular thrombosis, and disrupted cell membranes. Thrombi may provide iron, thereby promoting fungal growth. Elevated cytokine levels, particularly interleukin-6, in COVID-19 patients increase ferritin levels, leading to excess free iron.[4] This iron overload contributes to tissue damage and necrosis.

Several studies have indicated that diabetes and diabetic ketoacidosis were the most significant risk factors observed in the majority of mucormycosis in COVID-19 cases.[4,5] In this review, 13 of 16 articles mentioned diabetes as a risk factor. The current case, while lacking a diabetes history, presented with hypertension and corticosteroid immunosuppression during COVID-19 treatment. Cardiovascular disease was also mentioned as a risk factor for mucormycosis.[5] A systematic review of 144 COVID-19 and mucormycosis co-infection cases reported hypertension in 34.3%. However, hypertension and diabetes often co-exist in many patients. However, because hypertension and diabetes often coexist, attributing mucormycosis solely to hypertension might be overestimated due to the high prevalence of diabetes.[10]

Steroid use during COVID-19 treatment was stated as a risk factor related to fungal infection in eight of the 16 articles. Corticosteroids, such as dexamethasone, have proven effective in treating COVID-19 and reducing mortality in severe cases.[35] However, corticosteroids could cause drug-induced hyperglycemia, impairing granulocyte phagocytic capacity and potentially contributing to opportunistic fungal infections.[36] Some authors have suggested stopping steroid prescription in non-hypoxemic COVID-19 patients and limiting the steroid dose and duration in hypoxic patients.[37]

SARS-CoV-2 utilizes angiotensin-converting enzyme II (ACE2) for cell entry,[38] and its distribution, including in the lung, heart, kidney, oral mucosa, and tongue epithelial cells, suggests potential infection risks.[39] This indicates a direct impact on the oral cavity, making it a potentially high-risk area for COVID-19 susceptibility and a possible transmission route.[40] In this review, most cases reported mucormycosis in the maxilla, in contrast with only two cases in the mandible. The maxilla was rare osteomyelitis, attributed to its vascularity, thin cortical bone, and porous architecture. Notably, maxillary cases are often presented with hallmark signs such as pain and tooth mobility. These reviewed cases suggest an elevated incidence of mucormycosis in the jaws due to the combination of COVID-19 infection, diabetes mellitus, and steroid use during coronavirus treatment.

CAM onset varied from three10 to 90 days after confirmation,11 averaging around 25.6 ± 21 days.10 In a prospective study of 95 post-COVID patients, 98% developed invasive mucormycosis within 20 days of recovery. At the time of presentation, 91.5% of patients complained of local facial pain, 9.5% reported pain in the upper teeth, and 2.1% experienced pain in the lower teeth along with loosening.[12] From this review, the average onset of symptoms was approximately 30-60 days after COVID-19 detection. In the current case, maxillary infection symptoms emerged

around day 30 post-COVID confirmation, with a mucormycosis diagnosis on day 87.

Microscopy and culture methods continue to serve as the gold standard for identifying pathogenic fungi. These techniques offer several advantages, including the ability to identify specific species, thereby facilitating differentiation between septate molds (such as Aspergillus spp.), non-septate molds (such as Mucorales), and yeasts (such as Candida spp.). Moreover, these methods enable the assessment of antifungal resistance.[41] However, they are associated with certain drawbacks, including low sensitivity. Cultures from biopsy specimens or blood often yield negative results, and positive cultures may sometimes result from contamination rather than true infection. Additionally, these methods are characterized by long turnaround times.[42]

Quantitative polymerase chain reaction (qPCR) or real-time PCR in blood samples is now acknowledged as a non-invasive tool for early mucormycosis diagnosis. The assay demonstrated a sensitivity of 99.29% and a specificity of 83.84% for the diagnosis of invasive mucormycosis.[43] Quantitative polymerase chain reaction (qPCR) was conducted using both tissue samples, which were also utilized for cultures, and blood samples. The detection of circulating Mucorales DNA in serum or plasma holds superiority as it can be initiated promptly upon clinical suspicion of the diagnosis, and it may be carried out in all patients, including those unable to undergo a biopsy. qPCR is now highly valued for diagnosing fungal infections due to its easy handling, rapid turnaround time (approximately 3 hours), specificity, and cost-effectiveness.[44]

