Covid-19 vaccine tolerabilty in a patient with a delayed allergic reaction to polyethylene glycol: a case report

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Since the beginning of COVID-19 vaccinations in December 2020, multiple cases of suspected allergic reactions were reported with an initial estimation of 11.1 cases of allergic reactions (including anaphylaxis) occurring per 1 million doses [1,2]. The presence of the excipient polyethylene glycol-2000 (PEG-2000) has been considered as the potential cause of immediate drug hypersensitivity reactions to COVID-19 vaccines containing PEG-2000, as SPIKEVAX (Moderna's COVID-19 vaccine) or COMIRNATY (Pfizer-BioNTech's COVID-19 vaccine) [3,4]. PEG is a polyether compound that is widely used as an additive in pharmaceuticals, food, and cosmetics industry due to its stabilizing properties [5]. For medicines, the process of PEGylation involves binding of PEGs to systemic drugs to increase molecular weight, prolong circulation time, and shield the drug from the immune system by preventing opsonization [6]. In these vaccines, PEG-2000 is used to encapsulate messenger RNA (mRNA) into lipid nanoparticles to deliver it to cells [5]. Expert consensus statements have provided guidelines for diagnostic and therapeutic procedures used in COVID-19 vaccination in patients with allergic diseases and for patients that had an immediate reaction with a COVID-19 vaccine [2], but there is no information concerning COVID-19 vaccination in patients with PEG allergic contact dermatitis. We present the case of a patient diagnosed of contact dermatitis due to PEG that safely received a COVID-19 vaccine that contained PEG-2000. The patient gave her consent for publication of her case.

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A 41-year-old woman with no medical history of interest nor drug allergy background, was attended at the Dermatology Department because of symptoms of stomatitis that she suspected were related to toothpastes, mouthwash and chewing gums. An allergy study was performed using patch tests with the patient's suspected products (Oral-B ® toothpaste and mouthwash), the Spanish standard patch test series [7] and the cosmetics/vehicles and emulgents series (Supplementary Table 1). The results were mild positive at 96 hours to polyethylene glycol–400 and Oral-B ® toothpaste and mouthwash (which contain PEG-300, also named PEG-6 with the International Nomenclature of Cosmetic Ingredients), so she was diagnosed of allergic contact stomatitis to PEG. Avoidance of PEG-containing products (toothpaste and mouthwash) was recommended with subsequent resolution of the oral symptoms.

Some months later, she was referred to our Allergy Department to assess the possibility of receiving third dose of COVID-19 vaccination with PEG containing vaccines, which at that time, were the only ones available in our hospital. Previously, she had received two doses of VAXZEVRIA (AstraZeneca's COVID-19 vaccine) which does not contain PEG. We performed an allergy workup with skin prick test (SPTs) with PEG-1500 (100mg/mL, ROXALL Medicina España S.A., Zamudio, Spain) and 1:100 dilution of Polysorbate 80 (4mg/mL) and intradermal testing (IDT) with 1:100 and 1:1000 dilutions of PEG-1500 (1mg/mL, ROXALL Medicina España S.A., Zamudio, Spain) and 1:100 dilution of Polysorbate 80 (4mg/mL) with negative results in the immediate and late readings. The allergological study could not be performed with PEG-2000 since it is not commercially available.

Due to these results and taking into account the risk of insufficient immunization, the patient decided to receive a third dose of COVID-19 vaccine. She received SPIKEVAX (a PEG-2000 containing vaccine), at our hospital's vaccination center, and no immediate nor delayed adverse reactions were reported.

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In the present case, the stomatitis symptoms and positive patch test results confirmed a delayed type IV hypersensitivity mechanism to PEG. Some studies have reported that lower molecular weight (MW) PEGs (as 200-400 g/mol) are mainly implicated in allergic contact dermatitis, and cross-reactivity occurred between low-MW PEGs (<400 g/mol), but did not with the high MW PEGs (>1000 g/mol) [3,4]. In our case, the toothpaste and mouthwash contained PEG-300, considered a low MW PEG, which could explain the tolerability of PEG-2000 (a high MW PEG) presented at COVID-19 vaccines.

Similar scenarios were reported with other drug excipients like thimerosal. Thimerosal is a contact allergen composed of a mercury derivative and a thiosalicylic acid, used in cosmetics, vaccines, and eye care products [8]. Despite the apparent sensitization to mercurials, probably induced by vaccination, some clinical studies demonstrated that further vaccination of these individuals with thimerosal containing vaccines was safe with no hypersensitivity reactions reported, even in subjects with a positive patch test to thimerosal, suggesting that thimerosal hypersensitivity was not associated with an increased risk of vaccination reactions [8–10].

In conclusion, although we may have patients diagnosed with contact dermatitis due to PEG sensitization, we should not rule out the possibility of offering our patients a safe vaccination, even with PEG-2000 COVID-19 vaccines. Future studies will be needed to help us clarify the true role of PEG hypersensitivity with the risk of administering PEG containing vaccines, especially considering that the benefits of vaccination clearly outweigh the small risk of a local dermatitis.

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Conflict of Interest

The authors declare that they have no conflicts of interests to disclose.

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