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Oral lichen planus arising after BNT162b2 mRNA COVID-19 vaccine: report of 2 cases

Luca Raccampo, MD,^a Salvatore Sembrionio, MD, PhD, FEBOMFS,^a Alessandro Tel, MD,^a Veronica Cacitti, MD,^b and Massimo Robiony, MD, FEBOMFS^a

The ongoing COVID-19 pandemic required a firm and prompt effort in the development of an effective vaccine. Reports of adverse reactions are increasing. Lichen planus, as well as its oral variant, is a condition that has previously been reported to be associated with vaccines. This is one of the first reports of oral lichen planus (OLP) arising after any COVID-19 vaccine. Here the authors present 2 cases of OLP that occurred after BNT162b2 mRNA COVID-19 vaccination (Comirnaty, Pfizer, New York, NY, USA; BioNTech, Mainz, Germany). (Oral Surg Oral Med Oral Pathol Oral Radiol 2022;134:e54–e57)

Lichen planus (LP) is a chronic idiopathic inflammatory condition that involves both the skin and mucous membranes. LP has a reported prevalence of roughly 1%, with a female-to-male ratio of approximately 2:1.¹ Although the mean age of the patients affected by LP is older than 40 years, cases have also been reported in pediatric patients.² Oral lichen planus (OLP) is typically characterized by relapses and remissions, and it is chronic, whereas the cutaneous lesions are mostly pruritic and self-limiting. OLP clinical presentation is variable. The onset of the disease is insidious because most of the patients are unaware of the condition. The tongue and the gingiva are the most commonly involved parts of the oral cavity, and white reticular patches or ulcerations are the typical oral mucosal presentation. Patients usually complain about burning symptoms and hypersensitivity of the mucosa to hot and spicy food. Even though many etiologic theories have been proposed to explain the pathogenesis of LP, it is still considered an idiopathic disease.^{3,4} Growing evidence suggests that a T-cell-mediated response is implicated in its pathogenesis, triggered by the exposure of specific antigens on the surface of epithelial basal cells.^{3,5} This T-cell cross-reaction mechanism seems to be primed by chronic infections (hepatitis B virus [HBV], human immunodeficiency virus), drugs (thiazide diuretics, antimalarial agents, nonsteroidal anti-inflammatory drugs, etc.), contact allergens, and dental restorative materials (amalgam, gold, and nickel). LP has also been linked with vaccines, including HBV, influenza, rabies, diphtheria, tetanus, pertussis, and measles, mumps, and rubella.⁵⁻¹⁰ The vaccines

against COVID-19 were rapidly developed and approved; therefore, their short- and long-term effects as well as their safety and effectiveness were reported in clinical trials. Taking all of this into account, the authors present 2 cases of OLP that occurred after the administration of the BNT162b2 mRNA COVID-19 vaccination in the community setting (Comirnaty, Pfizer, New York, NY, USA; BioNTech, Mainz, Germany).

CASE PRESENTATION

Case 1

A 54-year-old woman presented with a bilateral white reticular pattern on the oral mucosa with no other reported skin or nail lesions. The lesions were asymptomatic, but the entity of clinical manifestation and the sudden appearance led the patient to visit her stomatologist. She had received the second dose of the COVID-19 vaccine 10 days before the oral lesions appeared. She did not report a history of any previous LP presentation or dermatologic disease. Her medical history did not reveal any disease or drugs taken by the patient. When asked about possible alternative triggers, the patient denied any dental procedures, signs of infection, changes in medication, or stressful events in the weeks before. She had received all the compulsory vaccinations, and she reported never having experienced any vaccine side effects. She had not been diagnosed with COVID-19. During clinical examination, the lesions presented as lacy, white, raised patches of tissue overlying the oral mucosa. Slightly white lacelike network lines (Wickham striae) were observed on the oral mucosae, with well-distributed pigmentation on the whole surface (Figure 1A). The patient underwent oral biopsy of the lesions under local anesthesia.

Case 2

A 56-year-old woman presented with a sudden onset of burning pain localized in the upper gingival mucosa, limiting normal daily activities, especially toothbrushing and swallowing. Clinical examination revealed an erythematous lesion with erosive aspects on the gingiva

^aMaxillofacial Surgery Department, Academic Hospital of Udine, Department of Medicine, University of Udine, Udine, Italy.

^bDepartment of Pathology, Santa Maria degli Angeli Hospital, Pordenone, Italy.

Corresponding author: Massimo Robiony E-mail address: massimo@robiony.it

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extending to the buccal vestibular mucosa (Figure 1B). No previous clinical manifestations of LP were reported by the patient. She denied any disease or ongoing medications. The patient was asked for other possible triggers, which were not found in her clinical history. The week before, the patient had received the second dose of the COVID-19 vaccine. A biopsy was performed with the patient under local anesthesia, and a sample of mucosa was harvested for histopathologic examination.

Case summary

In both cases, a topical corticosteroid treatment was prescribed with mouthrinses. At subsequent evaluations, both patients showed partial remission of their lesions and were scheduled for periodic 6-month follow-up. Clinical and histologic findings, combined with the timing of onset with respect to the vaccination, led us to the diagnosis of OLP, which was likely secondary to COVID-19 vaccination.

