

SARS-CoV-2 as a Trigger for De Novo Ulcerative Colitis

Key Words: inflammatory bowel disease, ulcerative colitis, SARS-CoV-2, epidemiology

To the Editor,

It has been thought that ulcerative colitis (UC) may be triggered by environmental factors, such as infections, in genetically susceptible patients.¹ We report on a patient with de novo UC onset after SARS-CoV-2 infection.

In May 2020, a nonsmoking male patient aged 55 years with an uneventful medical history was diagnosed with COVID-19 pneumonia. After treatment with steroids, azithromycin, and heparin, inflammatory markers rapidly normalized; 24 days later, two consecutive swabs resulted negative and he was discharged. One month later, he was completely asymptomatic, showing high antispikes antibody titers (IgG, 89.4 AU/mL).

In August, the patient developed abdominal pain and diarrhea. Shortly afterward, his symptoms worsened with severe abdominal pain and chronic bloody diarrhea (15 bowel movements per day). In September 2020, he was admitted to our gastroenterology department. After ruling out infections, including SARS-CoV-2, a diagnosis of de novo UC was made on the basis of bowel sonography (Figs. 1A, B), endoscopy (Figs. 1C, D), and histology (Figs. 1E, F).

Although SARS-CoV-2 infection most commonly affects the respiratory tract, it also causes gastrointestinal symptoms.² In fact, the gastrointestinal tract may be an extrapulmonary site for virus replication, leading to the deregulation of the gut–liver axis in these patients with SARS-CoV-2 infection.³ The angiotensin-converting enzyme 2 (ACE2) receptor is considered the key used by SARS-CoV-2 to enter the host³: Highly expressed in both the respiratory and gastrointestinal tracts, ACE2 plays a pivotal role in directing intestinal inflammation and microbiota.³ Through these mechanisms, SARS-CoV-2 alters the gut microbiota, leading to a reduction in *Bifidobacterium*, *Lactobacillus*, and *Eubacterium* and to an increase in *Corynebacterium* and *Ruthenibacterium*²: all these SARS-CoV-2-induced modifications in the gut microbiota reflect those described in patients who develop UC. Similarly, the overexpression of ACE2 induced by SARS-CoV-2 has been associated with increased colonic inflammation in UC.³

Therefore, we can speculate that SARS-CoV-2 infection, acting on ACE2 expression and gut microbiota composition in genetically susceptible patients, could be a trigger for de novo UC, as described in our patient. Recently, 2 patients with UC onset during SARS-CoV-2 infection have been reported.⁴ ⁵ Our patient had neither a significant history of intestinal disease nor gastrointestinal symptoms suspicious for inflammatory bowel disease before his symptoms appeared. Furthermore, he did not experience gastrointestinal symptoms during his SARS-CoV-2 infection, thus making previously

undiagnosed inflammatory bowel disease improbable.

In conclusion, several pathogenetic mechanisms could potentially lead to UC onset after SARS-CoV-2 infection, including ACE2 overexpression and gut microbiota alterations. Clinicians will need to pay close attention to the appearance of red flags in patients with a previous SARS-CoV-2 infection.

Nicola Imperatore, MD,*^{ID}

Raffaele Bennato, MD,*

Alfredo D'Avino, MD,[†]

Giovanni Lombardi, MD,* and

Francesco Manguso, MD*

From the *Gastroenterology and Endoscopy Unit, AORN Antonio Cardarelli, Naples, Italy; [†]Pathology Unit, AORN Antonio Cardarelli, Naples, Italy

Address correspondence to: Nicola Imperatore, MD, Gastroenterology and Endoscopy Unit, AORN Antonio Cardarelli, Via Cardarelli 9, 80131, Naples, Italy (nicola.imperatore@alice.it).

ACKNOWLEDGMENTS

The data underlying this article will be shared on reasonable request to the corresponding author.

REFERENCES

- Mann EA, Saeed SA. Gastrointestinal infection as a trigger for inflammatory bowel disease. *Curr Opin Gastroenterol*. 2012;28:24–29.
- Mohandas S, Vairappan B. SARS-CoV-2 infection and the gut–liver axis. *J Dig Dis*. Published online October 24, 2020. doi: [10.1111/1751-2980.12951](https://doi.org/10.1111/1751-2980.12951).
- Xiao F, Tang M, Zheng X, et al. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology*. 2020;158:1831–1833.e3.
- Calabrese E, Zorzi F, Monteleone G, et al. Onset of ulcerative colitis during SARS-CoV-2 infection. *Dig Liver Dis*. 2020;52:1228–1229.
- Taxonera C, Fisac J, Alba C. Can COVID-19 trigger de novo inflammatory bowel disease? *Gastroenterology*. Published November 19, 2020. doi: [10.1053/j.gastro.2020.11.026](https://doi.org/10.1053/j.gastro.2020.11.026).

