Infliximab for severe ulcerative colitis and subsequent SARS-CoV-2 pneumonia: a stone for two birds

Cristina Bezzio[1], Gianpiero Manes[1], Francesco Bini[2], Lucienne Pellegrini[1], Simone Saibeni[1]

[1]Gastroenterology Unit, Rho Hospital, ASST Rhodense, Rho, Italy

[2]Pneumology Unit, Garbagnate Milanese Hospital, ASST Rhodense, Garbagnate Milanese, Italy

Word count: 575

Keywords: COVID-19, coronavirus, inflammatory bowel disease, therapy, surgery

Abbreviations: COVID-19: coronavirus disease 2019; IBD: inflammatory bowel disease; CRP: C-reactive protein; SARS-CoV-2: severe acute respiratory syndrome corona virus 2; IL6: interleukin 6; CT: computed tomography

Corresponding author: Cristina Bezzio, MD, PhD

Gastroenterology Unit, Rho Hospital, ASST Rhodense

Corso Europa 250, I-20017, Rho (MI), Italy

Tel.: +39-02-99430-3264

Fax: +39-02-99430-3271

e-mail: cribezzio03@yahoo.it

We read with interest the article by Neurath (1) about the potential relationships between immunomodulating drugs for Inflammatory Bowel Disease (IBD) and COVID-19 (coronavirus disease 2019). The infection can cause pneumonia, which in some cases leads to acute respiratory distress syndrome with multiorgan failure. These life-threatening cases are attributable to a strong upregulation of cytokine production, known as “cytokine storm syndrome” (2). This is why anticytokine therapies have been proposed for this condition (3). However, so far, empirical evidence supporting the use of such therapies is lacking.

Here, we report the case of a 36-year-old man who was admitted to our hospital for a severe recurrence of ulcerative colitis.

At admission, he had been taking mesalazine in both oral and topical formulations and he reported up to 12 bowel movements with blood. Laboratory tests showed mild normocytic anemia (Hb, 12.3 g/dl), neutrophilic leukocytosis (neutrophils, 9420/μL), increased C-reactive protein (CRP) (17.1 mg/dL; normal values <0.5 mg/dL) and hypoalbuminemia (3.2 g/dL). Colonoscopy shown widely ulcerated mucosa, and a histological exam confirmed severely active ulcerative colitis. Chest and abdominal radiographs were normal. Intravenous methylprednisolone (60 mg/day), fluid replacement and anti-thrombotic prophylaxis with low-molecular-weight heparin were started. Stool culture, Cl. difficile toxin assay, and one nasopharyngeal swab test for SARS-CoV-2 were negative. Screening for infections, as recommended prior to prescribing biological therapies, was negative.

After 5 days of intravenous methylprednisolone, the patient’s general wellbeing and clinical conditions had slightly improved and CRP levels had dropped to 0.95 mg/dL. A proctosigmoidoscopy excluded cytomegalovirus infection. At this point, rescue therapy would have been appropriate (4), but the patient developed fever, dyspnea and cough. Laboratory tests showed the return of high CRP levels (3.98 mg/dL). High-resolution CT showed bilateral patchy ground-glass opacities, indicative of severe interstitial pneumonia (**Figure 1A**). A repeat nasopharyngeal

swab tested positive for SARS-CoV-2, and steroid therapy was tapered and moved to oral administration. We assessed IL-6 serum levels, which resulted abnormally high (37.4 pg/mL; normal values, 0-7 pg/mL) (5).

For the ulcerative colitis, we considered medical or surgical option. Surgery seemed contraindicated in a patient with COVID-19, which could complicate the postoperative course and be potentially fatal (6). So, we opted for infliximab at the dose of 5 mg/kg, also because our recent study found no association between the use of biological therapies and poor outcomes of IBD patients and COVID-19 (7).

After 7 days on infliximab, the patient's intestinal symptoms and general well being had markedly improved. High-resolution CT showed a clear improvement with reduced extent and density of the ground-glass opacities (**Figure 1B**). Laboratory tests indicated a normalization of CRP (0.12 mg/dL) and a drop of IL-6 levels to 15.9 pg/mL; two consecutive nasopharyngeal swab tests for SARS-CoV-2 were negative. The patient was discharged in good clinical condition, with 2 bowel movements without blood in the stools. The scheduled second infusion of infliximab has been performed and in few days he will complete induction regimen.

This is the first case of an adult patient with severe ulcerative colitis and COVID-19 pneumonia who was successfully treated for both conditions with infliximab. A similar case has been reported in a pediatric patient with active Crohn's disease and multisystem inflammatory syndrome related to COVID-19 (8).

