Reply

To the Editor:

We thank Dikici and Özdemir for the comments on our recent case series of patients developing chronic urticaria (CU) following coronavirus disease 2019 (COVID-19) vaccination.[1] CU has been reported following infections and vaccinations.[2] In the context of COVID-19 vaccinations, this rare event has been reported in our own and other case series following mRNA vaccinations, although other vaccine types have also been implicated.[3]

We acknowledge some of the identified nomenclature concerns and agree that given the inclusion of chronic inducible urticaria, use of "chronic" rather than "chronic spontaneous" urticaria would have resulted in a more precise title. However, we do not think that the clarity of our key messages has been affected, especially given the specialist target audience for our article, who likely have familiarity with the terminology. Similarly, we expected this allergy audience to be familiar with our reference to 43 IU/L as the cut point of the total IgE level that has been suggested as differentiating between autoallergic and autoimmune CU phenotypes rather than serving as a normal value.[4]

The pathophysiology of CU is complex. Skin mast cells are activated by autoimmune or autoallergic mechanisms, and the exact relationship between how viruses, drugs, and vaccines can precipitate or aggravate CU is not fully understood. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection itself can trigger acute urticaria and exacerbations of chronic urticaria, and more recently, it has been reported to also trigger the onset of new CU.[5,6] It is therefore entirely reasonable that COVID-19 vaccination could similarly trigger a similar spectrum of acute and chronic urticarias. We agree that the varying latencies between vaccine exposure and CU onset may underpin differing mechanisms and levels of certainty around vaccination as the only inciting driver. Consistent with the available literature on CU, the high total IgE levels seen in the majority of our patients with CU are consistent with an autoallergic CU phenotype, and the observed levels suggest that vaccination may induce cross-reactive IgE autoantibodies against skin antigens. Patients with CU have significantly higher rates of atopy than in the general population, and we do not believe that the presence of CU among these patients is evidence against COVID-19 vaccination as the trigger for new-onset CU. In our opinion, it is equally likely that an atopic predisposition to make IgE antibodies to exogenous antigens may also mean a predisposition to have autoallergic processes following environmental or immune triggers such as infection or vaccination.[3] However, this small case series and the limited laboratory data are insufficient to draw strong conclusions. We support further research into how infections or vaccination trigger immunologic pathways resulting in CU. Furthermore, we particularly support further work regarding how mRNA vaccines, which represent a rapidly expanding new vaccine platform, may led to pathologic autoallergic antibodies in susceptible individuals.

DISCLOSURE STATEMENT

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