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Oral Lessons From COVID

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Abstract

The oral microbiome plays a crucial role in maintaining oral health. Disturbed symbiosis of the participants contributes to various oral diseases. Viruses can manifest in the oral cavity through blisters, ulcers, or tumours. SARS-CoV-2 remains infectious in droplets and aerosols for up to an hour. "Long COVID" refers to persistent, recurrent, or newly emerging symptoms occurring one to nine months post-recovery, partially due to viral persistence in the oral epithelium and other organs. With the Omicron variant's high transmissibility, 10–35% of patients may develop long COVID. Oral symptoms include discoloration, ulcers, haemorrhagic lesions, tongue mycosis, aphthae, atrophic cheilitis, and altered salivary flow. This article presents two clinical cases involving altered taste, oral discomfort, and Herpes simplex reactivation. COVID-19 symptoms are believed to be closely linked to microbiota alterations. Notably, microbial diversity is not fully restored even 6–12 months after infection. Some oral manifestations may also be related to reactivated viruses. Greater attention to oral health during and after viral infections is essential to understand their systemic impact.

Keywords: oral cavity, ecology, long COVID, microbiota

Oral Ecology

Oral ecology examines all living organisms within the oral cavity and their interactions. The human oral microbiome is composed of archaea, bacteria, eukaryotes, and viruses. This microbiome plays a crucial role in maintaining oral health and is influenced by various factors, including diet, medications, and the immune system. It is a key focus in the study of conditions such as dental caries, candidiasis, gingivitis, and periodontal disease. The ratio of prokaryotic organisms to human cells ranges from 1:1 to 10:1, whereas virus-like particles among prokaryotes are found at significantly higher levels, reaching up to 100:1 (1). Despite the oral ecosystem's relative stability, a disruption in the symbiotic balance among its components can lead to oral diseases such as caries, periodontitis, and mucosal disorders, as well as certain systemic illnesses (2,3,4). While bacteria and fungi are commonly investigated in oral pathologies, viral metagenomics has revealed the presence of viruses capable of causing blisters, ulcers, and tumors within the oral cavity (1). Respiratory viruses, including SARS-CoV-2, can be transmitted via droplets and aerosols, both of which may be generated during dental procedures. Droplets are defined as airborne liquid particles

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>5 μm, while aerosols are <5 μm and can remain suspended in the air for hours. Larger droplets adhere to surfaces within a few minutes. SARS-CoV-2 has been shown to remain infectious in both droplets and aerosols, with a half-life of approximately one hour (5,6). Replication of SARS-CoV-2 occurs not only in the upper respiratory tract but also in the oral mucosa and salivary glands. Given the rich vascularization of the oral cavity, it may serve as a portal for infection to the lungs, gastrointestinal tract, and other organ systems (7,8).

COVID-19

As of September 2023, there have been over 770 million confirmed COVID-19 cases globally, resulting in approximately 7 million deaths (9). By 2021, 157 scientific studies had been published on COVID-19 patients, including many that explore the role of saliva in viral transmission (10). Dysgeusia (taste disturbances) in COVID-19 results from damage to taste receptors, while xerostomia (dry mouth) arises from salivary gland infection. Additional oral manifestations include pain, erythema, aphthous ulcers, herpetic lesions, oral herpes zoster, geographic tongue, white plaques, fungal infections, petechiae, gingivitis, bleeding gums, pemphigus, lichen planus, and Sjögren's syndrome (10,11). SARS-CoV-2 enters host cells through the angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed in the lungs, liver, kidneys, gastrointestinal tract, vascular endothelium, and sweat glands. The palate, tongue, and salivary glands—rich in ACE2 receptors—are particularly susceptible (12). The salivary glands, in particular, may act as a viral reservoir, facilitating transmission between individuals (13).

