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Original Research

Review on the oral manifestations of Covid-19 disease and Mucormycosis

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ABSTRACT:
Dysgeusia is that the first recognized oral symptom of novel coronavirus disease (COVID-19). during this review , we described oral lesions of COVID-19 patients. We searched PubMed library and Google Scholar for published .Finally, we selected few articles including case reports, case series and letters to editor. Oral manifestations included ulcer, erosion, bulla, vesicle, pustule, fissured or depapillated tongue, macule, papule, plaque, pigmentation, halitosis, whitish areas, hemorrhagic crust, necrosis, petechiae, swelling, erythema, and spontaneous bleeding. the foremost common sites of involvement in descending order were tongue (38%), labial mucosa (26%), and palate (22%). Suggested diagnoses of the lesions were aphthous stomatitis, herpetiform lesions, candidiasis, vasculitis, Kawasaki-like, EM-like, mucositis, drug eruption, necrotizing periodontitis , angina bullosa-like, angular cheilitis, atypical Sweet syndrome, and Melkerson-Rosenthal syndrome. Oral lesions were symptomatic in 68% of the cases. Oral lesions were nearly equal in both genders (49% female and 51% male). Patients with older age and better severity of COVID-19 disease had more widespread and severe oral lesions. Lack of oral hygiene, opportunistic infections, stress, immunosuppression, vasculitis, and hyper-inflammatory response secondary to COVID-19 are the foremost important predisposing factors for onset of oral lesions in COVID-19 patients[1]
There are increasing case reports of rhino-orbital mucormycosis in people with coronavirus disease 2019 (COVID-19), especially in India. Oral manifestations also are seen in mucormycosis ,Diabetes mellitus (DM) is an independent risk factor for both severe COVID-19 and mucormycosis. We aim to conduct a scientific review of literature to seek out out the patient's characteristics having mucormycosis and COVID-19.[6]
Keywords: COVID-19; Coronavirus, Oral manifestations,Mucormycosis ,Diabetes mellitus, Corticosteroids, systematic review

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may be a single-chain RNA virus that's the explanation for novel coronavirus disease referred to as COVID-19. the foremost common clinical symptoms are fever, headache, pharyngitis , dyspnea, dry cough, abdominal pain, vomiting, and diarrhea. Angiotensin converting enzyme 2 (ACE 2) receptor may be a known receptor for SARS-CoV-2 that's found within the lung, liver, kidney, gastrointestinal (GI) and even on the epithelial surfaces of sweet glands and on the endothelia of dermal papillary vessels. Todate, various cutaneous manifestations of COVID-19 disease are described including varicelliform lesions, pseudochilblain, erythema (EM)-liker lesions, urticaria form, maculopapular, petechiae and purpura, mottling, and livedo reticularis-like lesions.[1]
Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been related to a good range of opportunistic bacterial and fungal infections . Both Aspergillosis and Candida are reported because the main fungal pathogens for co-infection in people with COVID-19. Recently, several cases of mucormycosis in people with COVID-19 are increasingly reported world-wide, especially from India.[6]

ORAL SIGNS RELATED TO COVID-19

Cases of oral and skin signs in adults thanks to SARS-CoV-2 are documented. In Italy, a report shared that

severe patients developed skin signs, including erythematous rash ,generalized urticaria , and chickenpox-like vesicles (one patient), all of them with a bent directed to the trunk. In Spain, cases of oral signs related to SARS-CoV-2 are reported, depicting lesions like ulcers or ampules within the mouth . Another report documented three patients with macules and petechiae on the palate. In France, a patient was reported with tongue inflammation during the primary 24 h, with subsequent evolution to an erythematous macula, which resulted in an irregular and asymptomatic ulcer. The lesion probably derived from an inflammatory reaction triggered by vasculitis caused by COVID. [3]

Expression of the angiotensin-converting enzyme 2 receptor on oral mucosal epithelial cells

Transmission of SARS-CoV-2 can occur orally with saliva droplets or through nasal secretions in symptomatic and asymptomatic patients. The infection starts with the binding of the virus to the surface of the host cell. The spike protein (S) enables the virus to enter the target cell by binding its surface subunit S1 to the host cell's angiotensin-converting enzyme 2 (ACE2) receptor18. Therefore, cells expressing ACE2 can act as target cells and are highly vulnerable to SARS-CoV-2 infection. The S protein binds to ACE2 and is activated by the serine transmembrane protease 2. High expression of this enzyme has been identified in several areas of the physical body , like in pulmonary alveolar epithelial cells type II (AT2), upper esophagus stratified epithelium, ileum, and colon enterocytes, cholangiocytes, myocardial cells, mouth mucosa, proximal kidney tubule cells, and urothelial cells of the bladder.[3]

