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COVID-19 Induced Ulcerative Colitis: A Case Presentation and Review of Evidence

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Abstract

A 56-year old man presented to the hospital with a complaint of rectal bleeding, and sent home with a prescription for 1% hydrocortisone cream under the belief it was due to hemorrhoid irritation. He returned 6 months later with no resolution in symptoms, with the additive 1 month of watery diarrhea that transitioned to bloody diarrhea. Lower endoscopy was significant for severe, diffuse inflammation from the ileum to the rectum characterized by granular, friable, and ulcerated mucosa. After a significant work-up indicating the diagnosis of Ulcerative colitis, UC, he disclosed this started when he was diagnosed in clinic with COVID-19. This case report will review previously investigated case reports with similar findings of Ulcerative colitis post COVID-19 infection.

Keywords: ***COVID-19, 19IBD, UCUlcerative Colitis, ColitisViral induced proctitis, hemorrhagic, PAMPS, ACE-2, TNF-alpha***

Introduction

Ulcerative colitis (UC) is an Inflammatory Bowel Disease characterized by diffuse disruption of the colonic mucosa. The age of onset shows a bimodal distribution with two peaks: one between 15-30 years, and the other between 50-70 years. UC is a lifelong condition requiring immunomodulatory medication, such as 5-aminosalicylates, glucocorticoids, thiopurines and biologic agents. UC is thought to result from factors such as bacterial dysbiosis, epithelial barrier defect, aberrant immune response, and genetic predisposition [1]. This report will investigate the relationship between COVID-19 and the development of UC.

Previous research on the influence of microbiota suggests its ability to delay, or prevent serious manifestations of infections, as seen in COVID-19 [2,3]. COVID -19 patients have been found to have reduced anti-inflammatory bacterial species, and their feces contained higher levels of opportunistic pathogens; and PCR positivity for SARS-COV2. Of specific importance, it contained decreased populations of lactobacillus and Bifidobacterium. These bacteria are significant for their anti-inflammatory effects, through induction of FOXP3 T-reg proliferation [2,4]. Bacteroidetes populations, which can downregulate ACE-2 expression, were found to be reduced in this patient population and this negatively correlated with viral load [5]. Lack of appropriate microbiome diversity and their metabolites may contribute to the risk of developing UC [2].

SARS-COV2 can induce localized colonic inflammatory response by binding to ACE2 and TMPRSS2 receptors causing release of damage-associated molecular patterns. This induction of a cytokine storm-like response results in both localized and systemic inflammation, dysregulation of tight junctions, and disruption of the commensal relationship between bacteria and the host [3]. Inappropriate response of the host can provoke autoantigenic reaction through cross reactivity of host proteins and SARS-COV2 proteins [3]. Additionally, microbiota dysbiosis contributing to lack of anti-inflammatory mediators and mucosal irritation is a proposed contributor to the pathogenesis of UC in individuals with COVID-19 [2]. Intestinal expression of ACE-2 combined with direct binding of SARS-COV2 to the receptor may lead to blockage of the anti-inflammatory effects of the renin-angiotensin response, which normally mediates inflammation, fibrosis, and cellular proliferation. Increased binding of ACE-2 by the virus results in direct viral penetration into the intestinal epithelium which leads to fibrosis and inflammation. When the virus is transmitted, the receptors TLR3 and TLR7 recognize viral RNA and transmit signals to produce proinflammatory cytokines and further increase the permeability of the tight junctions, facilitating a poly-pathogenic state [6,7].

TLR4, which is associated with strong affinity for SARS-COV2 glycoprotein, has been implicated in the destructive effects in UC patients due to inflammatory cytokines [6]. IL-17, which is released by T-helper lymphocytes, is heavily involved in the pathogenesis of UC. SARS-COV2 induces interleukins and cytokines that are proinflammatory and highly implicated in the development in UC, such as TNF-alpha, IL-17, and IL-6. Synergistic effects of IL-6 and IL-17 may be implicated in the increased morbidity of UC patients with acute COVID-19 and could play a role in the development of UC after COVID-19 infection [2,3,8].

