

PERSONAL VIEWPOINT

Managing COVID-19 in patients with inflammatory bowel disease: navigating unprecedented challenges

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Abstract

The COVID-19 pandemic has demanded a rapid adaptation in healthcare provision, including patients with inflammatory bowel disease (IBD). This viewpoint discusses some of the unique challenges in managing comorbid IBD and COVID-19 experienced by our team at The Royal Melbourne Hospital, which was at the epicentre of the COVID-19 'second-wave' surge in Melbourne.

Introduction

The COVID-19 pandemic has necessitated rapid adaptation of healthcare service provision in metropolitan Melbourne. The Inflammatory Bowel Disease (IBD) unit at the Royal Melbourne Hospital was at the epicentre of the 'second wave' and faced unprecedented challenges. Of 11 IBD patients with COVID-19 within Australia included in the Surveillance Epidemiology of Coronavirus Under Research Exclusion (SECURE-IBD) registry, an international reporting database for IBD patients with COVID-19,¹ four were managed by our unit. Three of these are described in this article to inform ongoing IBD-specific and broader system-related COVID-19 care.

Personal experience and viewpoint

Case A was a 62-year-old man with steroid-dependent penetrating small bowel Crohn disease (CD) and severe chronic obstructive pulmonary disease (COPD). He was

admitted with an intra-abdominal collection associated with a complex parastomal fistula. This occurred as the second wave in Victoria was reaching its peak, with 200–700 COVID-19 cases being reported daily for the majority of admissions. Unbeknownst to the unit, on Day 23 of the patient's admission, a treating healthcare worker (HCW) was identified as positive for SARS-CoV-2. On this day, our health service had 78 confirmed HCW infections and was managing 87 COVID-19 cases. Case A proceeded to endoscopy 24 h after this exposure, given the unit's ignorance to potential exposure concerns. That evening, he underwent asymptomatic outbreak screening. Given previous anaphylaxis to infliximab, he received a loading dose of intravenous (i.v.) ustekinumab the following day for his CD. That evening, his screening test returned positive for SARS-CoV-2, prompting further staff testing across multiple departments. He symptomatically deteriorated from COVID-19 with requirement for high flow oxygen and dexamethasone treatment on Day 10 postexposure. He was discharged on Day 13 to a peripheral hospital. His CD remains stable with 8-weekly subcutaneous ustekinumab. Unfortunately, he has had repeated hospital admissions with post COVID-19 syndrome in the setting of comorbid COPD.

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Case B was a 25-year-old electrician with colonic and perianal CD in deep remission, maintained on adalimumab 40 mg fortnightly and azathioprine 75 mg daily. His partner, a nurse at a tertiary hospital, acquired COVID-19 at work. He tested positive after experiencing anosmia and fatigue. He was advised to withhold his azathioprine and adalimumab as suggested by international and local guidelines.²⁻⁴ He remained well without need for hospitalisation. His medications were recommenced utilising a symptom-based strategy. This advocates recommencing medications after at least 10 days have passed since symptom onset and at least 72 h have passed since clinical recovery, defined as resolution of fever without the use of antipyretic medications and with meaningful improvements in respiratory symptoms. He thus missed a total of two doses of adalimumab. He remains clinically well.

Case C was a 36-year-old tradesman with ischaemic heart disease and longstanding moderate to severely active Crohn colitis awaiting commencement of a clinical trial agent. He had prior anaphylaxis to infliximab, vedolizumab primary non-response and intolerance of thiopurines. He presented with a colitis flare in the context of having had mild COVID-19 infection 1 month prior. He tested negative for SARS-CoV-2 infection via nasopharyngeal and oropharyngeal PCR on admission. He was commenced on i.v. corticosteroid with rapid biochemical and clinical response, before being successfully bridged with a rapid steroid taper to ustekinumab.

The management of the aforementioned patients identifies numerous clinical and logistical challenges in the management of IBD during the COVID-19 pandemic.

Guidance on the cessation and resumption of biological agents in IBD patients with COVID-19

Cases A and C received ustekinumab, an IL12/23 p40 subunit monoclonal antibody, while affected with or closely following resolution of COVID-19. Case B acquired COVID-19 while on adalimumab combination therapy. Current international consensus recommendations state that IBD medications should not be stopped prophylactically in uninfected and asymptomatic patients, but advise withholding immunosuppressants and biologics in active COVID-19 infection.²⁻⁴

Importantly, current evidence refutes an association between the use of biologics to treat IBD and COVID-19 disease severity. The SECURE-IBD registry includes 226 patients managed with an IL12/23 inhibitor at the time of writing, with a 3% intensive care unit (ICU)/ventilator/death rate – comparing favourably to a 6% overall rate in the 2575 included patients.¹ The safety of anti-

TNF and vedolizumab monotherapy has also been demonstrated, with rates of severe COVID-19 of 2% and 7% respectively.^{1,5} These findings are reassuring, particularly given the long half-life of many of the IBD biologics. Furthermore, such agents are now being considered therapeutically for severe COVID-19, given their potential to suppress the aberrant systemic inflammatory response observed.³ Randomised interventional trials evaluating the role of biologics in COVID-19 are underway, including adalimumab.⁶ Such trials are warranted before the intentional use of biologics for management of COVID-19 can be advised; however, the underlying premise provides reassurance to treating clinicians and patients alike.