Histopathology

In both cases, the oral biopsy revealed the presence of the characteristic band-like lymphoid subepithelial infiltrate (Figure 2A). At a higher magnification, inflammatory infiltration into the basal layer and basal hydropic degeneration of epidermal basal cells could be seen. As it occurs in the skin lesion biopsy, colloid bodies, also known as Civatte bodies, formed as a result of the degeneration of keratinocytes, were visible in the oral epithelium (Figure 2B).

DISCUSSION

The COVID-19 pandemic represents the most challenging pandemic of the 21st century, and the study of a vaccine against severe acute respiratory syndrome coronavirus 2 has drawn global attention in order to stop the spread of the disease. The unusual rapidity in the development of various types of vaccines strengthened the hesitancy of people to be vaccinated and raised several doubts regarding both short- and especially long-term side effects. According to the Centers for Disease Control and Prevention, the most common side effects are local, such as pain, redness, and swelling on the site where the vaccine is injected, or systemic, such as tiredness, headache, muscle pains, nausea, chills, and fever. In order to determine whether possible short-term side effects are directly related to vaccination, first a temporal criterion should be satisfied, together with the nonexistence of other concurrent triggering factors.¹¹ In both the authors' cases, the oral lesions appeared just a few days after the injection, suggesting a possible correlation. As reported by Rotim et al.,¹² OLP and oral lichenoid reaction are similar entities both clinically and histopathologically.

Although the cause of OLP is supposed to be an autoimmune response to an unknown antigen, several factors are commonly attributed to oral lichenoid reaction, such as drugs, dental restorative materials, and dental plaque. Despite their clinical and histologic similarities, the 2 entities differ in treatment. The elimination of the causative agent represents the only possibility for lichenoid reaction (LR) remission, whereas OLP benefits from topical corticosteroid therapy. That is the reason why a detailed anamnesis is important, as well as periodic follow-up, which helps with the differential diagnosis. In both the authors' cases, the lichenoid reaction hypothesis is plausible, although the patients did not report any preexisting triggering factors and the lesions showed only partial remission after corticosteroid topical treatment; therefore, the authors lean toward their OLP hypothesis.

Although cutaneous or mucosal reactions represent a fairly rare event, the onset of oral and skin lesions is confirmed by the first studies conducted on health care workers in various countries.^{13,14} The first reports in the literature concerning LP after BNT162b2 mRNA COVID-19 vaccination did not report the occurrence of oral lesions. Hiltun et al.¹⁵ reported a single case of a 56-year-old woman who presented with pruritic lesions on the ankles extending to the periumbilical area and the mammary and axillary fold 48 hours after the second dose of the vaccine. Unlike the authors' patients, this woman had a history of LP diagnosed 7 years before and was successfully treated with topical therapy. A new-onset LP case was reported by Merhy et al.,¹⁶ who described the presentation of a middle-aged woman with no relevant previous medical history who came to their department for a pruritic eruption characterized by erythematous and squamous papules distributed mostly on the trunk, appearing 1 week after receiving the first dose of the Pfizer-BioNTech COVID-19 vaccine. Recently, Kaomongkolgit et al.,¹⁷ Sharda et al.,¹⁸ and Troeltzsch et al.¹⁹ reported 3 new-onset OLP cases that occurred after COVID-19 vaccination. The first case report described the case of a 28-year-old woman with a 6-week history of oral mucosal discomfort and burning sensations accompanied by a white papular and striated bilateral pattern on the buccal mucosa and tongue that had developed 1 week after the administration of the second dose of the BNT162b2 mRNA COVID-19 vaccine. The second and the third case reports described the cases of 2 patients with a history of oral mucosal discomfort, burning sensations, and desquamation 6 and 14 days, respectively, after COVID-19 vaccination.

In many cases, the clinical appearance of OLP is mild, and even a stomatologist could miss the diagnosis in initial stages; therefore, it is always difficult to establish whether this condition was pre-existent or a new