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Case Presentation

A 56-year-old male presented to clinic with chief complaint of rectal bleeding. His past medical history is significant for migraines, hypertension, eczema, and hemorrhoids. Outpatient medications include dupilumab, propranolol, galcanezumab, losartan, and zolmitriptan. Colonoscopy performed 1.5 years prior revealed sigmoid tubular adenoma and internal hemorrhoids. Vital signs included blood pressure 118/82 mmHg, pulse 68/minute, temperature 97.7 F, oxygen saturation 96% on room air. On initial evaluation, he reported that he had a small volume of blood noted when wiping as well as in his stool. Physical examination was significant for small palpable hemorrhoids on digital rectal exam. He was started on 1% hydrocortisone cream and asked to follow up if his symptoms did not improve.

6 months later he returned to the clinic complaining of over 1 month of watery diarrhea. Vitals included blood pressure of 148/90 mmHg, pulse 72/minute, temperature 98.3 F, oxygen saturation 98% on room air. He reported the stools were initially dark brown, but now had bright red blood. He also endorsed worsening diarrhea preceded by cramping and abdominal pain. Laboratory workup was ordered to evaluate for infectious and autoimmune etiologies, in addition to bidirectional endoscopy.

Laboratory workup was significant for elevated leukocyte count of 12.1, hemoglobin of 14.7 (1-year prior was 15.2), C-reactive protein 1.5 (reference <1.0), tissue transglutaminase IgA 22.7 U/mL (reference <15), and stool calprotectin 445 mcg/g (reference <50).

Bidirectional endoscopy was performed. Biopsies were taken from both the upper and lower gastrointestinal tracts to evaluate for celiac disease and colitis. Lower endoscopy was significant for severe, diffuse inflammation from the ileum to the rectum characterized by granular, friable, and ulcerated mucosa. Multiple sessile polyps were noted with no active bleeding. At the splenic flexure, few localized erosions were present with active bleeding. Mucus mixed with purulent material was seen throughout. Non-bleeding diverticula were also noted.

Biopsy of the colon was notable for non-necrotizing granulomatous inflammation with moderate active inflammation without dysplasia or malignancy. Based on his clinical presentation, a diagnosis of ulcerative colitis was made and the patient was started on vedolizumab and azathioprine.

When presenting back to the clinic several weeks after initiating therapy, he noted that he had been diagnosed with lab-confirmed COVID-19 a few months prior to the onset of his symptoms. Since starting the medications, he denies new episodes of bloody diarrhea, though he did still report occasional loose stools.

Discussion and case review

The case of this 56-year-old male is similar to other published case reports with a diagnosis of IBD made after COVID19 infection. A summary of these cases can be seen on Table 1. Review of the literature suggests that development of UC is more likely to occur in cases of COVID-19 with gastrointestinal involvement. One exception to this is the case of a patient with COVID-19 pneumonia without GI involvement who developed UC months after infection [4]. Based on the case reports of UC after COVID-19, there does not appear to be a predilection for males versus females. The distribution of COVID-19 related UC cases appears to be skewed towards the second peak of the bimodal distribution, with some outliers [12,10]. While the majority of reported cases document resolution of GI symptoms before presentation, there is a case in which the patient experienced continuous diarrhea after treatment and resolution of virus prior to the onset of bloody stool [14]. Of the cases reported, symptoms occurred anywhere from 14 days to 4 months after resolution of symptoms, with a range of complete resolution in symptoms to increase stool frequency prior to onset of blood in stool.

As discussed earlier, COVID-19 severity is associated with the gut microbiome, suggesting poor microbiome could predispose a patient to developing UC after COVID-19 infection. A report of a 71-year-old female returning from Egypt experienced severe hemorrhagic proctitis with negative UC histological image solely from COVID demonstrating the capability of the virus [19].

The mechanism of development of UC post-COVID is likely complex and related to ACE-2 receptor density, disruption of the gut microbiome, increased SCFA, and induction of a cytokine storm. Genetics may also play a role, but it is not a causal relationship. A case of two siblings, ages 9 and 10, who both developed COVID-19 and then an infectious colitis, one resolved completely and the other developed UC [12].

