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# Recurrent COVID-19 in a patient with ulcerative colitis on vedolizumab therapy

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**Abbreviations:**

IBD = inflammatory bowel disease

COVID-19 = Coronavirus Disease 2019

TNF = Tumour Necrosis Factor

IL 12/23 = interleukin-12/23

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

ACE2 = angiotensin I converting enzym 2

TMPRSS2 = transmembrane serine protease 2

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Dear editor,

Biological therapy seems not to lead to an increased risk of severe COVID-19 outcomes in IBD patients, moreover some may even have a protective effect.[1] The influence of these medications on a possible re-infection is, however, not yet determined.

We present a case of a 28-year-old Caucasian female with a medical history of ulcerative colitis for which she is treated with 300mg vedolizumab every 8 weeks. During ongoing clinical remission, she had an unexpected elevated fecal calprotectin of 1037 ug/g on July 31, 2020. On August 5 she developed a sore throat, runny nose and fatigue and the diagnosis COVID-19 was confirmed on August 7 by a positive polymerase chain reaction on a nasopharyngeal swab. Her symptoms disappeared after 5 days and she had a negative swab on August 14. On October 10 she developed diarrhea, nausea, coughing, sneezing, headache, myalgia, anosmia and dysgeusia but her nasopharyngeal swab tested negative on October 11. Due to a worsening of symptoms she underwent a second swab on October 17 which now tested positive.

It is unclear whether this second episode is caused by prolonged viral shedding or by a re-infection, especially since serological antibody testing or viral genome sequencing was not performed. However, given the clinical course and duration between positive tests the latter seems most likely. One could speculate that an altered expression of angiotensin I converting enzym 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) in the gut of our patient due to vedolizumab or subclinical inflammation may have played a role.

The entry of SARS-CoV-2 into target cells is conducted by the binding of the virus to the ACE2 receptor, which is afterwards cleaved by TMPRSS2 to induce cell entry.[2] IBD disease activity may alter the expression, leading to an elevated colonic and rectum ACE2 and TMPRSS2 expression but also a decrease of ileal ACE2 expression.[2, 3] Although contradicting results, demonstrated by a downregulation of ACE2, were also reported.[4]

Medication may possibly influence the expression as well. Studies demonstrated that post-infliximab there is a decrease in colonic ACE2 without modulation of TMPRSS2 expression, while ileal ACE2 expression significantly increased.[2, 3] Although not much is known about the influence of vedolizumab on the expression, it was demonstrated that during treatment patients had lower levels of ACE2 and increased expression of TMPRSS2.[4] Contradictory to anti-TNF treatment, ACE2 expression did not significantly change post-vedolizumab .[2]

Overall the effect of both inflammation and vedolizumab on ACE2 and TMPRSS2 expression is complex and not completely elucidated but one could hypothesize that an altered gene expression, caused by inflammation and vedolizumab therapy, could have made our patient more susceptible for re-infection. Although larger studies are needed to confirm or invalidate our speculation.

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**Conflicts of interest:**

FC, PW and HB have nothing to declare. NdB has served as a speaker for AbbVie and MSD and has served as consultant and principal investigator for TEVA Pharma BV and Takeda. He has received a (unrestricted) research grant from Dr. Falk, TEVA Pharma BV, MLDS and Takeda

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**Authors contribution**

FC wrote the first draft of the manuscript. NdB, PW and HB critically revised the manuscript. All authors approved the final version of the article, including the authorship list.

**Data availability Statement**

*The data underlying this article are available in the article*

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