

LETTER TO THE EDITOR

Oral lesions postinjection of the first administration of Pfizer-BioNTech SARS-CoV-2 (BNT162b2) vaccine

To the Editor,

A 34 year-old healthy woman, with no medical history of allergic reactions and not undergoing chronic systemic pharmacological therapies, presented with diffuse and painful oral lesions. These appeared two days after the first administration of Pfizer-BioNTech SARS-CoV-2 (BNT162b2) vaccine. She reported no fever after the shot, but mild diffuse joint pain, asthenia and local pain in the injection site. At clinical examination, diffuse ulcerative lesions on the floor of the mouth were observed, associated with oral erythema of the ventral surface and anterior area of the tongue. The lip mucosa appeared dry and inflamed, with mild signs of angular cheilitis (Figure 1a,b).

The patient also referred swelling of the lips and oral gingiva, where multiple small erosive ulcers were present (Figure 1c-f). The lesions were treated with topical antibacterial agents and moisturizing lip balm. At the one-week follow-up, the lesions were gradually healed, but still present on both margins of the tongue and lower lip. Signs of angular cheilitis remained. At day 15, complete mucosal healing was achieved. Subsequently, the patient underwent allergological cutaneous tests, planned before the second vaccine administration. These resulted positive for polysorbate 80, in particular ID 1:10 with refresh-sterile eye drops, used an alternate source of polysorbate. Other allergy testing for pegilate was negative. The day after allergy test, the patient reported swelling of the lips and diffuse oral burning sensation, which lasted for 2 days. Due to the reaction following the first administration of the vaccine and the positive allergological results of proven allergy to the excipient, patient did not receive the second administration of the vaccine.

COVID-19 has been strongly associated with dysgeusia, but several oral manifestations have also been described in patients infected by SARS-CoV2 (Iranmanesh et al., 2021). There is growing evidence that angiotensin-converting enzyme 2 (ACE2), the main host cell receptor of SARS-CoV-2, is highly expressed on the epithelial cells of the tongue and of the salivary glands, which may explain the development of dysgeusia: it is possible that SARS-CoV-2 can infect and replicate in oral keratinocytes and fibroblasts, causing oral manifestations (Brandão et al., 2021). However, there is still a question in COVID patients about whether oral lesions may be also a secondary manifestations resulting from

the patient's systemic condition (Amorim Dos Santos et al., 2020; Tomo et al., 2020).

Given the clinical picture of the patient, it could not be excluded during the first clinical examination that the lesions could be due to a COVID-19 infection already ongoing at the time the first administration of the vaccine, although the patient recently had confirmation of negative nasopharyngeal swab. Furthermore, the oral lesions appeared after 48 hr since the first injection with BNT162b2 vaccine.

In addition, allergic reactions can also occur after vaccination, although oral side effects of systemically administered vaccines are extremely rare (Tarakji et al., 2014).

Few reports are present about BNT162b2 vaccine adverse reactions in the orofacial district (Cirillo, 2021).

Recently, a case of oral mucositis due to a hypersensitivity triggered by ChAdOx1 COVID-19 vaccination has been reported (Azzi et al., 2021), with similar lesions to those here described. However, these two vaccines differ: ChAdOx1 consists of a nonreplicating viral vector while BNT162b2 is a m-RNA vaccine and they consist of different excipients triggering the human immune system with different pathways.

Since the patient showed an important reactivity to polysorbate 80 during allergological tests with evident skin reaction and reappearance of oral signs and symptoms, it is plausible to associate the oral manifestations with the administration of the vaccine (Banerji et al., 2021).

Polysorbate 80 is used to make the m-RNA fat-soluble, and it is generally used to encapsulate the monofilament of the m-RNA, which otherwise is unstable in physiological conditions, and otherwise, it could not perform its function. It is known to be able to cause a cross-link reaction with one of the components of the BNT162b2 vaccine. The nano-particle possibly involved in the cross-link reaction with Polysorbate 80 is named Poly(ethylene glycol) (PEG), which has been proven to improve stability and immunogenicity of vaccine particles. Although different hydrogel cross-linking mechanisms are known to result in distinct network structures, it is still unknown how these various mechanisms influence biomolecule release (Lee et al., 2016).

Possible adverse reactions to PEG are already known in literature and have already been specifically indicated as a possible adverse effect to the BNT162b2 vaccine (Sellaturay et al., 2021).

The continuation of the vaccination campaign and the increasing number of doses administered could lead to an increase in reports of oral adverse reactions.