When recommending biologics and immunosuppressants post COVID-19 infection, a symptom-based strategy taking into consideration the clinical severity of both IBD and COVID-19 should be adopted.² Utilising this strategy, recommencement occurs after at least 10 days from symptom onset, with a minimum of 72 h following infection recovery. The latter is defined as resolution of fever without the use of fever-reducing medications and clinical meaningful improvement in respiratory symptoms.² Although the SECURE database has been integral in demonstrating the relative safety of continuing biologics during the COVID-19 pandemic, such retrospective observational data cannot currently inform the safety of intentional biologic continuation in the context of symptomatic COVID-19. Further evidence is awaited to guide recommendations for therapy cessation during, and recommencement following, COVID-19.

HCW exposure of patients to COVID-19

These cases highlight the inadvertent risk HCW may pose to inpatients through asymptomatic COVID-19 infection. Seroprevalence in HCW is high, particularly in frontline HCW, with up to 41% of HCW infections thought to have been hospital acquired.⁷⁻⁹ Asymptomatic SARS-CoV-2 infection occurs in 15.6% (95% CI, 10.1–23.0%) of individuals, with pre-symptomatic infection (SARS-CoV-2 detection while asymptomatic with later development of symptoms) occurring in almost 50%.¹⁰ Protocolised screening of both asymptomatic patients and HCW in areas of high prevalence may seem logical, but has not yet proven efficacious for transmission reduction. Although presently lacking high-quality supportive evidence, recent consensus recommendations from the British Society of Gastroenterology recommend keeping all in-patients with acute severe ulcerative colitis in isolation precautions throughout the course of their admission, irrespective of COVID-19 status.¹¹ Additionally, repeated COVID-19 swabs prior to escalation in

medical therapy are advocated for.¹¹ These guidelines reflect an undeniable need to mitigate the risk to patients through HCW exposure needs, particularly during times of high community (and thus realistically hospital) COVID-19 prevalence. Promotion of telehealth consultations to minimise healthcare exposure is prudent, but must be tailored to meet the individual's culture, linguistic and clinical needs and technological capacity.¹² Additionally, we advocate for a candid and expedient reporting system for ward-based outbreaks within healthcare services, so as to limit unnecessary exposure of multiple staff, and thus secondarily patients to COVID-19.

Corticosteroids in COVID-19

Case A underscores the contradictory effects of corticosteroid in different stages of COVID-19. Chronic corticosteroid use is a risk factor for severe COVID-19 infection in patients with IBD, with an adjusted odds ratio for ICU admission, ventilator use and/or death of 6.9 (95% CI, 2.3–20.5).⁵ Paradoxically, dexamethasone plays an important role in treating COVID-19 with associated respiratory failure.¹³ Viral shedding occurs relatively early in COVID-19, with the deleterious inflammatory response evolving subsequently.¹³ Early corticosteroid use may allow for enhanced viral replication and hence higher viral loads.¹³ Conversely, corticosteroids in the second week of infection, when the immunopathological phenomenon predominates, may be beneficial.¹³ Given that active IBD and corticosteroids both serve as risk factors for severe COVID-19,^{1,12} prudent and expedited use of biologics to optimise corticosteroid free disease control is essential. Achieving this control further serves to minimise COVID-19 exposure risk associated with emergent hospitalisation.

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COVID-19 infection mimicking or precipitating IBD flare

Up to 17.6% of patients with COVID-19 experience gastrointestinal symptoms, including diarrhoea in 12.5%.¹⁴ Alarming, up to 28% with gastrointestinal symptoms do not have typical respiratory symptoms, and thus initial COVID-19 testing may not be performed.⁷ Whether SARS CoV-2 infection can precipitate IBD flare is uncertain.³ However, the virus is known to infect epithelial cells, including those of the gastrointestinal tract, via membrane-bound ACE2 receptor.¹⁵ Thus, SARS CoV-2 may precipitate colonic inflammation directly, as evidenced by reports of endoscopically demonstrable colitis in a patient with COVID-19.¹⁵ SARS CoV-2 stool testing in patients with known IBD and symptomatic flare in highly prevalent settings is not yet recommended.³ However, due to implications on treatment and infection control, our unit has routinely tested all flaring IBD patients for COVID-19 with oropharyngeal and nasopharyngeal PCR during the COVID-19 'waves'.

Conclusion

The COVID-19 situation is rapidly evolving, and fortunately appears to be improving markedly in Australia. Flexibility and rationality in approach to patient care where evidence is perpetually emerging is paramount. IBD patients need to be supported in continuing maintenance therapies to optimise disease control and thus avoid harmful corticosteroid exposure. A conscientious approach to inpatient screening for COVID-19 is prudent. Furthermore, bureaucratic transparency within the healthcare system regarding infection control concerns and outbreak management must be prioritised, thereby ideally minimising healthcare associated infection and ensuring patient and staff safety.

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