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CORRESPONDENCE

Reply to correspondence: Basophil reactivity to BNT162b2 in COVID-19 convalescence

We thank Perkins et al. for their comments[1] and acknowledge that further studies related to the basophil response are warranted.

Whether the reaction to vaccine components is likely due to the spike protein translated from mRNA, we have further evaluated the reaction to these proteins in some cases, and we have found positive basophil activation to protein S only in those with post-COVID-19 independently of the hypersensitivity reaction to the vaccine. Sampath et al. reviews some studies where patients who have recovered from SARS-CoV-2 infection have stable virus-specific memory B cells that recognize the spike or nucleocapsid proteins of the SARS-CoV-2 virus for at least eight months post-infection, and another study found that neutralizing antibody titers against the SARS-CoV-2 spike protein persisted for at least 5 months after infection. This information could explain why our patients who have suffered from COVID infection show positive BAT results to the vaccine and s-spike protein.[2] In fact, we observed that 3 out of 5 patients had positive BAT results to both, vaccine and s-spike protein. One of the 3 patients with positive BAT had suffered from COVID-19 infection. This information shows that around 33% of patients with post-COVID infection had positive BAT results to the vaccine and s-spike protein. These results were confirmed in controls since in the group of controls with post-COVID infection, 4 were positive to s-spike protein (40%). Interestingly, all these controls showed also positive results in BAT to BNT162b2 vaccine. Moreover, all controls who not suffered from COVID-19 showed negative results in BAT to both BNT162b2 vaccine and s-spike protein.

Alexandre Troelnikov et al. explained basophil reactivity in patients with PEG allergy,[3] this agrees with our results. Additionally, in our article, we also found basophil reactivity in patients with no allergic reaction to PEG, probably related to the SARS-CoV-2 infection.[4]

Thus, these results confirm our previous conclusion that positive results in BAT to the vaccine are somewhat related to a post-COVID-19 infection instead of an allergy.[4]

Alternatively, we did not find a reduction in the threshold for basophil activation or an increase in the spontaneous degranulation related to COVID-19 infection.

Indeed, we agree, and as Perkins G et al. indicate, there are case reports of urticaria and angioedema in patients with COVID-19 infection.[5] We have observed these cases in our clinical setting. Although the exact aetiology of COVID-19-related skin manifestations is still unclear, SARS-CoV-2 may behave like other viruses and initiate a state of mast cell activation, leading to histamine release. Moreover, another plausible explanation for the development of angioedema in these patients could be the excessive activation of the bradykinin pathway by angiotensin-converting enzyme 2, increasing vascular permeability and leading to angioedema. These mechanisms are also responsible for the skin manifestation after COVID-19 vaccination remain to be fully determined. Nevertheless, these patients have tolerated the 2nd dose of the vaccine and even continue experiencing urticaria episodes non-related to the vaccine, which is not in accordance with an IgE mechanism.

Moreover, it has been reported an effect of COVID-19 infection on basophils, reducing their number in the acute phase but increasing in the recovery phase.[6] On the other hand, as demonstrated by Rodriguez L et al.[7] circulating basophils can be associated with anti-CoV-2-IgG responses. Therefore, we could think that in the cases of subjects with post-COVID-19, the basophil response may also be related to an IgG mechanism.

Finally, we agree that further studies are necessary to elucidate the mechanisms involved in basophil responses to the vaccine and their relation to a post-COVID-19 infection, giving answers to why reactors to the vaccine tolerate the second dose.

CONFLICT OF INTEREST

None of the authors have any conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

M.L., JA.C., I.D, MH.S., I.A., C.M., and MJ.T. contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

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