New onset and exacerbation of oral lichenoid mucositis following SARS-CoV-2 infection or vaccination

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1 | INTRODUCTION

Oral lichen planus (OLP) and lichenoid mucositis (LM) are immune-mediated mucosal reactions (Alrashdan et al., 2016). Multiple factors were proposed to cause OLP and LM, including autoimmunity, medications, dental restorations, stress, and hepatitis C. OLP/LM have been associated with infectious agents such as hepatitis C and human papillomavirus (Lodi et al., 2010; Shang et al., 2020).

Following the description of coronavirus disease 2019 (COVID-19) and its causative agent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), case reports of oral mucosal reactions to SARS-CoV-2 infection have been published (Amorim Dos Santos et al., 2021; Brandão et al., 2021; da Mota Santana et al., 2022; Fidan et al., 2021; Iranmanesh et al., 2021), including new onset or exacerbation of OLP/LM following SARS-CoV-2 infection or vaccination (Burgos-Blasco et al., 2021; Diaz-Guimaraens et al., 2021; Fidan et al., 2021; Sharda et al., 2021; Troeltzsch et al., 2021). Here, we report OLP/LM in three categories (Table 1): 1) new-onset OLP/LM following COVID-19 infection (case 1), 2) new-onset OLP/LM following COVID-19 vaccination (cases 2 and 3), and 3) exacerbation of known OLP/LM following vaccination (cases 4–7).

2 | CASE REPORTS

2.1 | Case 1

A 41-year-old male was diagnosed with COVID-19 in December 2020. Two weeks after his diagnosis, he developed oral sensitivity. He had no history of prior mucosal lesions. Lichenoid striations with erythema were present on the buccal mucosa and gingival margins (Figure 1A–C). Fluocinonide 0.05% gel was prescribed, and he experienced symptomatic resolution within 1 month (Figure 1D–F).

2.2 | Case 2

A 56-year-old female was diagnosed with COVID-19 in March 2021. She was hospitalized and received hydroxychloroquine. She received two Pfizer-BioNTech vaccines in April 2021 and experienced oral sensitivity beginning in April 2021. She had no history of oral mucosal lesions. Striations on the bilateral buccal mucosa with erythema were noted. The assessment included a reaction to hydroxychloroquine or OLP/LM secondary to COVID-19. Fluocinonide 0.05% gel was prescribed.

2.3 | Case 3

A 72-year-old male received Moderna vaccines in February and March 2021. He developed new onset of symptoms in April 2021. He had no prior symptoms or mucosal changes. Erythema of the gingiva and upper lip were noted. A biopsy was performed which was consistent with lichenoid mucositis. He was begun on high potency topical steroids and his symptoms improved within 3 months.

2.4 | Case 4

A 61-year-old male with gingival OLP (Figure 2A–D), which was previously controlled with topical pimecrolimus 1% cream once daily,
received Pfizer-BioNTech vaccine in April 2021, and a second dose of Moderna vaccine in June 2021. He experienced a flare of oral lesions in mid-July 2021 presenting with erythema and striations involving the gingiva and tongue (Figure 2E–H). His signs and symptoms recovered to baseline 12 weeks after the second vaccine.

2.5 | Case 5

A 65-year-old female with a history of carcinoma-in-situ of the left lateral border of tongue, had ongoing follow-up in the oral medicine clinic for lichenoid changes. She had been originally managed with topical vitamin A 0.025% gel and clobetasol 0.05% gel twice daily with excellent response. One week after receiving the second dose of the Pfizer-BioNTech vaccine, she developed sensitivity and ulceration of the buccal mucosa and tongue. Oral findings resolved after 4 weeks of the original topical therapy at an increased frequency to 4 times daily.

2.6 | Case 6

A 65-year-old female with a history of oral and cutaneous lichen planus managed with topical steroids received the Pfizer-BioNTech vaccine in February and March 2021. Twenty-four hours following the second dose, she reported a feeling of “mouth on fire” which continued for 2 weeks. She was seen in July 2021; she had gingival erythema and striations extending into vestibular mucosa (Figure 3A–C). Saliva production was reduced (resting 0.3 mg/3 min and stimulated 2.1 mg/3 min). She has prescribed topical clobetasol and bethanechol for dry mouth. At one month follow-up, a significant reduction in erythema was seen (Figure 3D–F).

