Dear Editor,

MRNA COVID-19 vaccine anaphylactoid reactions to Omalizumab prevents...

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Omalizumab prevents anaphylactoid reactions to mRNA COVID-19 vaccine

Dear Editor,

Within the first days of initiating mass vaccination with the novel COVID-19 vaccines several anaphylactic reactions have been reported. We present two cases experiencing angioedema with or without urticarial rash after the first dose of the mRNA-1273 vaccine. Both patients tolerated the second vaccination after a pretreatment with the anti-IgE antibody omalizumab.

The first patient, a 27 years old woman with no known allergies, developed dyspnoea, throat tightness, lip and tongue swelling, and flushing within the first hour after administration of the first vaccination. After treatment with intravenous antihistamines and glucocorticoids, the symptoms resolved. The second case, a 31 years old woman, developed an urticarial rash and subsequently a swelling of tongue and upper eye lids 10 days after receiving the first dose of the vaccine (Fig. 1). The symptoms reoccurred during the period of 9 days but resolved after 7 days of treatment with oral glucocorticoids as well as oral antihistamines. The patient reported on no other allergies apart from a type IV-sensitization to nickel.

In both patients, serological quantifications of total IgE, specific IgE to aeroallergens and tryptase levels revealed no hints of pre-existing type I-sensitizations or mast cell activation disorders (Table 1).

After a washout period of >14 days upon cessation of systemic anti-allergic treatments, skin prick tests using residuals of the mRNA-1273 vaccine displayed no positive response (Fig. 1). In addition, flow-assisted basophil activation assays determining CD63 expression showed no sensitizations neither to polyethylene glycol (PEG) nor to the mRNA-1273 vaccine (Table 1).

Thus, we found no evidence of pre-existing or newly acquired hypersensitivities to the mRNA-1273 vaccine or its components explaining the reactions in these cases. Hence, the immunological mechanisms behind the anaphylactoid reactions remain unclear. Acute allergic reactions to the novel mRNA COVID-19 vaccines have been described based on self-reports. However, so far no type I-sensitization has been proven. Several publications reported on the efficacy of omalizumab, a recombinant humanized monoclonal anti-IgE antibody, in preventing hypersensitivity reactions even in cases without known triggers.

Against this background, both patients were pretreated with a single dose of 300 mg omalizumab 2 and 7 days, respectively, prior to the second vaccination. Neither patient experienced angioedema or urticarial rashes as immediate reactions after the second dose of the vaccine. The second patient showed a delayed reaction with fever and subsequent development of urticaria 8 days following the vaccination. However, this time the rash was by far less severe and thus no treatment with systemic glucocorticoids was required. Based on the clinical course and allergologic examinations, one could argue that the urticaria in the second case was most likely triggered by the delayed reactogenicity symptoms the patient experienced after the vaccination. Further, McMahon et al reported on urticarial rashes showing low second-dose recurrences. Hence, we cannot rule out that our second patient would have experienced less symptoms even without pretreatment with omalizumab.
To exclude any negative effect of omalizumab on the efficacy of the vaccination, the patients were tested for antibody titres: both exhibited high SARS-CoV-2 spike protein-specific antibody titres related to the vaccination (>384.00 BAU/mL on Euroimmun Anti-SARS-CoV-2-QuantiVac-ELISA) as well as moderate to high SARS-CoV-2 neutralizing antibody titres of 1:80 and 1:320, respectively, as determined by a serial dilution endpoint test in Vero cells (Table 1). Both patients were tested for SARS-CoV-2 nucleocapsid protein-specific antibodies beforehand using the SARS-CoV-2 IgG chemiluminescence microparticle immunoassay from Abbott to exclude an undetected infection prior to the vaccination.

Our two cases indicate that pretreatment with omalizumab could be a way of ensuring a safe and effective vaccination even after experiencing anaphylactoid reactions following the initial dose of a COVID-19 vaccine.

Acknowledgement
The patients in this manuscript have given written informed consent to publication of their case details.

Conflict of interest
SM reports personal fees and/or grants from Novartis, LEO Pharma, Almirall, AbbVie, Sanofi, UCB, Eli Lilly, Janssen Cilag, Milan and Pfizer, and BH reports personal fees and/or grants from Novartis, LEO Pharma, AbbVie, Sanofi, UCB, Eli Lilly, Janssen Cilag, Union Pharma and Pfizer. All COI are outside the present work. AS, SS, LM, OA and PA did not report any COI.
**Small vessel vasculitis related to varicella-zoster virus after Pfizer-BioNTech COVID-19 vaccine**

Dear Editor,

We read with great interest the article by Ackerman et al.\(^1\) regarding the occurrence of persistent maculopapular rash few hours after receiving the vaccine.\(^1\)

We herein report a case of atypical varicella-zoster virus skin infection inducing a small vessel vasculitis after first dose of Pfizer-BioNTech COVID-19 vaccine. An 84-year-old female patient, with medical history of chronic kidney disease and depressive disorder, received the first dose of Pfizer-BioNTech (Mainz, Germany) COVID-19 vaccine. Few hours later, she developed burning pain on the distal part of right leg and foot, followed by multiple non-confluent purpuric papules and vesicles in the same sites (Figs 1 and 2). Clinical examination did not show signs of systemic involvement and serum tests showed varicella-zoster virus (VZV) IgM and IgG antibodies positivity and high levels of liver enzymes (2N). Punch biopsy of right lower leg was performed and histopathologic examination showed intraepidermal spongiosis with acantholytic keratinocytes.

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**References**

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