Long COVID

A considerable proportion of patients continue to experience symptoms after recovering from the initial infection. Post-COVID-19 syndrome (PCS), also known as "long COVID," can manifest up to nine months after recovery (14), as SARS-CoV-2 can persist in the oral epithelium as well as in other organs/systems (15). This condition is defined by the persistence, recurrence, or appearance of new symptoms at least 30 days following infection (16). Although the incidence of long COVID has decreased, it remains above 10%. Cases associated with the Omicron variant tend to be less severe, but due to its high transmissibility, between 10% and 35% of infected individuals may develop long COVID (7). The underlying causes of long COVID may include persistent viral particles, immune dysregulation, alterations in gut microbiota, and microthrombus formation (9).

Most Common Oral Symptoms of Long COVID

In a study of 1,256 patients by B. Rafalowicz, L. Wagner, and J. Rafalowicz, the following oral manifestations were observed:

- 32% had discoloration, ulceration, or hemorrhagic lesions of the oral mucosa
- 29.7% had mycosis of the tongue
- 25.8% had aphthous ulcers on the hard palate
- 12.5% presented with atrophic cheilitis (14).

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Approximately 60% of patients reported reduced salivary secretion at the onset, with 7% continuing to experience this up to four months after resolution of systemic symptoms. Most oral lesions resolved spontaneously within three weeks. However, elderly, hospitalized, and severely ill patients experienced more extensive and persistent oral changes (14). PCS-related oral manifestations may also be linked to stress, poor oral hygiene, vasculitis, multi-organ involvement, opportunistic infections, reinfection, or immune dysfunction (17). Reported long COVID-related oral lesions include aphthous ulcers with inflamed borders, palatal hemorrhages, extensive wounds, spontaneous bleeding, cheilitis, bright red or violet mucosa, depapillated tongue, angioma-like lesions, and fungal infections of the tongue (14). We present two cases of oral changes following COVID-19 infection (Figures 1 and 2).

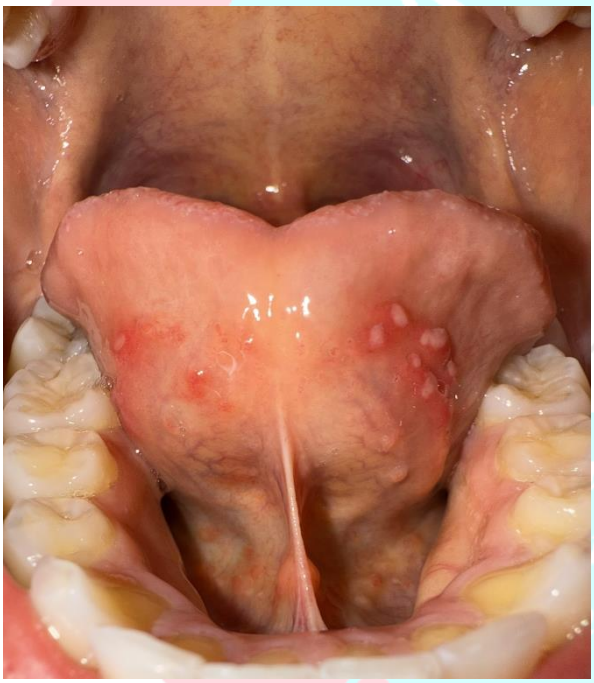

Fig. 1. A 20-year-old man with a history of COVID-19 infection two years ago presents with a burning sensation in the mouth, consistent with reactivation of Herpes Simplex Virus type 1 (HSV-1).