FIGURE 1 From upper left corner: (a) Ulcerative lesion on the floor of the mouth. (b) Angular cheilitis. (c) Multiple small erosive ulcers on lip's mucosa. (d) Diffuse erythema and multiple small erosive ulcers on oral gingiva: upper right jaw. (e) Diffuse erythema and multiple small erosive ulcers on oral gingiva: upper left jaw. (f) Diffuse erythema and multiple small erosive ulcers on oral gingiva: lower right jaw

CONFLICT OF INTERESTS

None to declare.

AUTHOR CONTRIBUTIONS

Maddalena Manfredi: Conceptualization; Investigation; Validation; Writing-review & editing. **Giulia Ghidini:** Writing-original draft. **Erminia Ridolo:** Writing-review & editing. **Silvia Pizzi:** Supervision.

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REFERENCES

- Amorim dos Santos, J., Normando, A. G. C., Carvalho da Silva, R. L., De Paula, R. M., Cembranel, A. C., Santos-Silva, A. R., & Guerra, E. N. S. (2020). Oral mucosal lesions in a COVID-19 patient: New signs or secondary manifestations? *International Journal of Infectious Diseases*, 97, 326–328. <https://doi.org/10.1016/j.ijid.2020.06.012>
- Azzi, L., Toia, M., Stevanello, N., Maggi, F., & Forlani, G. (2021). An episode of oral mucositis after the first administration of the ChAdOx1 COVID-19 vaccine. *Oral Diseases*. <https://doi.org/10.1111/ODI.13874>
- Banerji, A., Wickner, P. G., Saff, R., Stone, C. A., Robinson, L. B., Long, A. A., Wolfson, A. R., Williams, P., Khan, D. A., Phillips, E., & Blumenthal, K. G. (2021). mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: Current evidence and suggested approach. *The Journal of Allergy and Clinical Immunology: In Practice*, 9(4), 1423–1437. <https://doi.org/10.1016/j.jaip.2020.12.047>

- Brandão, T. B., Gueiros, L. A., Melo, T. S., Prado-Ribeiro, A. C., Nesrallah, A. C. F. A., Prado, G. V. B., Santos-Silva, A. R., & Migliorati, C. A. (2021). Oral lesions in patients with SARS-CoV-2 infection: Could the oral cavity be a target organ? *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, 131(2), e45–e51. <https://doi.org/10.1016/j.oooo.2020.07.014>
- Cirillo, N. (2021). Reported orofacial adverse effects of COVID-19 vaccines: The knowns and the unknowns. *Journal of Oral Pathology and Medicine*, 50(4), 424–427. <https://doi.org/10.1111/jop.13165>
- Iranmanesh, B., Khalili, M., Amiri, R., Zartab, H., & Aflatoonian, M. (2021). Oral manifestations of COVID-19 disease: A review article. *Dermatologic Therapy*, 34(1), e14578.
- Lee, S., Tong, X., & Yang, F. (2016). Effects of the poly(ethylene glycol) hydrogel crosslinking mechanism on protein release. *Biomaterials Science*, 4(3), 405–411. <https://doi.org/10.1039/C5BM00256G>
- Li, Q., Gong, S., Yao, W., Yu, Y., Liu, C., Wang, R., Pan, H., & Wei, M. (2021). PEG-interpenetrated genipin-crosslinked dual-sensitive hydrogel/nanostructured lipid carrier compound formulation for topical drug administration. *Artificial Cells, Nanomedicine, and Biotechnology*, 49(1), 345–353. <https://doi.org/10.1080/21691401.2021.1879104>
- Sellaturay, P., Nasser, S., Islam, S., Gurugama, P., & Ewan, P. W. (2021). Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine. *Clinical and Experimental Allergy*. <https://doi.org/10.1111/cea.13874>
- Tarakji, B., Umair, A., Alakeel, R., Ashok, N., Azzeghaibi, S. N., Darwish, S., Mahmoud, R. S., & Elkhatat, E. (2014). Hepatitis B vaccination and associated oral manifestations: A non-systematic review of literature and case reports. *Annals of Medical and Health Sciences Research*, 4, 829–836. <https://doi.org/10.4103/2141-9248.144870>
- Tomo, S., Miyahara, G. I., & Simonato, L. E. (2020). Oral mucositis in a SARS-CoV-2-infected patient: Secondary or truly associated condition? *Oral Diseases*. <https://doi.org/10.1111/odi.13570>

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