

## CORRESPONDENCE

# Safely use of omalizumab during SARS-CoV-2 infection in patients with chronic spontaneous urticaria

To the Editor,

We read the recent article by Yildirim et al.<sup>1</sup> entitled 'Retrospective evaluation of patients with chronic spontaneous urticaria using omalizumab during the COVID-19 pandemic' with great interest. In this retrospective cohort -research article, Yildirim et al.<sup>1</sup> reported that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has impacted a substantial fraction of the chronic spontaneous urticaria (CSU) cases, and the data about using omalizumab (OMZ) during the coronavirus disease 19 (COVID-19) pandemic are limited. Their findings also have shown that omalizumab treatment in CSU cases during the COVID-19 pandemic does not increase the risk of SARS-CoV-2 infection and omalizumab can be utilized safely.<sup>1</sup> After reading this enlightening study, we also want to share our limited experience with SARS-CoV-2 infection and COVID-19 disease along with a case with CSU under omalizumab therapy for the last 4 years in the light of current literature.

In our outpatient pediatric allergy clinic, omalizumab treatment is given to a total of 11 patients with the diagnosis of CSU. Although the mean age of our patients who received omalizumab for CSU was 17.4 years; 8 (72%) were girl and 3 (28%) were boy. One of these patients, a 20-year-old girl, was found to have PCR test positivity for SARS-CoV-2 and received omalizumab treatment during COVID-19 infection. Consistent with this retrospective cohort study by Yildirim et al.,<sup>1</sup> our patient had the SARS-CoV-2 infection at home with mild symptoms without using any medication for COVID-19 as well as without having an exacerbation of CSU.

In addition to the fact that SARS-CoV-2 such as in Herpesvirus and Norovirus infections may trigger urticaria, the course of the COVID-19 disease was carefully followed in our case, which was also under the influence of monoclonal antibody therapy. COVID-19 might lead to the development of new-onset urticaria or exacerbation of pre-existing urticaria through activation of the mast cells and basophils directly or indirectly by the virus.<sup>1-5</sup> Kritas et al. evaluated mast cell role in SARS-CoV-2 infection and decided that the SARS-CoV-2 enters mucosal mast cells and excites them to secrete proinflammatory chemokines and cytokines (TNF- $\alpha$ , IL-1, IL-6, IL-33, and proteases), exacerbating available inflammation. Therefore, CSU might deteriorate during SARS-CoV-2 infection, as reported by some authors.<sup>6</sup> Furthermore, mast cells express the ectoprotease angiotensin-converting enzyme 2 required for SARS-CoV-2 binding,

and serine proteases, including TMPRSS2, are required for priming of the SARS-CoV-2 spike protein, thus defining a route by which mast cells could also become hosts for this virus.<sup>7</sup>

Omalizumab as a monoclonal anti-immunoglobulin E antibody is approved for use in patients with CSU resistant to antihistamine therapy. Although the data on the use of omalizumab treatment in SARS-CoV-2 infection are limited, both its effect on the course of urticaria and the effect of immunological mechanisms on the course of infection are of interest. Nevertheless, there is literature mentioning that omalizumab use diminishes inflammation by hindering proinflammatory cytokines and might even have antiviral effects. By affecting mast cells, omalizumab blocks the secretion of inflammatory mediators, for example, histamine and serine proteases besides proinflammatory cytokines e.g. IL-1, IL-6, and IL-33.<sup>8</sup> Gill et al.<sup>9</sup> also noticed that omalizumab restored type I interferon responses by reducing IgE receptors in dendritic cells to respiratory viruses, for example, rhinovirus and influenza. This helps to initiate a strong antiviral immune response to inhibit SARS-CoV-2 replication and even limit the spread of infection in the early stage of the disease.<sup>9-11</sup>

Several observational studies indicate that treatment with biologics such as omalizumab was not associated with a higher risk of SARS-CoV-2 infection, COVID-19 severity, or a more severe clinical course of CSU.<sup>1,8,10</sup> There are also publications in the literature suggesting that omalizumab can be tried for the treatment of urticaria and vascular lesions caused by COVID-19 patients and that the risk of severe course can be reduced by inhibiting pro-inflammatory mediators.<sup>10</sup> We aimed to benefit from the effect of omalizumab on both preventing exacerbation of urticarial lesions and alleviating the course of acute infection by administering omalizumab treatment to our patient during the beginning of SARS-CoV-2 infection.

This case is one of the cases to report a favorable outcome of omalizumab in a patient having CSU with COVID-19, without deterioration of clinical status and excellent response.<sup>1,4</sup> This case report further supports the safety of omalizumab use in allergic diseases, especially CSU, asthma, and allergic bronchopulmonary aspergillosis during the COVID-19 pandemic.<sup>12-16</sup> Similarly, it has been suggested that continuing treatment with omalizumab is advisable in patients affected with mild-to-moderate COVID-19; in the severe form of the disease, prolongation of the dosing interval or treatment interruption was recommended in a position paper.<sup>17</sup>

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chronic spontaneous urticaria, COVID-19, omalizumab, SARS-CoV-2

**CONFLICT OF INTEREST**


No conflict of interest.

**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**INFORMED CONSENT**

The patient in this manuscript has given written informed consent to publication of these case details. Responsibility for all opinions, conclusions, and data interpretation lies with the authors.

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