Correspondence

Chronic spontaneous urticaria exacerbation in a patient with COVID-19: rapid and excellent response to omalizumab

Dear Editor,

During the COVID-19 pandemic, physicians may not feel comfortable managing dermatological conditions with biological agents. No literature describing behavior of pre-existing chronic spontaneous urticaria (CSU) in COVID-19 patients has been reported up to June 20, 2020, in PubMed.

We present a 54-year-old female with CSU and angioedema since September 2019. Her medical history was negative for use of nonsteroidal anti-inflammatory drugs or analgesics, and atopic diathesis (asthma, rhinitis, or dermatitis). Full urticaria work-up including C-reactive protein, serum IgE, complete blood count, D-dimer, thyroid, renal, and hepatic profile were within normal limits. At initial visit, uriticaria activity score (UAS) = 6 and urticaria control test (UCT) = 0, demonstrating severe CSU. She had previously failed levocetirizine 15 mg daily. After starting bilastine 80 mg daily, CSU activity decreased to UAS7 (UAS 7 days score = 06 and UCT = 12). In March 2020, after symptoms of fever, sore throat, cough, fatigue, anosmia, and ageusia, and a positive nasopharyngeal swab for SARS-CoV-2 PCR, she was diagnosed with COVID-19. Shortly after symptom onset, she noticed exacerbation of urticaria and angioedema (UAS7 = 42 and UCT = 6). Peripheral O2 saturation was 95%, and thorax computed tomography (CT) demonstrated mild thickened lobular septum (Fig. 1a). She received a 7-day course of amoxicillin-clavulanate, and follow-up CT showed bilateral lung involvement with ground-glass opacities (Fig. 1b).

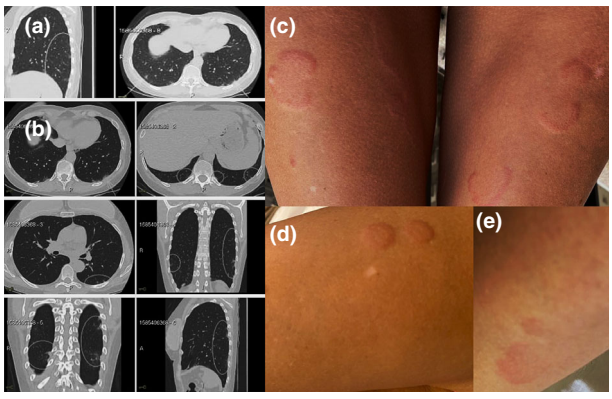

Figure 1 Chest computed tomography (CT) and urticaria lesions aggravated during COVID-19. (a) First thorax CT images without significant findings on March 18, 2020. (b) Second thorax CT images showed ground-glass opacities (GGO) in both lungs in peripheral pattern. (c) Several urticaria lesions involving the thighs. (d) Urticaria lesions involving upper extremity. (e) Urticaria lesions on lateral aspect of the thigh

During COVID-19, her CSU was refractory to deflazacort 30 mg/day, bilastine 80 mg/day, and ketotifen 2 mg/day (Fig. 1c–e), when anosmia and ageusia were still present. Omalizumab 300 mg subcutaneously was initiated, with complete resolution of urticaria and itching after 72 hours. Improvement of all COVID-19 symptoms was also noted. She remained on bilastine 80 mg/day and omalizumab 300 mg every 4 weeks, with a total of three injections, without new flares. (Fig. 2).

This case demonstrates the treatment challenge of patients with aggravation of their cutaneous condition during SARS-CoV-2 infection as well as the unknown response to biological agents in this setting.

Viral infections can worsen CU or represent a trigger to acute urticaria.[1] In a systematic review of association between urticaria and viral infections, Imbalzano *et al.*[1] concluded that CU was aggravated by Herpesvirus and Norovirus infections, the latter known for causing outbreaks in schools, nursing homes, and hospitals.[2] In CU, inflammation of the gastrointestinal tract, as occurs during Norovirus infections,[2] leads to T-cell activation and subsequent induction of inflammatory mediators (interferon, IL-1, IL-2, and TNF-alpha).[2] Skin mast cells (MCs) have receptors for TNF-α and IL-1. This milieu of cytokines then induces MC degranulation and urticaria.

After exposure to SARS-CoV-2, median incubation period is 5 days.[3] Fever starts at onset of clinical disease and can last up to 3 weeks.[3] At this point, clinical symptoms start to resolve; however, some patients may develop Acute Respiratory Distress Syndrome (ARDS) requiring mechanical ventilation. In our

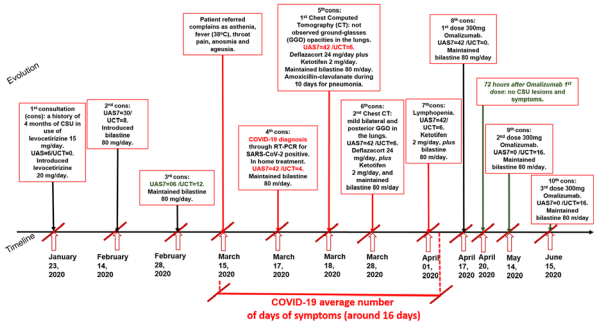

Figure 2 Timeline of CSU progression in our patient since first visit, development of COVID-19, CSU aggravation, and omalizumab use

patient, lung involvement was mild, and the COVID-19 course was not severe.[3]

Alizadeh *et al.*[4] demonstrated that omalizumab decreases FcεRI expression on the surface of basophils, plasmacytoid, and myeloid dendritic cells (DCs) in CSU patients, leading to increased interferon production.

Kritas *et al.*[5] reviewed MC involvement in coronavirus infection and concluded that the virus invades mucosal MCs and stimulates them to release proinflammatory cytokines (TNF-α, IL-1, IL-6, IL-33, and proteases), aggravating the inflammatory state. In this clinical proinflammatory scenario, CSU may worsen during COVID-19, as experienced by our patient.

This is the first case to report a favorable outcome of omalizumab in CSU in a patient with COVID-19, without deterioration of clinical status and excellent response.

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