A 71 year old female post mortem revealed in addition to plasma cells and lymphocytes infiltrating the lamina propria of the rectum and duodenum, as well as stool samples testing positive for PCR, a new mechanism not previously mentioned in other case studies of an aberrant PD1/PD-L1, and suggested the synergistic effects of the aberrancy in irritated mucosa with COVID-19 induced cytokine storm in the induction of procto-hemorrhagica [18].

COVID-19 can alter immune responses in multiple ways that range from hyperinflammation, immune dysregulation and dysfunction at the level of white blood cells. The reaction to the infection can cause cytokine storm which can consequentially cause damage to organ function. The immune dysregulation that results from induction of cytokine storm and change in microbiota signaling, can additionally lead to molecular mimicry and cross damage to healthy, normal functioning cells. Amongst fighting the infection, reports of lymphopenia, and T- cell dysfunction have been found [2,3,6,7,8,20].

While there has been no direct causal effect between COVID and UC, it can be postulated that the relationship is due to both microbiota dysbiosis and immunologic dysfunction. Additionally, the clear immunologic dysfunction that occurs as a result of microbiota disturbance. Due to the wide range of symptoms that occur with the infection, the differing strains and the unclear long-term sequela, this relationship will continued to be seen and should be studied more extensively. What is evident is that the interplay among the cytokine storm, the potential for immune suppression, and the complex interaction between an individual's genetics and environmental factors, the potential for evoking IBD is evident [2,3,8].

In summary, physicians should keep IBD on the differential in patients who present with COVID and change in bowel habits, especially if infectious colitis has been ruled out. An elevated index of suspicion may reduce time to colonoscopy and subsequent treatment for IBD, improving quality of life. Further research is needed to explore the increased risk of development of ulcerative colitis in the context of COVID-19.

Table 1: Summary of Case

Age, Sex	Presenting Sxs covid	Time since COVID IBD symptoms presented	presenting sxs prior to IBD Dx + CRP +Calprotectin	Findings on endoscopy	Treatment	Smoker	Co-morbidities
50,M[9]	Fever, SOB, Tachypnea, Tachycardia	2 weeks	Blood diarrhea Normal CRP 1800 Calpro	diffuse micro ulcerated, granulated	5-ASA	Y	N
37, M[10]	Respiratory symptoms	8 weeks	Abd pain, bloody diarrhea CRP65 Cal pro 325	moderate protcodigmoidtis	5-ASA	N	N
64, M[10]	constitutional symptoms followed by respiratory symptoms	3 weeks	Abd pain, bloody diarrhea CRP 98 Cal pro 350	moderate protcodigmoidtis	5-ASA	Y	DM, HTN
74 M[5]	rhinorrhea, fever, diarrhea (subsided after 2 weeks)	4 weeks	Fever, Blood diarrhea, CRP 20.3 Cal pro N	Diffuse and active cryptitis	5-ASA	N	-
84, M[11]	Bloody diarrhea, no respiratory sx, found incidentally	1 week	Continuous severe bloody diarrhea Cal pro 3,160	Severe ulcerations, inflammation	Methylpredinsolone 5-ASA	–	bullous emphysematous COPD, HTN, DM2, Abd aneurysm, prior infectious colitis
9,F[12]	Diarrhea, hematochezia, abd pain	4 weeks	worsening Abd pain, diarrhea, hematochezia Fecal Pro 1401 CRP 1.2	Moderate pancolitis	5-ASA	N	N
19,F[13]	F, N, V, Diarrhea, anosmia, bloody diarrhea	1 week	Anemia, no other symptoms	extensive colitis	Beclomethasone and MMX-mesalamine	N	N
55, M[4]	Pneumonia	3 months	Abd pain, bloody diarrhea	Extensive colitis with spontaneous bleeding	—	N	—
** 47, F[14]	weakness, myalgia, diarrhea	4 months	Large volume diarrhea CRP 39 cal pro 290	Erosions at terminal ileum	oral budesonide		—
"Youn g" F[15]	F, myalgia, watery diarrhea, sore throat	4 months	Worsening diarrhea that became bloody	Extensive erosions. confluent involvement for 35 cm from anal verge	oral and topical mesalamine	N	–
21, M[16]	Sore throat, ha, cough, fever	one week	6x daily diarrhea with abd pain; CRP 57 Cal Pro 649	Erythematous and edematous superficial ulceration and loss of vascular pattern, suggestive of moderate colitis	5-ASA rectal and oral with azathioprine and prednisolone in hospital and home azathioprine and 5-ASA	N	N
18 M[17]	Acute respiratory symptoms	1 month	CRP 3.8 calpro 1700 bloody diarrhea	proximal transverse to anorectal diffuse granular colitis	5-ASA	-	-
71 F[18]	dyspnea and sepsis	concurrent	calpro 38 procal 26 hemorrhagic defecation requiring transfusions	mucosal and submucosal ulcerations	subtotal colectomy due to hemorrhage	N	N