Taste alteration has been reported as an early sign of SARS-CoV-2 infection in adults. Expression of ACE2 is that the main factor for viral entry into the host cell in SARS-CoV-2 infection. ACE2 is expressed in epithelial cells from different sites within the mouth . the very best expression was found within the tongue and lesser amounts within the oral and gingival tissue.Expression of ACE2 has also been detected in salivary glands22, which could identify the mouth as a highly susceptible site for SARS-CoV-2 infection. Although the mechanism for the alteration within the perception of taste by this coronavirus isn't clear, this symptom might be considered an early manifestation in infected adults.[3]

DISCUSSION

Appearance of oral lesions was simultaneously found with loss of taste and smell within the patients and more severe and disseminated oral lesions were reported in older patients and in severe COVID-19. In another study, enanthema was reported in 29% of cases with confirmed COVID-19 and cutaneous exanthema.[1]

4.1 Aphthous-like lesions

Aphthous-like lesions appeared as multiple shallow ulcers with erythematous halos and yellow-white pseudomemberanes on the both keratinized and nonkeratinized mucosae. Regression of oral lesions was in parallel association with improvement of systemic disease. Increased level of tumor necrosis factor (TNF)-α in COVID-19 patients can cause chemotaxis of neutrophils to oral mucosa and development of aphthous-like lesions. Stress and immunosuppression secondary to COVID-19 infection might be other possible reasons for appearance of such lesions in COVID-19 patients.[1]

4.2 Herpetiform/zosteriform lesions

Herpetiform lesions presented as multiple painful, unilateral, round yellowish-gray ulcers with an erythematous rim on the both keratinized and nonkeratinized mucosae. Manifestations of those lesions preceded, coincided with, or followed systemic symptoms. In one case, geographic tongue appeared after recovery of herpetiform lesions. Stress and immunosuppression related to COVID-19 was the suggested cause for appearance of secondary herpetic gingivostomatitis.[1]

4.3 Ulcers and erosion

Ulcerative or erosive lesions appeared as painful lesions with irregular borders on the tongue, surface , and labial mucosa. various factors including drug eruption (to NSAID in one case), vasculitis, or thrombotic vasculopathy secondary to COVID-19 were suggested as causes for development of ulcerative and erosive lesions.[1]

4.4 White/red plaques

White and red patches or plaques were reported on dorsum of tongue, gingiva, and palate of patients with confirmed or suspected COVID-19. Candidiasis thanks to long-term antibiotic therapy, deterioration of general status, and decline in oral hygiene are often the explanation for white or red patches or plaques.[1]

4.5 EM-like lesions

EM-like lesions appeared as blisters, desquamative gingivitis, erythematous macules, erosions, and painful cheilitis with hemorrhagic crust in patients with cutaneous target lesions within the extremities. Lesions appeared between 7 and 24 days after the onset of systemic symptoms and recovered after 2 to 4 weeks.[1]

4.6 Angina bullosa-like lesions

Angina bullosa-like lesions presented as asymptomatic erythematous-purple blisters without spontaneous bleeding on the tongue and surface in two confirmed cases of COVID-19. [1]

4.7 Kawasaki-like disease

Oral lesions including cheilitis, glossitis, and erythematous and swollen tongue (red strawberry tongue) appeared in COVID-19 patients with Kawasaki-like disease (Kawa-COVID). [1]

4.8 Necrotizing periodontitis

Oral lesions including painful, diffuse erythematous and edematous gingiva with necrosis of inter-papillary areas. The suggested diagnosis was necrotizing periodontitis thanks to bacterial coinfections (especially prevotella intermedia) along side COVID-19. [1]

Vesicles and pustules and petechiae also are seen[1]

More about the loss of taste

Firstly, the peripheral systema nervosum is suffering from the coronavirus, and as gustatory buds are innervated by cranial

nerves, related functions could also be impaired, leading to taste disorders . Secondly, SARS-CoV-2 may bind essential salivary

mucin components, like sialic acid, consequently accelerating taste particle degradation and disturbing taste . Furthermore, ACE2 high expression was demonstrated

in the taste buds of rats and was related to angiotensin II production in mice taste buds. These findings may additionally point to

the inability of ACE2 to interrupt down this protein during COVID-19 infection, leading to the erratic taste responses. Researchers have also found with a point of evidence that taste disorders are related to COVID-19 positivity.[4]

