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SARS-CoV-2 infection in a psoriatic patient treated with IL-23 inhibitor

Editor

Since December 2019, an outbreak of 2019 novel coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been spreading worldwide. This has risen concern among patients undergoing biologics and physicians who administer them, as far as the possible increase of incidence and severity of COVID-19 in this delicate population concerns.[1]

We describe the case of a 32-year-old woman, affected by psoriasis and psoriatic arthritis since 18 years, previously treated with several conventional and biologic drugs, including cyclosporine, methotrexate, infliximab, etanercept, adalimumab, secukinumab and ixekizumab. She had no other medical conditions.

In April 2019, she developed a severe Crohn's disease while taking ixekizumab. Therefore, she switched to ustekinumab, with improvement of Crohn's disease but a worsening of both psoriasis and psoriatic arthritis. On 6th November, we added methotrexate 10 mg/week, which was further increased to 25 mg/week after 4 weeks because of an unsatisfactory response. On 23rd December, since psoriasis was still worsening, we switched ustekinumab to guselkumab, while maintaining methotrexate at 25 mg/week.

On February 26, after two injections of guselkumab the patient showed a marked improvement of psoriasis and arthritis.

On February 29, she went out for dinner with some friends and, 2 days later, one of them was discovered to be affected by COVID-19. On March 4, she had mild rhinorrhea and fever (37.4°C), and the next day, she was tested positive for SARS-CoV-2.

The day after the body temperature lowered to 36.3°C, and the rhinorrhea was still mild. We advised her to interrupt methotrexate and to postpone the next guselkumab injection, which was originally scheduled for March 16.

In the following days, the body temperature never rose above 36.5°C and she never developed sore throat, cough, shortness of breath or other symptoms of the infection. Her blood tests revealed increased erythrosedimentation rate (120 mm/h), C-reactive protein (4.76 mg/dL), D-dimer (381 μg/L) and fibrinogen (701 mg/dL). All the other parameters were normal.

On March 13, the rhinorrhea subsided. On March 20, RT-PCR was still positive for SARS-CoV-2. On March 28 and March 30, the tests resulted negative, meeting the criteria to be considered successfully healed.

In COVID-19, inflammatory cytokines assume a double role: firstly, they stimulate the activation of an effective immune response, while later they can mediate the development of an exaggerated systemic inflammation. This 'cytokine storm' is both ineffective towards the pathogen and detrimental for the body, eventually leading to acute respiratory distress syndrome and potentially to death.[2]

Available data suggest that the adaptive response towards SARS-COV-2 develops mainly in a Th1-polarized fashion, being CD8+ cytotoxic cells the main effectors of the antiviral response.[2] With the progression of the disease, the worsening of clinical conditions is associated to a marked increase in proinflammatory cytokines, such as IL-1, IL-6 and TNF-alfa.[2,3]

Interestingly, the IL-23/IL-17 axis does not seem to be pivotal in an effective immune response. On the contrary, observations carried on both coronavirus and non-coronavirus pneumonia patients show that an aberrant Th17 polarization may correlate with a worse outcome.[4,5]

Based on these observations, a clinical trial investigating the use of ixekizumab associated with antiviral therapy is currently ongoing in China as a possible treatment for COVID-19 infection.[6]

In conclusion, we reported the first case of COVID-19 infection in a psoriatic patient treated with a biologic. The outcome of this case and data from currently available literature suggest that IL-23/IL-17 axis inhibition might not be detrimental in the setting of COVID-19 infection. Further data are needed to support this hypothesis.

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The patient in this manuscript has given written informed consent to publication of her case details.

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LETTERS TO THE EDITOR

Ocular surface disease during dupilumab treatment in patients with atopic dermatitis, is it possible to prevent it?

Dear Editor,

Atopic dermatitis (AD) is the most common inflammatory skin disease that affects up to 20% of children and 2–5% of the adult population. This disorder can have a dramatic impact on the quality of life, in fact, negatively affects sleep, productivity, mood and quality of life. Recently, encouraging results have been obtained with the use of dupilumab. This drug is a human monoclonal antibody directed against the shared α subunit of the interleukin (IL)-4 and IL-13 receptor approved for adult patients affected by moderate-to-severe AD.[1,2]

Clinical trials and real-life data have demonstrated efficacy and safety of this treatment; however, trials have also shown an increased incidence of conjunctivitis.[3] Indeed, it would be more correct to use the term of ocular surface disease (OSD), an umbrella term that includes all types of dupilumab-induced ocular inflammation including dry eye, conjunctivitis and keratitis. Interestingly, the incidence of OSD is not observed in patients with asthma, chronic sinusitis and eosinophilic esophagitis treated with Dupilumab.[4] It was hypothesized that dupilumab may have different effects on AD, or that this may be due to properties specific to the eye; periocular dermatitis has also been attributed to contact allergen hypersensitivity due to dupilumab induced increased of T helper 1 response. Another observation, consider the possibility that Demodex mites may prosper due to the decreased IL-4 and IL-13 levels of ocular cytokines,[5] leading to IL-17-mediated inflammation and a disease similar to ocular rosacea. However, IL-17 is decreased in dupilumab-treated patients and the disease course of conjunctivitis is too short in comparison with ocular rosacea. Moreover, blocking α subunit of the IL-4 receptor causes increased systemic bioavailability of free IL-4 and IL-13. This maybe causes inflammatory symptoms whether by stimulating the CD40-dependent IgE production via B cells or by activating the IL-13 R alpha 2 receptor that has not been blocked by dupilumab or both.[6] Why OSD occurs exclusively in patients with AD remains unclear; however, some authors have found, through conjunctival biopsies, the decreased density of intraepithelial goblet cells suggesting that OSD occurs secondary to tear film alteration and subsequent conjunctival irritation.[7] Based on these observations, we hypothesized that the use of artificial tears could prevent the occurrence of ocular complications.

Since February 2019, we have observed 30 adult patients with severe AD undergoing dupilumab treatment. These patients received the drug as recommended dosage, an initial dose of 600 mg followed by 300 mg injected every other week. During the first administration of the monoclonal antibody, patients were instructed to instil artificial tears, one drop per eye two times a day, and they were advised to avoid too dry environments and abuse of smartphones or similar devices. After 6 months of treatment, nobody of the patients examined reported ocular symptoms or the appearance of conjunctivitis and keratitis. It should be noted that among the patients they were not present visual display terminal workers and contact lens users.

Conjunctivitis and other ocular complications that develop after the administration of dupilumab for AD may be severe enough to necessitate stopping the therapy, indicating the importance of early prevention. Surely, our experience is limited due to the small number of patients examined, but it would be advisable to try to gather everyone's experiences, and create an *ad hoc* protocol, possibly in collaboration with ophthalmologist specialists, to prevent the onset of this worrying complication.

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