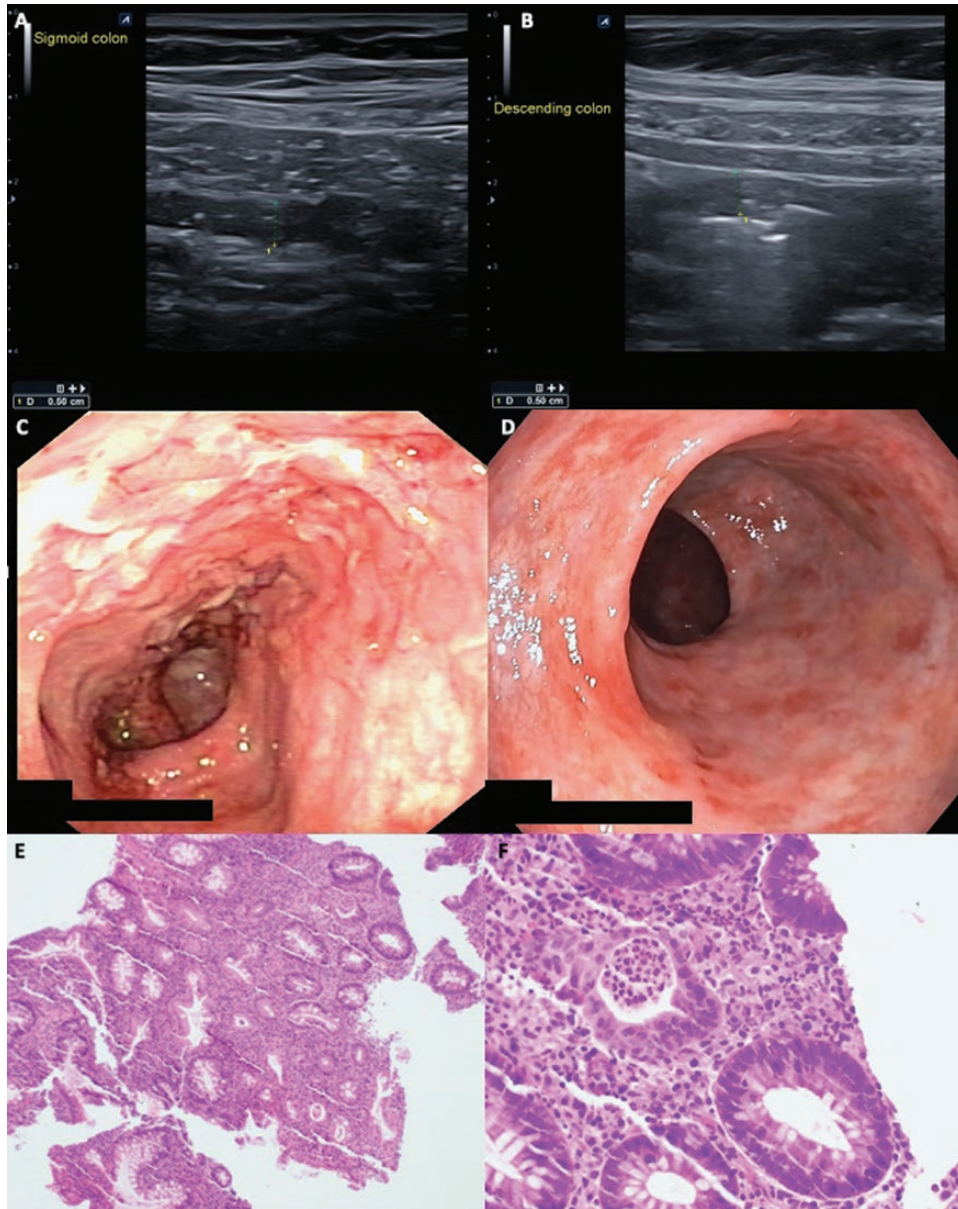


FIGURE 1. Small bowel ultrasound showing increased sigmoid (A) and descending (B) colon thickness. Endoscopic view showing an extensive colitis with ulcerations, erosions, mucosal friability, and spontaneous bleeding at rectosigmoid junction (C) and descending colon (D). Histopathology showing active inflammation with cryptitis and crypt abscesses, crypt architectural distortion, and ulcerations (E-F).