*** Crohn's disease*

Cal pro= Calprotectin

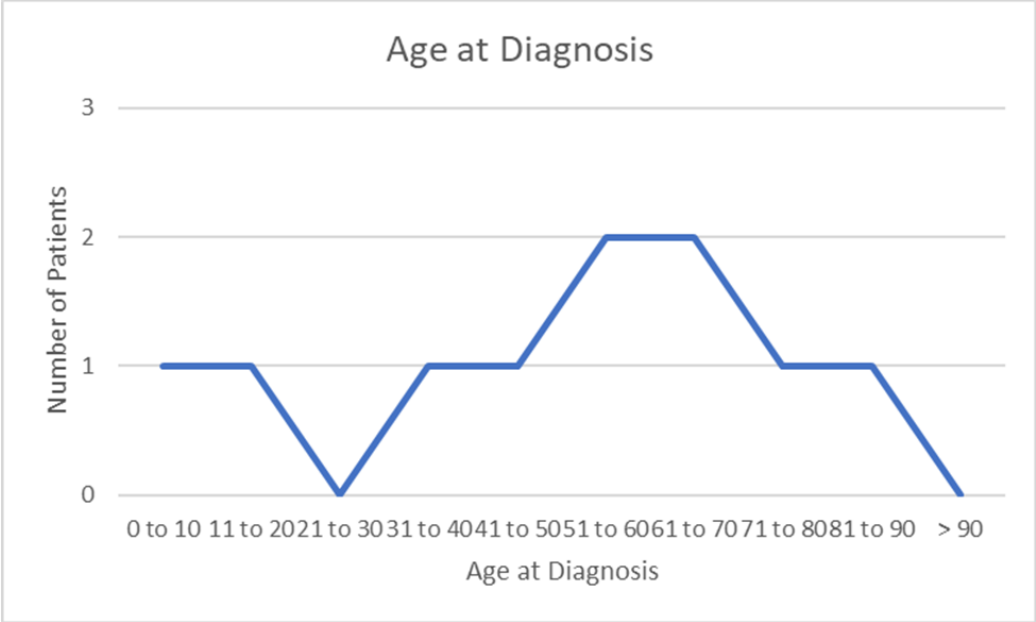

Fig 1: Age at Diagnosis

Ethical Clearance

Not required.

Conflict of Interest

The author declares that there is no conflict of interest regarding the publication of this article.

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References

[1] Lynch WD, Hsu R. Ulcerative Colitis. In: StatPearls. StatPearls Publishing; 2022.

[2] Wang B, Zhang L, Wang Y, et al. Alterations in microbiota of patients with COVID-19: potential mechanisms and therapeutic interventions. Signal Transduct Target Ther. 2022;7(1):143.

[3] Dvornikova KA, Bystrova EY, Churilov LP, Lerner A. Pathogenesis of the inflammatory bowel disease in context of SARS-COV-2 infection. Mol Biol Rep. 2021;48(7):5745-5758.