Successful management of mucormycosis encompasses both surgical and medical interventions. A standard daily dose of Liposomal amphotericin B suggested by current guidelines of less than 5 mg/kg/day, is considered the drug of choice for invasive mucormycosis,[32] with several studies reporting overall survival rates of up to 72%.[45] However, a significant limitation of amphotericin B is that it can only be administered parenterally, and its safety profile is associated with increased nephrotoxicity and electrolyte imbalances.[46] In such cases, newer triazoles, namely posaconazole and isavuconazole, are recommended.[32]

In vitro studies have shown that posaconazole exhibits varying activity against Mucorales, with its effectiveness being species-dependent.[47] Posaconazole is currently available only as an oral suspension and is preferably taken with a high-fat meal to enhance bioavailability.[48] These dietary requirements pose challenges for critically ill patients who may not be able to eat. On the other hand, isavuconazole is a newer broad-spectrum antifungal agent with minimum inhibitory concentration (MIC) values for Mucorales that are 2- to 4-fold higher than those of posaconazole.[49] Isavuconazole is available in both intravenous and oral formulations, is associated with less hepatotoxicity and no nephrotoxicity, and exhibits excellent oral bio-availability with no specific food requirements.[46]

To the best of our knowledge, this is the first literature review on fungal infections of the jaws related to COVID-19. For the case report, this initial presentation of the patient mimicked chronic periodontitis. Computed tomography was chosen over cultures and plain imaging for detecting mucormycosis. A definitive diagnosis relied on histological investigation from a biopsy, which detailed fungus morphology, tissue reaction, and blood vessel invasion. Treatment involved addressing underlying conditions, extensive surgical debridement, and antifungal therapy (amphotericin B). Aggressive debridement, facial reconstruction, and supportive therapy were crucial for restoring the patient's quality of life.

The precise pathogenesis remains unknown. Mucormycosis is an exceedingly rare infection in healthy individuals. It is plausible that the patient may have inadvertently consumed contaminated food. Concurrently, the patient had been administered corticosteroids during COVID-19 treatment, comprising dexamethasone (16 mg/day for ten days), followed by prednisolone (40 mg/day for three days) and then prednisolone (20 mg/day for three days). A systematic review and meta-analysis of 958 cases revealed that the majority of patients with CAM were treated with corticosteroids (78.5%), particularly dexamethasone, which was the most commonly prescribed drug (46.6%). These findings are consistent with the treatment regimen of our patient.[50]

Due to the common presenting complaints of CAM of the jaws, such as gingival swelling (18.5%) and palatal necrosis or ulcer (12.7%),[51] prompt detection is facilitated, enabling immediate treatment initiation, and potentially reducing mortality rates. The overall mortality rate of CAM related to the head and neck area was 38.32%,[52] which was lower than that of pulmonary mucormycosis (80%),[53] and disseminated mucormycosis (96%).[54] However, limitations of this study include the inability to differentiate outcomes based on glycemic control status due to the lack of information on HbA1C and limited data on the fungal culture.

Conclusion

Typical pain and swelling in the oral region should raise suspicion for a cautious diagnosis in individuals with a history of previous COVID-19 infection. Biopsy plays a crucial role as a diagnostic tool in such cases. It is crucial to differentiate mucormycosis from other infections to initiate early and appropriate treatment, thereby improving outcomes. Patients with suspected mucormycosis should be referred immediately to a facility with the highest care level. This article aims to raise awareness among clinicians about this rare yet potentially fatal fungal infection.

Ethical approval and consent to participate

The research project was approved by the Human Research Ethics Committee of the Faculty of Dentistry, XXX (HREC-XXX 2022-065). A written consent for publication was obtained from the patient.

Consent for publication

The authors affirm and agree to the submission of this paper. The human research participants provided informed consent for publication of the images in Fig. 1A-1D, Fig. 2A-2E, Fig. 3A-3B, Fig. 4A-4B, Fig. 5A-5D, Fig. 6A-6Cc, and Fig. 7A-7C.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Boosana Kaboosaya, Napat Damrongsirirat, Saraporn Koosrivinij and Atiphan Pimkhaokham. The first draft of the manuscript was written by Boosana Kaboosaya, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

The authors declare that data supporting the findings of this study are available.

Declaration of Competing interests

All authors confirm they have no competing interests in the publication of this paper.

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