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

We read with interest the article by Neurath[1] about the potential relationships between immunomodulating drugs for IBD and COVID-19. 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 anaemia (haemoglobin, 123 g/L), neutrophilic leucocytosis (neutrophils, 9420/μL), increased C reactive protein (CRP) (17.1 mg/dL; normal values <0.5 mg/dL) and hypoalbuminaemia (3.2 g/dL). Colonoscopy showed widely ulcerated mucosa, and a histological examination confirmed severely active ulcerative colitis. Chest and abdominal radiographs were normal. Intravenous methylprednisolone (60 mg/day), fluid replacement and antithrombotic prophylaxis with low-molecular-weight heparin were started. Stool culture, *Clostridium 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 well-being 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, dyspnoea 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 interleukin 6 (IL-6) serum levels, which was 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

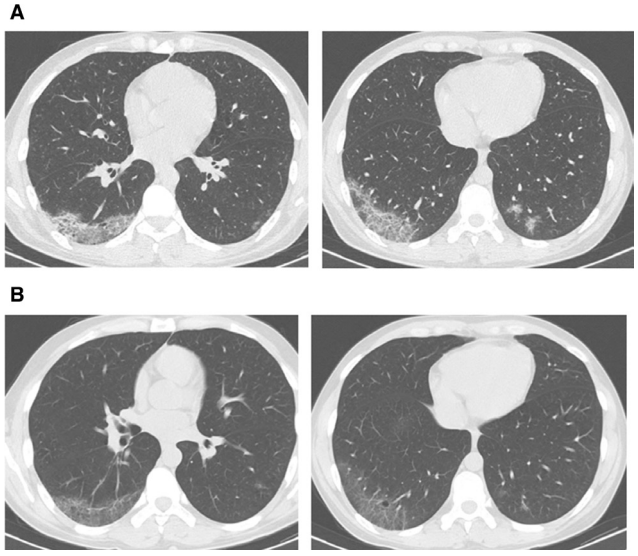

Figure 1 Transverse High Resolution CT scans of the chest of a patient with ulcerative colitis and COVID-19. (A) At the onset of symptoms of COVID-19, CT shows patchy ground-glass opacities affecting the subpleural lung parenchyma bilaterally, indicating interstitial pneumonia. (B) After 10 days (7 days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

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 normalisation 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 two 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 paediatric patient with active Crohn's disease and multisystem inflammatory syndrome related to COVID-19.[8]

The improvement of pulmonary symptoms suggests that anti-tumour necrosis factor alpha (TNF-α) 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.

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