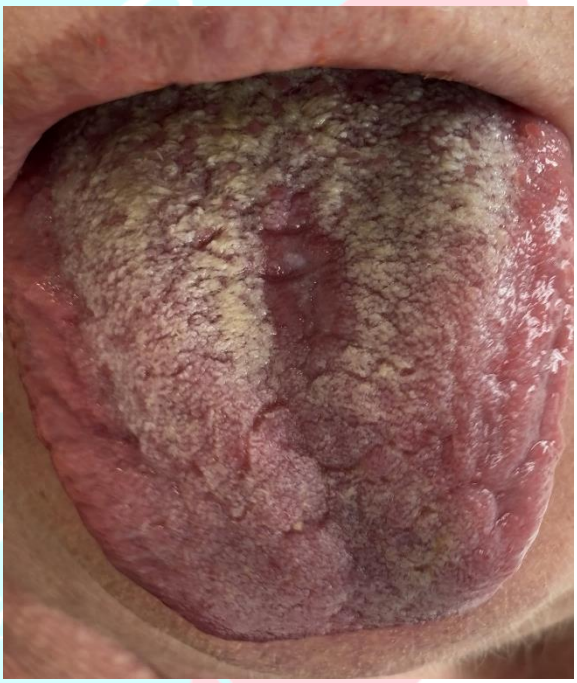

Fig. 2. A 67-year-old woman with a history of breast cancer, treated surgically and with six cycles of chemotherapy. She has had COVID-19 four times. Since her second COVID infection, she has experienced altered taste, gingivitis, and stomatitis, despite being sanitized and having no focal infections.

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Oral Lesions and COVID-19

It is not yet possible to establish a definitive causal relationship between prior SARS-CoV-2 infection and the development of oral lesions. However, similar to patients with human immunodeficiency virus (HIV), individuals infected with SARS-CoV-2 appear to be more susceptible to oral lesions due to virus-induced immunosuppression (18).
Research on oral manifestations in SARS-CoV-2 infection has demonstrated associations with thrombocytopenia, disseminated intravascular coagulation (DIC), and systemic inflammation (19). According to Martín Carreras-Presas et al., Long COVID may be driven by vascular and hematological alterations, including lymphocytic thrombotic arteritis (20). The potential for reinfection should also be considered (14). A case report by P. Heidari and Vl. Panov (21) describes a sequela of an aphthous lesion on the lower lip in a patient with acute COVID-19. The lesion appeared on the first day of illness, reached peak pain on day seven (coinciding with disease progression), and resolved by day ten. However, localized pain persisted, and two months later, the patient continued to experience a noticeable depression in the affected area.

Oral Microbiota

The microbiota has a well-established role in human health and immune system regulation. COVID-19 has been shown to alter both gut and oral microbiota compared to healthy individuals (22, 23). Notably, microbial diversity in COVID-19 patients may remain disrupted for 6 to 12 months following recovery (24, 25).
A recent study conducted by a Chinese research team investigated the oral flora of individuals who had recovered from the Omicron variant, as well as patients experiencing Long COVID. Tongue coating samples were collected and analyzed via DNA extraction and 16S rRNA gene sequencing. Interestingly, patients with Long COVID exhibited greater microbial diversity and abundance than those without prolonged symptoms (9). Bacterial taxa such as Prevotellaceae, Neisseria, Veillonella, Haemophilus, Prevotella, Fusobacterium, Porphyromonas, Rothia, Streptococcus, and Leptotrichia were commonly detected in post-COVID tongue samples. In particular, Prevotella, Haemophilus, Veillonella, and Neisseria were strongly associated with COVID-19 infection. Prevotella and Veillonella produce lipopolysaccharide (LPS), and their elevated presence may contribute to the pathogenesis of Long COVID. These findings suggest that the oral microbiome may influence both the acute phase and the recovery trajectory of SARS-CoV-2 infection (9).

Other Viruses Affecting the Oral Cavity

The presence of oral lesions long after recovery from COVID-19 also raises the question of coinfections or reactivations involving other viruses known to affect the oral mucosa. A systematic review of 53 articles on viral reactivation and coinfections in COVID-19 examined data on 12 viruses: Influenza A (IAV), Influenza B (IBV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), varicella-zoster virus (VZV), and human herpesviruses HHV-1, HHV-2, HHV-6, HHV-7, HHV-8, as well as hepatitis B virus (HBV) and parvovirus B19. Among these, EBV, HHV-1, and CMV were

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most frequently reactivated, while IAV and EBV were the most commonly reported coinfections (26).

Conclusion

Oral health research during the COVID-19 pandemic highlights the significant impact of systemic viral infections on both oral and general health. These findings underscore the importance of maintaining vigilant oral care during viral illnesses and further investigating the connections between oral manifestations and broader systemic involvement. Future research should aim to clarify the mechanisms linking oral changes to immune dysregulation, microbiome alterations, and viral persistence across multiple organ systems.

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