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A case of delayed allergy to polyethylene glycol 2000 and polysorbate 80 confirmed by patch test: Consequences for anti-SARS-CoV2 vaccination?

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Among the anti-SARS-CoV2 vaccines currently used in Italy, polyethylene glycol (PEG) 2000 [H(OCH₂CH₂)_nOH; CAS 25322-68-3] is contained in Pfizer-BioNTech BNT162b2 and Moderna mRNA-1273, and polysorbate 80 (PS80) [C₆₄H₁₂₄O₂₆; CAS 9005-65-6] in AstraZeneca AZD1222 and Johnson & Johnson Ad26.COV2.S.¹ These two excipients are also contained in several other drugs and in daily topical products and have been reported as sensitizers.^{2,3}

Herein, we report a patient with delayed hypersensitivity to the anti-SARS-CoV2 vaccine excipients PEG2000 and PS80 who experienced in the past two episodes of maculopapular eruptions following the administration of two different drugs, each of which containing the two previously mentioned excipients.

CASE REPORT

A 57-year-old woman referred to us for history of two generalized maculopapular itching eruptions which had occurred after taking

ibuprofen and zolpidem tablets 4 and 2 years before. The two drugs contained PS80 and PEG400, respectively. The patient denied contact dermatitis from cosmetics and topical medications. Due to this history and to assess the potential risk of adverse reactions related to anti-SARS-CoV2 vaccination, a patch test with PEG2000 and PS80 (5% in petrolatum) was performed. The allergens were obtained from Sigma-Aldrich and prepared by our hospital Pharmacy according to GMP procedures. Patch tests were occluded for 2 days with the Haye's Test Chambers (Haye's Service) on Soffix tape (Artsana) and readings were performed on Day (D)2 and D4.⁴ The patient resulted positive to PEG2000 (++) and PS80 (++) on D2 and D4 (Figure 1). Ten healthy volunteers resulted negative to the same patch tests. Since no anti-SARS-CoV2 vaccines without these two excipients are available in Italy, we advised the patient to refrain from anti-SARS-CoV2 vaccination.⁵ Finally, we recommended to our patient to avoid all systemic drugs and topical preparations containing PEGs or PS80 either.



FIGURE 1 Positive patch test to polyethylene glycol 2000 and polysorbate 80 (5% pet)

DISCUSSION

PEGs and PS80 are extensively used as excipients in drugs and cosmetics. PEGs are hydrophilic polymers of ethylene oxide and are also used as osmotic laxatives. PS80 is a PEGylated sorbitan and is also used as emulsifier in the food industry. Delayed hypersensitivity to PEGs and PS80 is rarely reported in contact dermatitis to dressings and topical and inhalation drugs.^{6,7} To the best of our knowledge, this is the first report of delayed hypersensitivity to both PEG2000 and PS80 confirmed by patch test in the same patient. Our patient experienced in the past two maculopapular eruptions caused by a non-steroidal anti-inflammatory drug and by a sedative and hypnotic drug, two different drugs containing the structurally similar polymers PEG400 and PS80, respectively. Thus, a cross-reactivity between these excipients could not be excluded, as reported for immediate hypersensitivity to PEGs and PS80.⁸

Regarding the role of PEG2000 and PS80 in anti-SARS-CoV2 vaccine allergy, Phases 2 and 3 clinical trials on anti-SARS-CoV2 vaccines excluded patients with proven allergy to excipients contained in these vaccines.⁹ While patients with documented immediate hypersensitivity to PEGs and PS80 are recommended to avoid vaccination with the vaccine containing the culprit excipient,¹⁰ data on delayed hypersensitivity are not available and the question is still challenging. Even if our patient had experienced no life-threatening reactions to drugs sharing the same or similar excipients contained in all currently available anti-SARS-CoV2 vaccines in Italy, we recommended avoidance of anti-SARS-CoV2 vaccination. In fact, to obtain an efficient vaccination coverage at least two vaccine doses are needed, potentially increasing the risk of a delayed severe skin adverse reaction due to the repeated immune stimulation.

AUTHOR CONTRIBUTIONS

Marta Tramontana: Conceptualization; writing – original draft; data curation; supervision. **Leonardo Bianchi:** Conceptualization; writing – original draft; writing – review and editing; data curation. **Filippo Biondi:** Conceptualization; writing – original draft; data curation. **Katharina Hansel:**

Conceptualization; writing – original draft; writing – review and editing; methodology. **Nicolò Malatesta:** Conceptualization; writing – original draft; data curation. **Rossella Marietti:** Conceptualization; writing – original draft; data curation. **Luca Stingeni:** Conceptualization; writing – original draft; writing – review and editing; methodology; data curation; supervision.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICS STATEMENT

Written informed consent was provided by patient to the data publication.

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