COVID-19 infection in chronic spontaneous urticaria treated with omalizumab: two case reports

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Dear Editor,

Chronic spontaneous urticaria (CSU) is an inflammatory skin disease characterized by itchy pomphi associated or not with angioedema and occurring with daily or near-daily frequency for more than six weeks.[1] It is divided into two entities, an autoimmune form determined by the presence of immunoglobulin (IgG) specific for FcεRI receptors on tissue mast cells and circulating basophils, and an idiopathic form.[1] It affects 0.5-1% of the world's population and has a major impact on patient's quality of life.[1] Several environmental factors can induce flare-ups, the most important of which include drugs (especially nonsteroidal anti-inflammatory drug), infections, and foods.[1] To date, the first-line therapy is with a second-generation anti-H1 antihistamine at the standard dose; if there is no response after 2-4 weeks, it is possible to increase the dosage to 4 times the standard dose. Treatment with systemic glucocorticoids is indicated only for short periods in severe flare-ups.[1] In case of therapeutic failure, in patients older than 12 years, it is possible to use an immunomodulating biological drug called omalizumab (OMZ), which is a humanized recombinant IgG1 monoclonal antibody able to bind and neutralize IgE but also to indirectly reduce the expression of the FcεRI receptor on tissue mast cells and circulating basophils.[1,2] It is a safe medication with few side effects and can control the disease in many patients. Studies have shown that it does not increase the risk of COVID-19 or other airway infections.[3,4] Current SARS-CoV-2 infection represents a major healthcare challenge, especially in managing patients with chronic disease. The impact and safety of 3biological treatment and the course of CSU during SARS-CoV-2 infection are poorly understood. We want to further clarify these aspects by reporting two cases of COVID-19 infection in patients with CSU treated with OMZ.

Case 1: a 22-year-old woman with a history of CSU for three years was treated with little success with an anti-H1 second-generation antihistamine (bilastine) with a dosage up to 4 times the standard. She did not suffer from other pathologies and, over the years, has made several cycles of therapy with systemic corticosteroid (deltacortene) with partial benefit; the symptoms, in fact, always relapsed when discontinued. Since antihistamines did not control the clinic, it was decided to start treatment with OMZ, an injection of 300 mg every four weeks. The score at baseline of urticaria activity over seven days (UAS7) was 26; this score reduced to 0 after only one month. After two months, the patient contacted us saying she had become COVID-19 positive and developed a paucisymptomatic form with moderate fever, pharyngodynia, ageusia, and anosmia. She had not had a COVID-19 vaccine. In agreement with the data already available in the literature,[5,6] it was decided to continue with OMZ therapy. The family doctor prescribed the patient antibiotic coverage (azithromycin) and low-dose cortisone (betamethasone). Symptoms resolved within three days, and the patient never developed urticarial lesions. Four months after the resolution, she still maintained clinical remission.

Case 2: a 42-year-old man with seasonal allergic rhinoconjunctivitis and SCU for 1.5 years uncontrolled with second-generation anti-H1 antihistamine (loratadine) at four times the standard dosage and cycles of systemic corticosteroid (deltacortent), it was decided to start OMZ therapy with 300 mg injections every four weeks. The score at baseline of 7-day urticaria activity (UAS7) was 34; this score reduced to 0 after two months. Two months before OMZ initiation, the patient had double-dosed with the SARS-CoV-2 vaccine Comirnaty - BioNTech/Pfizer, when clinical worsening of UAS occurred. Despite the vaccination, three months after the first dose of OMZ, he contacted us reporting being positive for COVID-19 with the development of high fever, asthenia, cough, pharyngodynia, and headache. In this case, we decided to continue the therapy with OMZ. The patient took only

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paracetamol, and within five days, the symptoms completely resolved without the appearance of pomphoid lesions. At three months after the resolution, he still maintained clinical remission.

These two cases provide additional evidence to that already found in the literature on the safety of OMZ treatment in patients with mild-to-moderate COVID-19.[5,6] Both of our patients did not experience worsening of the infection, which resolved within a few days. However, in patients with severe infection, given the few studies available, discontinuation of the drug or reduction in the frequency of injections is recommended, seven but such a procedure could be wrong and unnecessary, even in light of recent work that hypothesizes an even protective role of OMZ against COVID-19 disease.[8] We would also like to point out that there was no exacerbation of pomphoid lesions during the infection. However, the literature reports a tendency to worsen the SCU during infection with COVID-19, especially in severe forms.[9] This is probably attributable to the protective action of OMZ, which, if possible, should be maintained to ensure freedom from disease for the patient.

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