

## LETTER TO THE EDITOR

## Herpetic gingivostomatitis in a patient with COVID-19: Is this mutual relationship possible?

Dear editor,

Along with dermatologic lesions reported by numerous authors, Carreras-Presas et al (2020)<sup>1</sup>, in one of them, suggested that oral ulcers in SARS-CoV-2-positive patients represent an oral manifestation of COVID-19. Since then, various reports have emphasized the SARS-CoV-2 as the primary agent in developing oral lesions. However, the issue of such a role has generated much controversy among authors.<sup>2,3</sup> Given the difficulties in addressing the issue, we wish to highlight a case of herpetic gingivostomatitis exacerbated by COVID-19 with a 5-month follow-up to collaborate with authors in the comprehensive discussion.

A 15-year-old male with a history of mental illness presented on 18 August 2020, with fever, cough, intestinal complications and suspected COVID-19. Physical examination revealed a 37.5°C body temperature and 95% oxygen saturation in room air, and the nasopharyngeal swab went to the laboratory for analysis. The clinician prescribed azithromycin 500 mg, dipyron 500 mg, ivermectin 6 mg and prednisolone 20 mg for 5 days, and then discharged the patient under home quarantine and monitoring. Five days later, he returned to the hospital due to painful blisters and gingival erythema (Figure 1A), whose investigation led to the diagnosis of recurrent herpes. When the RT-PCR result confirmed the diagnosis of COVID-19, the team maintained supportive

care for the patient and implemented acyclovir 400 mg for 7 days and 0.12% chlorhexidine mouthwashes 3×/day. Two weeks following the onset of COVID-19 symptoms, the patient no longer presented symptoms, and the mouth displayed no gingiva blisters (Figure 1B). In the 5-month follow-up, no signal of lesions was observed.

A brief search performed in PubMed® and Science Direct databases (16 January 2021) using the descriptor “Oral manifestations and COVID-19” retrieved 1319 results. The authors mostly reported intraoral lesions such as ulcers, blisters, erosions, macules and petechiae in various sites, especially palate, tongue and lips<sup>4</sup>, but no evidence has convincingly demonstrated an association between the oral conditions and COVID-19. Four studies investigated the oral tissue responses to SARS-CoV-2 infection microscopically and, as a result, they identified mainly nonspecific inflammatory infiltrates and thrombosis<sup>5–8</sup> (Table 1). However, only two among these reported the negative serological results for herpes simplex virus (HSV) type 1 and type 2 antibodies, thus really backing the possibility that COVID-19 directly caused the oral conditions.<sup>5,7</sup>

Undeniably, numerous characteristics of COVID-19 require further elucidation. Widely accepted, COVID-19 exacerbates the inflammatory response of individuals by a ‘cytokine storm’<sup>4</sup>, which, along with an immunosuppressive



**FIGURE 1** (A) Initial presentation. Gingiva blisters delimited by erythematous halos and diffuse redness areas. (B) Final presentation. Complete healing and absence of herpetic lesions after remission of COVID-19 symptoms

TABLE 1 Brief summary of the four clinicopathologic studies of COVID-19 in English literature

Author	Patient description	Country	COVID-19 diagnostic tests	Anatomic locations/ clinical presentation	Microscopic features	Analysis technique
Ansari et al 2020 <sup>5</sup>	56 years/F; 75 years/M	Iran	PCR/nasopharyngeal swab	Hard palate and tongue/ulcers	Granulation tissue and invasion of mononuclear cells and neutrophilic cell invasion secondary to bacterial infection. Negative serological tests for herpes simplex virus type 1 and type 2 antibodies	H&E; IHC
Cruz Tapia et al 2020 <sup>6</sup>	51 years/F; 41 years/F; 55 years/F; 42 years/M	Peru	PCR/nasopharyngeal swab	Hard palate and tongue/blisters and macules	Keratinocyte vacuolization in the spinous cell layer, vascular congestion, haemorrhage, lymphocytic and inflammatory infiltrates in the lamina propria	H&E
Soares et al 2020 <sup>7</sup>	42 years/M	Brazil	PCR/nasopharyngeal swab	Hard palate, tongue and lips/ulcer	Epithelial vacuolization, exocytosis, chronic diffuse inflammatory, necrotic and haemorrhagic areas; CD34-positive expression in small vessel thrombi. CD3 positivity in most inflammatory cells in the connective tissue and the basal layer of the epithelium, CD8 highlighting lymphocytes in the lamina propria. Negative serological tests for herpes simplex virus type 1 and type 2 antibodies	H&E; IHC
Kämmerer et al. 2021 <sup>8</sup>	46 years/M	Germany	PCR/nasopharyngeal swab	Gingiva and buccal mucosa/erosion	Lymphocytic and inflammatory infiltrates in the lamina propria, apoptotic keratinocytes and exocytosis. Nuclei with positive staining for HSV-1 and -2 antibodies	H&E; IHC

F, Female; M, male; H&E, haematoxylin and eosin; IHC, immunohistochemistry.

action, could predispose the patients to the advent and aggravation of secondary conditions, such as herpes.<sup>1</sup>



As COVID-19 is a systematic disease, the pandemic emergency has motivated an unbridled search to characterize the disease's full epidemiological profile to speed up a timely therapy. However, a drawback of the situation has been the amount of superficial, fragmented and speculative conclusions. Robust epidemiological studies are lacking, and new ones, especially regarding oral conditions, should be conducted to clarify controversial points.

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#### CONFLICT OF INTEREST

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