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Failure of desensitization with Pfizer-BioNTech COVID-19 vaccine in two asthmatic patients

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Summary
Since December 2020, in various countries of the world, many cases of severe allergic reactions after administration of PfizerBioNTech COVID-19 vaccine, were reported. A great concern has arisen among the doctors who administer the vaccine and the allergic patients who undergo vaccinations. In Italy guidelines were published in order to stratify the risk in the allergic population.
In mRNA vaccines, the component currently suspected of causing allergic reactions is the polyethylene glycol excipient (PEG or macrogol). In patients who have shown an immediate allergic reaction to vaccine and who are negative to skin tests for PEG, desensitization with the same vaccine is proposed. In this paper we describe two cases of asthma after the first COVID vaccine administration in which desensitization has failed.

Impact statement
Subjects with particular conditions, such as asthma, can carry out the anti COVID vaccination, but need a more specific and individualized management.

Introduction

As of December 23, 2020, 175 case reports were identified as possible cases of severe allergic reactions in the United States, including anaphylaxis, after administration of PfizerBioNTech COVID-19 vaccine (1). The median interval from vaccine receipt to symptom onset was 13 minutes (range 2-150 minutes). Among persons with follow-up information available, all had recovered or been discharged home. Most of the patients had suffered from a prior history of allergy or anaphylaxis.
Subsequently, millions more doses of Pfizer-BioNTech vaccine were administered, with an updated reported anaphylaxis rate of 4.7 cases per 1 million doses (2).
Furthermore, a recent study has found the vast majority of people who have a prior history of anaphylaxis are unlikely to have a serious adverse reaction after receiving Pfizer's COVID-19 vaccine (3). In the updated AIFA (Italian Drug Agency) report on the surveillance of COVID-19 vaccines, out of 84.010.605 doses of vaccine administered in Italy in the period between 12/27/2020 and 09/26/2021, were reported 3 cases of anaphylaxis per million doses of Comirnaty (4).
Nevertheless, a great concern has arisen among the doctors who administer the vaccine and the allergic patients who undergo vaccinations. In Italy, guidelines were readily published in order to stratify the risk in the allergic population. Specific guidelines are given on the management of allergic reactions to the vaccine (5) and rule out allergy to polyethylene glycol (PEG), present in Pfizer vaccines to help stabilize the mRNA, a possible cause of these reactions. In patients who have shown an immediate allergic reaction and who are negative to skin tests for PEG and polysorbates (6), compounds structurally related to PEG, desensitization with the same vaccine is proposed, according to the guidelines proposed by EAACI (7). We describe below two cases of asthma after the first COVID vaccine administration in which desensitization has failed.

Case 1

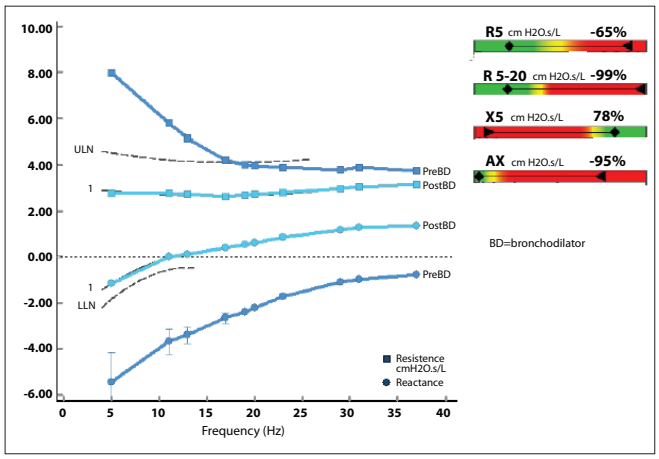
ML is a 60-year-old, nonsmoker woman, suffering from asthma in PET allergy (not present at home). In March 2020 after SARS CoV2 infection she developed an exacerbation of asthma treated with oral steroids. After this episode she started LABA/ICS therapy. In January 2021 she had immediate mild urticaria and asth-

ma (dyspnea and cough) after the first dose of Pfizer-BioNTech vaccine. The patient underwent skin tests to rule out allergy to the vaccine additives, with negative results. Subsequently she underwent desensitization. Asthma was in good control with LABA/ICS therapy, and Asthma Control Test (ACT) and oscillometry were normal. We performed desensitization starting with 0.05 mL of the 1:10 dilution of the vaccine and then with 0.05 ml – 0.1 ml – 0.15 ml of the undiluted vaccine every 20 minutes. She developed asthma at the last dose of the vaccine. The patient was subjected to oscillometry, which showed an increase in peripheral and central resistances and reactance, then she was treated with intravenous steroids and inhaled ICS/formoterol, with significant reversibility after administration of therapy (**figure 1**).

Case 2

FL is a 44-year-old professional nurse with atopic asthma to dust mites and grasses well controlled with daily low inhaled corticosteroid according to the 2020 Global Initiative for Asthma (GINA) guidelines approved at the time of the desensititazion. She has no known diagnosis of COVID-19 disease. In January 2021, a few minutes after the Pfizer-Biontech COVID-19 vaccine, she experienced a respiratory reaction (dry cough and a sensation of a lump in the throat) with biphasic trend. The PEG and polysorbate skin testing were negative. We carried out desensitization with Pfizer-BioNTech vaccine previously performing an asthma control test that indicated a well- controlled asthma, because lung function test was not available due to the COVID-19 pandemic. During the subsequent immunization in graded doses, she showed cough and tightness in the throat twenty minutes after the third dose (0.1 mL of the indiluted vaccine). The symptoms resolved after treatment with intravenous steroid and antihistamine. Desensitization was discontinued.

Figure 1 *- Oscillometry modification in case 1: the increase in peripheral and central resistances and reactance, and the significant reversibility after administration of therapy.*



Conclusions

No current research highlights that the COVID-19 vaccines worsen asthma symptoms. Not even all immediate reactions that occur in association with vaccines are true allergic reactions. This is described in a CDC report demonstrating that out of 175 possible severe allergic reactions, 86 (49%) were non anaphylactic allergic reactions (1). People with asthma, as with other vaccine recipients, may experience temporary side effects after getting the vaccine, like fever or flu-like symptoms, which can act as an asthma trigger. This could explain the failure of desensitization in the cases described above. We emphasize the importance of asthma stabilization in asthmatic patients who are subject to vaccination, particularly in those with severe asthma and who have a previous history of allergy. Patients who have developed asthma after the first dose of the vaccine should be monitored carefully when the second dose is given, despite negative skin tests for vaccine additives. Another chance is to consider administering an alternative vaccine. At the moment the limitation of diagnostics is due to the impossibility of carrying out tests with the vaccine in its entirety.

Conflict of interests

The authors declare that they have no conflict of interests.

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