Safe Administration of SARS-CoV-2 Vaccine After Desensitization to a Biologic Containing Polysorbate 80 in a Patient With Polyethylene Glycol–Induced Severe Anaphylaxis and Sensitization to Polysorbate 80

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Polyethylene glycols (PEGs) and structurally related polysorbates (PEG sorbitans) are polyether compounds derived from ethylene oxide that are widely used as excipients and conjugated pharmaceuticals. The role of PEG as an unsuspected, high-risk "hidden" allergen that can cause systemic allergic reactions was recently assessed [1].

In November 2020, a 61-year-old man developed a severe allergic reaction to a PEG-based colonoscopy preparation containing PEG 3350 (Moviprep). Immediately after taking the drug, he experienced generalized urticaria with labial angioedema, vomiting, dysphagia, presyncope, hypotension, and tachycardia. He was treated with intravenous fluids, metoclopramide 10 mg, methylprednisolone 40 mg, and dexchlorpheniramine 5 mg. His condition barely improved, and he was treated in the emergency room with a second dose of the same drugs together with intravenous hydrocortisone 200 mg. His symptoms resolved completely. It should be noted that despite the severity of the reaction, epinephrine was not administered. The patient reported that he had previously developed pruritic erythematous macules when using some shower gels.

In January 2021, an allergy work-up was carried out in the allergy department. Skin prick tests (SPTs) performed with undiluted Moviprep and PEG 2000 (0.16 mg/mL) yielded positive results (wheals of 7×7 and 4×5 mm, respectively). The patient was diagnosed with anaphylaxis due to Moviprep and sensitization to PEG 2000 and advised to avoid all drugs and vaccine preparations containing PEG of any molecular weight.

Two months later, the patient was diagnosed with stricturing Crohn's disease, and the gastroenterologist indicated treatment with the biologic adalimumab. Given the need for vaccination against COVID-19 before starting adalimumab, he was referred back to our department, since all available vaccines against SARS-CoV-2 contain PEG or polysorbate. Of note, adalimumab also contains polysorbate 80 (PS80) as an excipient.

SPTs performed with the vaccines Comirnaty (Pfizer-BioNTech) and Vaxzevria (AstraZeneca), trometamol, PS80, and PS20 yielded negative results. Intradermal testing was negative with trometamol (0.1 mg/mL) and positive with PS80 (0.04 mg/mL) and PS20 (0.04 mg/mL) (both wheals of 7×7 mm).

A basophil activation test (BAT) yielded positive results to Comirnaty vaccine (10% basophil activation), Vaxzevria vaccine (9.6%), PEG 2000 (18.8%), PS20 (21.8%), PS80 (9.4%), PEG 3350 (13%), and adalimumab (8.4%).

Since all the available anti-TNF-α treatments for Crohn's disease contained polysorbates as excipients, we decided to perform a desensitization procedure with infliximab, an intravenous biological drug containing PS80, after consultation with the gastroenterologist and signing of the informed consent by the patient. The protocol was based on that designed by Lee et al [2] and adjusted to the dose prescribed by the gastroenterologist (Table). The drug was administered according to the manufacturer's protocol (infliximab dose of 470 mg containing 2.35 mg of PS80, maintenance schedule every 8 weeks). The patient tolerated all 6 infliximab desensitization procedures without incident; in the last procedure, the dose of infliximab was doubled and was also well tolerated. On the second day of desensitization, the Janssen SARS-CoV-2 vaccine, which contains 0.16 mg of PS80, was also administered at the end of the infliximab schedule. The drug was well tolerated. The Janssen vaccine was chosen because it contained PS80 as an excipient and only 1 dose was needed to immunize the patient.

After some time, a new dose of Jansen or AstraZeneca SARS-CoV-2 vaccine was requested, although it was not available. A study of the immune response against SARS-CoV-2 carried out by the immunology department revealed good levels of humoral and cellular response to the virus. The cellular immunity pattern showed that the patient had been in contact with the SARS-CoV-2 virus after vaccination.

From 1989 through 2017, the US Food and Drug Administration (FDA) received 53 reports of anaphylactic reactions in which PEG-containing bowel preparations or laxatives were the primary or only suspected causative agent. Reports to the FDA of anaphylaxis induced by biologics have increased in the last 20 years. The mechanisms of the underlying reactions are not clear, although PEG or polysorbates were involved in many of them [3].

In the case we report, where the anaphylactic reaction was due to PEG 3350 contained in a laxative, it is interesting that sensitization to PEG 3350 and PEG 2000 was detected together

Table. Outpatient Desensitization Protocol for a Total Infliximab Dose of 470 mg[a]

Solution		Dose in each solution		Volume	Solution concentration		
A (1/100)		0.94 mg		50	0.0188 mg/mL		
B (1/10)		9.4 mg		50	0.188 mg/mL		
C		470 mg		250	1.88 mg/mL		
Step	Solution	Rate, mL/h	Time, min	Infliximab dose administered	Infliximab cumulative dose	PS80 dose administered	PS80 cumulative dose
1	A	3	15	0.0141	0.0141	0.0000705	0.0000705
2	A	6	15	0.0282	0.0423	0.000141	0.0002115
3	A	12	15	0.0564	0.0987	0.000282	0.0004935
4	A	25	15	0.1175	0.2162	0.0005875	0.001081
5	B	5	15	0.235	0.4512	0.001175	0.002256
6	B	10	15	0.47	0.9212	0.00235	0.004606
7	B	20	15	0.94	1.8612	0.0047	0.009306
8	B	40	15	1.88	3.7412	0.0094	0.018706
9	C	9	15	4.23	7.9712	0.02115	0.039856
10	C	19	15	8.93	16.9012	0.04465	0.084506
11	C	39	15	18.33	35.2312	0.09165	0.176156
12	C	77	180	434.28	469.5112	2.1714	2.347556

[a]Premedication with intravenous acetaminophen 1 g, methylprednisolone 20 mg, and dexchlorpheniramine 5 mg was administered 30 minutes before the protocol, according to the manufacturer's regimen.

with sensitization to PS80 and PS20 and demonstrated by skin tests and a BAT. Although there is limited evidence that PEGs cross-react with certain polysorbates, cross-reactivity between PEG 3350 and PS80 has been reported in patients who reacted to both [4] and has been demonstrated in patients with positive skin test results to both excipients and a history of immediate hypersensitivity reactions to PEG [5].

Given the risk of cross-reactivity and the history of severe anaphylaxis, as well as the need to use a biological drug for the patient's underlying disease, desensitization with a biological drug containing PS80 was the best option. In addition, infliximab was chosen for desensitization because it can be administered intravenously, in contrast with other biologics, which must be administered subcutaneously.

The Pfizer-BioNTech and Moderna SARS-CoV-2 vaccines were approved in December 2020. Since then, there have been reports of anaphylaxis following administration [6]. While PEG and polysorbate have been thought to cause these potential IgE-mediated reactions, causality has been demonstrated in very few cases [7,8]. In the present report, the patient had risk factors for a severe reaction to both vaccines; therefore, administration of one of them during the desensitization regimen with infliximab/PS80 was adequate.

In conclusion, we report the safe administration of a SARS-CoV-2 vaccine and a PS80-containing biologic drug to a PS80-sensitized patient after a desensitization regimen. To our knowledge, this is the first report of such a procedure.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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