DOI: 10.1111/apt.16240

AP&T Alimentary Pharmacology & Therapeutics WILEY

Letter: how frequently does COVID-19 mimic an IBD flare when community transmission of SARS-CoV-2 is active?

EDITORS,

We read with interest the case series by Taxonera et al on the gastrointestinal symptoms accompanying SARS-CoV-2 infection[1] in patients with inflammatory bowel disease (IBD). The authors reported SARS-CoV-2 infection in 12 patients with IBD, nine of whom reported diarrhoea at initial presentation, with two reporting diarrhoea as their only presenting symptom.

Gastrointestinal (GI) symptoms are frequently reported in COVID-19, with incidence of diarrhoea ranging from 2 to 49%.[2] Both the SARS-CoV-2 receptor, angiotensin-converting enzyme 2 (ACE-2), as well as the SARS-CoV-2 nucleocapsid protein have been detected in gastrointestinal epithelial cells.[3] This suggests a role for direct viral infection[4-6] resulting in cytokine release and neutrophil degradation[7] in GI presentation of COVID-19. These data raise concerns that the high prevalence of diarrhoea reported in COVID-19 could potentially mask an underlying IBD flare in susceptible individuals. Indeed, faecal calprotectin (FC), a biomarker of intestinal inflammation frequently used in assessment of IBD,[8] rises in patients with SARS-CoV-2 RNA detected in stool samples.[9]

We performed a prospective, single centre study of IBD patients who reported symptoms suggestive of an IBD flare during the first wave of the COVID-19 pandemic (March-June 2020). Patients provided a stool sample as part of routine clinical care to measure FC. Following research ethics committee approval, a subset of patients provided a second stool sample for SARS-CoV-2 RNA testing. FC levels >150 g/dl were considered positive for an IBD flare, and 50-150 g/dl indeterminate.

Of 249 patients reporting IBD flares during the study period, 158 (63.5%) provided a stool sample for FC testing as part of their clinical assessment and 38 consented to providing an additional tool sample for SARS-CoV-2 RNA testing, of whom 21 (55%) complied. Of those providing two stool samples, there was a male preponderance (14/21, 66%) with a median age of 35.5 years (IQR 22-47). Crohn's disease and ulcerative colitis accounted for 57% (12/21) and 43% (9/21), respectively, with a median duration of disease of 10.4 years (IQR 7-11). Seven patients were treated with biologic therapy alone, six with combination therapy, three with mesalazine (mesalamine) (5-ASA) and an immunomodulator, two with 5-ASA alone, and three with no therapy.

FC was positive in 8/21 (38%) and indeterminate in 4/21 (19%). SARS-CoV-2 RNA was not detected in any stool samples. Of the eight patients with suspected IBD flares and positive FC, one had Cryptosporidium, two were non-compliant with treatment, one was given a steroid enema, one commenced an immunomodulator and three had no change in their therapy.

Patients with IBD continue to present with disease flares during the COVID-19 pandemic. Our index of suspicion for considering COVID-19 as a possible cause of diarrhoea when SARS-CoV-2 community transmission should remain high. However, and reassuringly, we did not detect SARS-CoV-2 RNA in any stool samples, whether FC levels were elevated or not. These limited data suggest that SARS-CoV-2 infection is not a common cause of disease flare in patients with IBD, even during periods of high SARS-CoV-2 community transmission.

ACKNOWLEDGEMENT

Declaration of personal interests: None.

Declaration of funding interests: Neil O'Morain has received support to attend international meetings from Abbvie, Janssen, Takeda and Ferring pharmaceuticals, and received speaker's fees from MSD. Patrick Mallon has received funding for Advisory Boards, speaker panels, preparation of educational materials and/or research grants to his institution from Gilead Sciences, ViiV Healthcare, BMS, MSD, Abbvie and Janssen-Cilag. Glen Doherty has served as speaker, a consultant and an advisory board member for Abbvie, MSD, Pfizer, Amgen, Janssen, Shire, Takeda, Tillotts and has received funding from Abbvie, MSD and Pfizer. Carolann Coe, Patrick Twomey and Cillian de Gascun have no disclosures.

LINKED CONTENT

This article is linked to Taxonera et al paper. To view this article, visit https://doi.org/10.1111/apt.15804

Neil O'Morain[1]
Carolann Coe[1]
Patrick Mallon[2,3,4]
Patrick Twomey[4,5]
Cillian F. De Gascun[6]
Glen A. Doherty[1,4]

AP&T correspondence columns are restricted to letters discussing papers that have been published in the journal. A letter must have a maximum of 500 words, may contain one table or figure, and should have no more than 10 references. It should be submitted electronically to the Editors via http://mc.manuscriptcentral.com/apt.

[1]Centre for Colorectal Disease, St Vincent's University Hospital, Dublin, Ireland
[2]Department of Infectious Disease, St. Vincent's University Hospital, Dublin, Ireland
[3]Centre for Experimental Pathogen Host Research, University College Dublin, Dublin, Ireland
[4]School of Medicine, University College Dublin, Dublin, Ireland
[5]Department of Clinical Chemistry, St Vincent's University Hospital, Dublin, Ireland
[6]National Virus Reference Laboratory, University College Dublin, Dublin, Ireland
Email: neilmoran@gmail.com

ORCID

Neil O'Morain https://orcid.org/0000-0003-2542-9455

REFERENCES

1. Taxonera C, Sagastagoitia I, Alba C, Mañas N, Olivares D, Rey E. 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases. *Aliment Pharmacol Ther*. 2020;52:276–283.
2. Tian Y, Rong L, Nian W, He Y. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. *Aliment Pharmacol Ther*. 2020;51:843–851.
3. Wu F, Zhao SU, Yu B, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020;579:265–269.
4. Wong SH, Lui RNS, Sung JJY. Covid-19 and the digestive system. *J Gastroenterol Hepatol*. 2020;35:744–748.
5. Hoffmann M, Kleine-Weber H, Schroeder S. et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181:271–280.e8.
6. Zhang H, Kang Z, Gong H, et al. Digestive system is a potential route of COVID-19: an analysis of single-cell coexpression pattern of key proteins in viral entry process. *Gut*. 2020;69:1010–1018.
7. Effenberger M, Grabherr F, Mayr L, et al. Faecal calprotectin indicates intestinal inflammation in COVID-19. *Gut*. 2020;69:1543–1544.
8. Roseth AG, Schmidt PN, Fagerhol MK. Correlation between faecal excretion of indium-111-labelled granulocytes and calprotectin, a granulocyte marker protein, in patients with inflammatory bowel disease. *Scand J Gastroenterol*. 1999;34:50–54.
9. Reuken PA, Wüst M, Löffler B, Bauer M, Stallmach A. Letter: SARS-CoV-2-induced gastrointestinal inflammation. *Aliment Pharmacol Ther* 2020;52:1748–1749.