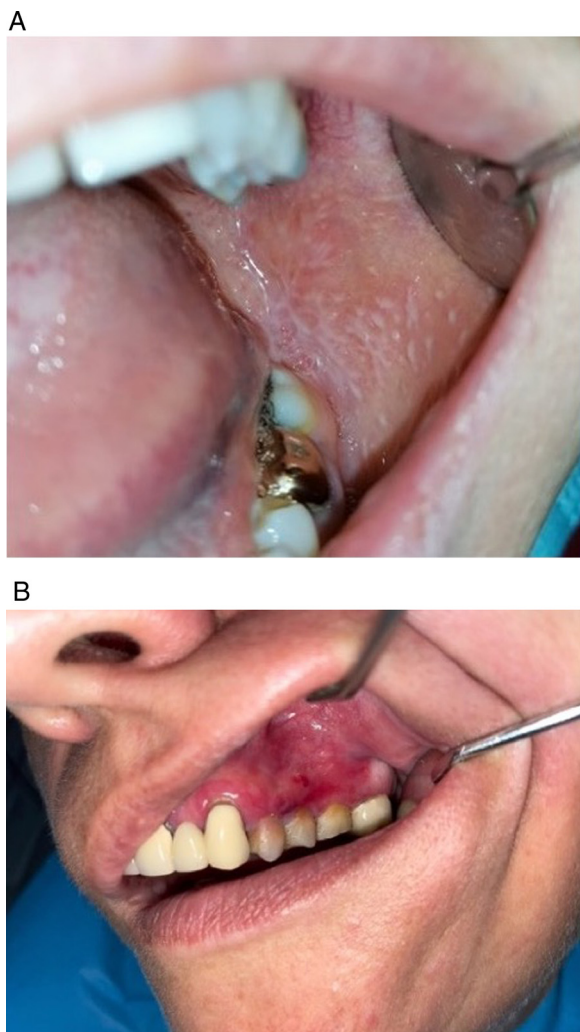


Fig. 1. (A) Clinical pattern of the first patient's lesions, with the white lacelike network that identifies the Wickham striae. (B) The erythematous aspect of the second patient's lesions on the left upper soft and hard gingiva.

onset. In both the authors' reported cases, they cannot rule out a prior subclinical form of OLP; however, the lesions became evident 2 weeks after the vaccine, suggesting an enhanced immune response independent of whether the condition was preexistent.

LP is an immune-mediated inflammatory condition whose progression depends on a T-cell-dominated, antigen-specific system. This persistent activation of CD8 autotoxic T lymphocytes against epidermal and mucosal cells may provoke apoptosis of basal layer cells and stimulate the production of various cytokines (e.g., interferon- γ , interleukin-5) to increase expression of major histocompatibility complex class II molecules and antigen presentation to CD4 T cells.^{19,20,21} The mechanisms involved in its pathogenesis remain partially unknown, even though several theories have been proposed. It is believed that proinflammatory

cytokines play a key role, also stimulating the production of reactive oxygen species, leading to apoptosis of the basal layer cells.²² Moreover, Yang et al.²³ investigated the potential involvement of the OLP pathogenesis of T-cell-derived exosomes that cause an elevation of the production of macrophage inflammatory protein-1 α/β , which in turn may guide the trafficking of CD8⁺ T cells after binding with chemokine receptors 1/5 in OLP, contributing to the development of OLP. Although it is considered, as mentioned earlier, a T-cell-mediated idiopathic inflammatory disease that has often been associated with drugs and even vaccines, especially HBV and influenza vaccination, the specific component responsible for the onset of LP is still unknown.⁹ It is likely that the cytokine production secondary to the Th1 response that triggers the vaccination may play a fundamental role in the LP outbreak in these patients, even if the exact pathogenic mechanism remains unclear.

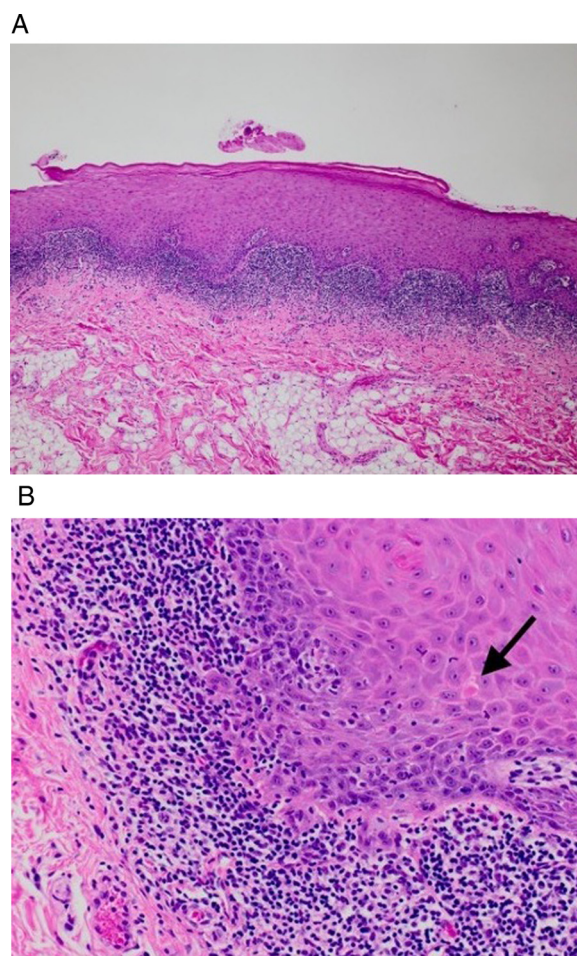


Fig. 2. (A) Typical histological pattern with the bandlike lymphoid subepithelial infiltrate. (B) Histological finding of Civatte bodies (arrow) as a result of the degeneration of keratinocytes.

CONCLUSIONS

Every clinician engaged in oral care should be aware of the possible complication of OLP after COVID-19 vaccination. OLP might represent an adverse event, considering the magnitude of the worldwide vaccination campaign that is ongoing. It is, however, a very rare side effect that should not discourage people from being vaccinated against COVID-19.

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