CLINICAL DILEMMA IN CHILDREN

Although much remains unknown about the full-fledged effects of COVID-19, literature from the first stages of the COVID-19 pandemic (spring and summer 2020) shows a post-viral immunologic reaction leading to a multisystem inflammatory syndrome in children (MIS-C). The case definition of MIS-C consistent with the Centers for Disease Control and Prevention (CDC) may be a patient lesser than 21 years aged with fever, laboratory evidence of inflammation, and clinical evidence of severe illness requiring hospitalization, including involvement of two or more organ systems. These patients also should be positive for SARS-CoV-2 infection, confirmed either by reverse transcription polymerase chain reaction (RT-PCR), serology, or antigen testing, and will not have the other imminent explanation for their symptoms .Interestingly, oral mucosa changes also appear to be a crucial finding in MIS-C(7).It are often confused with Kawasaki disease , which may present in children with Strawberry tongue .

The intraoral findings during a child suffering from the disease are usually nonspecific which may flow from to the milder sort of COVID-19 in children . there's not much literature yet available that delineate the intraoral findings during a COVID positive child. Paediatric dentists

should therefore be vigilant while examining COVID positive children thanks to the paucity in information. Also, children are generally asymptomatic carriers of COVID-19, then universal

precautions should be followed by pedodontists. [4]

IN MUCORMYCOSIS

The most common oral sign of mucormycosis is ulceration of the palate, which ends up from necrosis thanks to invasion of a palatal vessel.Extension from the sinuses into the mouth causes painful, black necrotic ulcerations within the surface . The lesion is characteristically large and deep, causing denudation of the underlying bone .Ulcers from mucormycosis have also been reported on the gingiva, lip and gum ridge .[6]

Oral manifestations of mucormycosis are frequently the primary clinical signs to arise, probably due to the highly vascularized structure of oral soft tissues. Furthermore, it's been suggested that vascular ruptures and bleeding thanks to dental extractions may create a portal of entry for fungi into the maxillofacial regions.Intraorally, the surface is typically affected due to its proximity to the infection of the nasal fossa and paranasal sinuses. additionally , isolated intraoral involvement is extremely rare.

The maxilla rarely undergoes necrosis thanks to its rich vascularity. Maxillary necrosis can occur thanks to bacterial infections like osteomyelitis, viral infections like herpes zoster or fungal infections like mucormycosis, aspergillosis etc.Location of mucormycosis on the palate may be a rare and late occurance.[5]

It is an opportunity that such lesions are often early signs of the disease without the classic presentation of other symptoms. during this case, it becomes the responsibility of dental practitioners to acknowledge and investigate

such symptoms and regard every patient as potentially infectious. Dental practitioners should follow strict precautionary measures particularly at a time the society is

opening and COVID-19 remains a threat. Current studies suggest that oral lesions could also be atypical manifestation of COVID-19 Knowledge of those lesions by the attending dentist may aid in early detection of patients with asymptomatic disease and should be helpful in stopping the spread of the virus.[2]

Management

The management of oral mucosal lesions included one or more of the following: topical or systemic corticosteroids, diphenhydramine, mouthwashes, and antibiotics. altogether cases, the reported orofacial manifestations completely resolved within a few of days (range: 3-21 days) from the day of diagnosis.[3]

Treatment of mucormycosis consists of surgical debridement; systemic antifungal

therapy(amphotericin-B)and treatment of any underlying condition are most effective methods. Control and prevention of opportunistic fungal infection in patients suffering from debilitating diseases such as diabetic ketoacidosis, immunodepression, blood dyscrasia, solid organ transplant, patients on long term steroids and bone marrow transplant is very important. Once mucormycosis infection diagnosed in debilitated patients, it must be treated proptly, without any delay, by different modalities, medically and surgically.[5]

CONCLUSION

Aphthous-like lesions, herpetiform lesions, candidiasis, and oral lesions of Kawasaki-like disease are the most common oral manifestations of COVID-19 disease. An older age and severity of COVID-19 disease seem to be the most common factors that predict severity of oral lesions in these patients. Lack of oral hygiene, opportunistic infections, stress, underling diseases (diabetes mellitus, immunosuppression), trauma (secondary to intubation), vascular compromise, and hyper-inflammatory response secondary to COVID-19 could be are the foremost important predisposing factors for the development of oral lesions in COVID-19 patients.

Increase in mucormycosis in Indian context appears to be an unholy intersection of trinity of diabetes (high prevalence genetically), rampant use of corticosteroid (increases blood sugar and opportunistic fungal infection) and COVID-19 (cytokine storm, lymphopenia, endothelial damage). All efforts should be made to take care of optimal hyperglycemia and only judicious evidence-based use of corticosteroids in patients with COVID-19 is suggested so as to scale back the burden of fatal mucormycosis.

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