[4] Imperatore N, Bennato R, D'Avino A, Lombardi G, Manguso F. SARS-CoV-2 as a Trigger for De Novo Ulcerative Colitis. Inflamm Bowel Dis. 2021;27(7): e87-e88.

[5] Kartsoli S, Vrakas S, Kalomoiris D, Manoloudaki K, Xourgias V. Ulcerative colitis after SARS-CoV-2 infection. Autops Case Rep. 2022;12: e2021378.

[6] Tripathi K, Godoy Brewer G, Thu Nguyen M, et al. COVID-19 and Outcomes in Patients with Inflammatory Bowel Disease: Systematic Review and Meta-Analysis. Inflamm Bowel Dis. 2022;28(8):1265-1279.

[7] Akbaş E, Akın MS. SARS-Cov-2 Infection in Patients with Inflammatory Bowel Disease: A Single-Center Study. Med Sci Discov. 2022;9(5):288-292.

[8] Viganò C, Mulinacci G, Palermo A, et al. Impact of COVID-19 on inflammatory bowel disease practice and perspectives for the future. World J Gastroenterol. 2021;27(33):5520-5535.

[9] Aydın MF, Taşdemir H. Ulcerative Colitis in a COVID-19 Patient: A Case Report. Turk J Gastroenterol. 2021;32(6):543-547.

[10] Elbadry M, Medhat MA, Zaky S, El Kassas M. Ulcerative colitis as a possible sequela of COVID-19 Infection: The endless story. Arab J Gastroenterol. 2022;23(2):134-137.

[11] Fonseca Mora MC, Abushahin A, Gupta R, Winters H, Khan GM. Severe Ulcerative Colitis as a Complication of Mild COVID-19 Infection in a Vaccinated Patient. Cureus. 2022;14(6): e25783.

[12] Preziosi NA, Rizvi AH, Feerick JD, Mandelia C. De Novo Pediatric Ulcerative Colitis Triggered by SARS-CoV-2 Infection: a Tale of 2 Sisters. Inflamm Bowel Dis. 2022;28(10):1623-1625.

[13] Calabrese E, Zorzi F, Monteleone G, Del Vecchio Blanco G. Onset of ulcerative colitis during SARS-CoV-2 infection. Dig Liver Dis. 2020;52(11):1228-1229.

[14] Tursi A, Nenna R. COVID-19 as a Trigger for De Novo Crohn's Disease. Inflamm Bowel Dis. 2022;28(6): e76-e77.

[15] Taxonera C, Fisac J, Alba C. Can COVID-19 Trigger De Novo Inflammatory Bowel Disease? Gastroenterology. 2021;160(4):1029-1030.

[16] Xia C, Dissanayake J, Badov D. A New Onset of Ulcerative Colitis Post-COVID-19: A Case Report. Cureus. 2023;15(3): e36257.

[17] Lee A, Elbaum P. S2468 Inflammatory Bowel Disease After COVID-19 Infection. Official journal of the American College of Gastroenterology | ACG. 2021;116: S1042.

[18] Rutigliani M, Bozzo M, Barberis A, et al. Case Report: A Peculiar Case of Inflammatory Colitis After SARS-CoV-2 Infection. Front Immunol. 2022; 13:849140.

[19] Carvalho A, Alqusairi R, Adams A, et al. SARS-CoV-2 Gastrointestinal Infection Causing Hemorrhagic Colitis: Implications for Detection and Transmission of COVID-19 Disease. Am J Gastroenterol. 2020;115(6):942-946.

[20] Suryawanshi P, Takbhate B, Athavale P, Jali P, Memane N, Mirza S, Karandikar M, Kakrani AL, Kanitkar S, Gandham N, Barthwal MS, Dole S, Chaturvedi S, Pawale S, Tripathy A, Bhawalkar JS, Tripathy S. Lymphopenia with Altered T Cell Subsets in Hospitalized COVID-19

Patients in Pune, India. Viral Immunol. 2023 Apr;36(3):163-175. doi: 10.1089/vim.2022.0123. Epub 2023 Mar 10. PMID: 36897333.