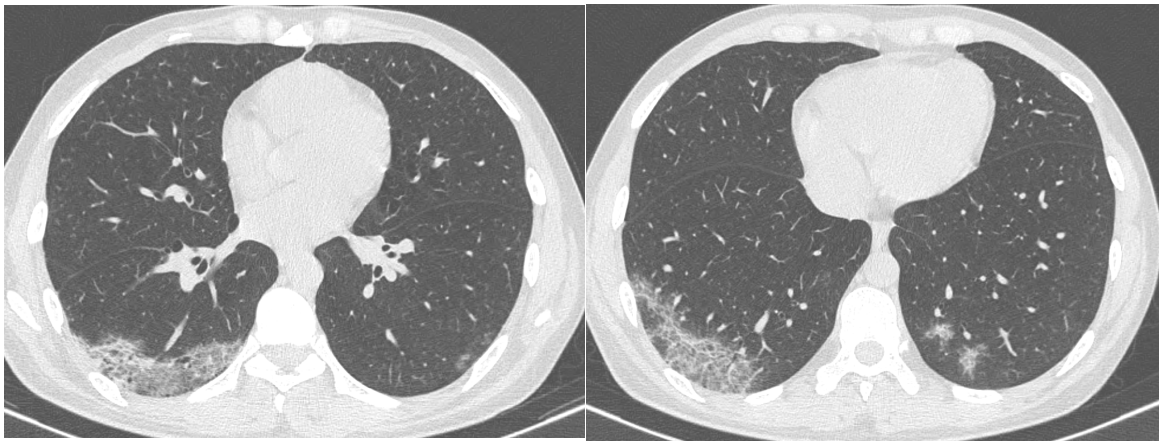
The improvement of pulmonary symptoms suggests that anti-TNF alpha agents may be an effective therapy for COVID-19. Furthermore, the positive outcome is a reassuring message for clinicians considering the initiation or continuation of anti-TNF alpha therapy in IBD patients with active disease and COVID-19.

REFERENCES

1) Neurath MF. Covid-19 and immunomodulation in IBD. Gut. 2020 Apr 17:gutjnl-2020-321269. doi: 10.1136/gutjnl-2020-321269. [Epub ahead of print]
2) Henderson LA, Canna SW, Schulert GS, et al. On the alert for cytokine storm: Immunopathology in COVID-19. Arthritis Rheumatol. 2020 Apr 15. doi: 10.1002/art.41285 [Epub ahead of print]
3) Perricone C, Triggianese P, Bartoloni E et al. The anti-viral facet of anti-rheumatic drugs: lessons from COVID-19. J Autoimmun. 2020 Apr 17:102468. doi: 10.1016/j.jaut.2020.102468. [Epub ahead of print]
4) Harbord M, Eliakim R, Bettenworth D, et al.; European Crohn's and Colitis Organisation [ECCO]. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 2: Current Management. J Crohns Colitis. 2017;11: 769-84.
5) Cunningham L, Kimber I, Basketter DA, et al. Why judiciously timed anti-IL 6 therapy may be of benefit in severe COVID-19 infection. Autoimmun Rev. 2020 May 4:102563. doi: 10.1016/j.autrev.2020.102563. [Epub ahead of print]
6) Aminian A, Safari S, Razeghian-Jahromi A et al. COVID-19 outbreak and surgical practice: unexpected fatality in perioperative period. Ann Surg. 2020 Mar 26. doi: 10.1097/SLA.0000000000003925. [Epub ahead of print]
7) Bezzio C, Saibeni S, Variola A et al. Outcomes of COVID-19 in 79 patients with inflammatory bowel disease in Italy: an IG-IBD study. Gut 2020, in press. doi: 10.1136/gutjnl-2020-321411 [Epub ahead of print]
8) Dolinger MT, Person H, Smith R, et al. Pediatric Crohn's Disease and Multisystem Inflammatory Syndrome in Children (MIS-C) and COVID-19 Treated with Infliximab. J Pediatr Gastroenterol Nutr 2020 May 22. doi: 10.1097/MPG.0000000000002809. Online ahead of print.

Figure 1: Transverse High Resolution CT scans of the chest of a patient with ulcerative colitis and COVID-19. (A) At the onset of symptoms of COVID-19, CT shows patchy ground-glass opacities affecting the subpleural lung parenchyma bilaterally, indicating interstitial pneumonia. (B) After 10 days (7 days after Infliximab therapy), CT shows a reduced extent and density of the ground-glass opacities.

A)



B)