2.7 | Case 7

A 51-year-old male with a history of OLP and oral squamous cell carcinoma of the tongue received the second dose of the Pfizer-BioNTech vaccine in May 2021. He developed increasing oral sensitivity in the buccal mucosa bilaterally 2 weeks following the second dose. Clinical findings include erythema and striations of the posterior buccal mucosal bilaterally. Topical pimecrolimus cream with turmeric supplementation was prescribed. At the 2-month follow-up, clinical signs and symptoms returned to baseline.

3 | DISCUSSION

We present a case series of oral lichenoid reactions following vaccination or infection by SARS-CoV-2. New onset of OLP/LM was noted in 1 case following infection and 2 cases following vaccination. Exacerbation of existing OLP/LM was noted in 4 cases following vaccination. Although a biopsy was performed on one case only,
the diagnosis of OLP/LM is generally based on history and clinical features (Alrashdan et al., 2016).

OLP/LM are common conditions with a prevalence of 0.2%–5.0% (Gorouhi et al., 2014). Although the etiopathogenesis of OLP/LM is not fully understood, type 1 immune response appears to play a major role (Wang et al., 2016). Autoimmunity has been proposed to be the underlying mechanism of OLP/LM development (Ebrahimi et al., 2010). This series suggests that OLP/LM may be aggravated due to immune response to COVID-19/vaccination. Both SARS-CoV-2 infection and vaccination elicit type 1 immune response (Alter et al., 2021; Prompetchara et al., 2020). Therefore, it is not surprising for OLP/LM to ensue or be exacerbated by COVID-19 infection/vaccination.

Lichen planus is reported to follow vaccinations for other viral pathogens, such as hepatitis B, influenza, and herpes zoster (Lai & Yew, 2017). Furthermore, autoimmunity induced by vaccination is not limited to the COVID-19 vaccine but also in hepatitis B and H1N1 vaccines (Segal & Shoenfeld, 2018). Two theories were proposed to explain this phenomenon, immune hyperstimulation, and molecular mimicry. Immune hyperstimulation following COVID-19 infection as evidenced by the increase of inflammatory cytokines, including IL-6 and IL-10 (Wang et al., 2020). In addition, previous work has shown

**FIGURE 1** New-onset lichenoid reaction following SARS-CoV-2 infection (Case 1). (a–c) Bilateral reticulations of the buccal mucosa and erythema of the soft palatal mucosa. (d–f) Resolution of oral changes following 1-month treatment with fluocinonide gel (0.05%)

**FIGURE 2** Exacerbation of oral lichen planus following vaccination against SARS-CoV-2 virus (Case 4). (a–d) Mild reticulations of the marginal gingiva prior to vaccination. (e–h) Erythema and reticulations of the marginal gingiva 4 weeks following vaccination.
structural homology between SARS-CoV-2 surface peptides and human proteomes, further justifying the occurrence or exacerbation of immune-mediated conditions following SARS-CoV-2 infection (Kanduc & Shoenfeld, 2020).

This case series suggests that COVID-19 infection and host response to SARS-CoV-2 vaccination not only can aggravate known oral immune-mediated reactions but also can lead to de novo presentation of oral immune-mediated conditions. While it is not possible to establish causality between COVID-19 infection/vaccination and OLP/LM development/exacerbation, the timing of events is an important consideration. Whether COVID-19 infection/vaccination and OLP/LM development/exacerbation are directly or indirectly related, it is important to be aware of the occurrence of such events for diagnosis and management.

AUTHOR CONTRIBUTIONS
Lama Alabdulaaly: Writing – original draft; writing – review and editing. Herve Sroussi: Supervision; writing – review and editing. Joel B. Epstein: Conceptualization; data curation; supervision; writing – review and editing.

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CONFLICT OF INTEREST
None.

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