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 eritema 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 were negative. The day after allergy test, the patient reported swelling of the lips and diffuse oral burning sensation, which lasted for two days. The 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 B, 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 TB, 2020). However, there is still a question about whether oral lesions may be also a secondary manifestations resulting from the patient's systemic condition (Amorim Dos Santos , 2020; Tomo, 2020).

Given the clinical picture of the patient, it could not be excluded 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 had recently had confirmation of negative nasopharyngeal swab. Furthermore, the oral lesions appeared after 48 hours 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, 2014).

Few reports are present about BNT162b2 vaccine adverse reactions in the orofacial district (Cirillo, 2020) .

Recently, a case of oral mucositis due to a hypersensitivity triggered by ChAdOx1 COVID-19 vaccination has been reported (Azzi, 2021), with similar lesions to those here described. However, these two vaccines differ: ChAdOx1 consist in a non replicating 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 symtoms, it is plausible to associate the oral manifestations with the administration of the vaccine (Banerji, A, 2021).

Polysorbate 80 is used to make the m-RNA fat-soluble, 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 crosslinking mechanisms are known to result in distinct network structures, it is still unknown how these various mechanisms influence biomolecule release (Lee, 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, 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.

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Figure:

From upper left corner:

1a) Ulcerative lesion on the floor of the mouth.

1b) angular cheilitis.

1c) multiple small erosive ulcers on lip's mucosa.

1d) diffuse eritema and multiple small erosive ulcers on oral gingiva: upper right jaw.

1e) diffuse eritema and multiple small erosive ulcers on oral gingiva: upper left jaw.

1f) diffuse eritema and multiple small erosive ulcers on oral gingiva: lower right jaw.