

Newly diagnosed Crohn's Disease after COVID-19 Infection: A Case Report

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Abstract: Viral infections are recognized as potential triggers for immune-mediated diseases, and an increasing number of reports have described newly diagnosed inflammatory bowel disease (IBD) following COVID-19. We report a previously healthy 23-year-old man who was diagnosed with Crohn's disease (CD) shortly after symptomatic SARS-CoV-2 infection. Within two weeks of the confirmed infection, he developed severe gastrointestinal symptoms, followed by a perianal abscess and fistulizing disease. Ileocolonoscopy revealed patchy erosive colitis with predominant rectosigmoid involvement, while histological examination demonstrated chronic active granulomatous ileocolitis. He required surgical drainage, corticosteroids, azathioprine, and ultimately infliximab, achieving complete mucosal healing within one year. A literature review identified 19 previously reported cases of newly diagnosed IBD following COVID-19, most of which were ulcerative colitis; none of the reported CD cases presented with perianal fistulizing disease or required anti-TNF therapy. Proposed pathophysiological links between COVID-19 and IBD include altered epithelial ACE2 expression, gut dysbiosis, barrier disruption, and post-infectious immune dysregulation, providing biological plausibility for a possible association. This rare case of severe, newly diagnosed CD temporally associated with COVID-19 highlights the need to investigate persistent gastrointestinal symptoms after infection, although causality and the possibility of previously subclinical disease cannot be established from a single case.

Keywords: Case Report; Crohn's Disease; COVID-19; Inflammatory Bowel Disease.

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1. Introduction

The SARS-CoV-2 pandemic has profoundly impacted global healthcare, including the management and understanding of immune-mediated diseases such as inflammatory bowel disease (IBD). Viral infections are recognized as potential triggers for autoimmune disorders including IBD. Only few reports have described newly diagnosed IBD following COVID-19, raising the possibility of an association between these etiologies [1]. Furthermore, complex interactions between COVID-19 and IBD exist at a molecular level. Epithelial expression of angiotensin converting enzyme 2 (ACE2) appears to be both essential for viral entry of SARS-CoV-2 into host enterocytes [2] and is also credited to be intrinsically related to IBD pathological aspects.

Here, we report a young adult who presented classical Crohn's disease (CD) shortly after symptomatic COVID-19 and summarize previously reported cases of post-COVID newly diagnosed IBD.

2. Case Report

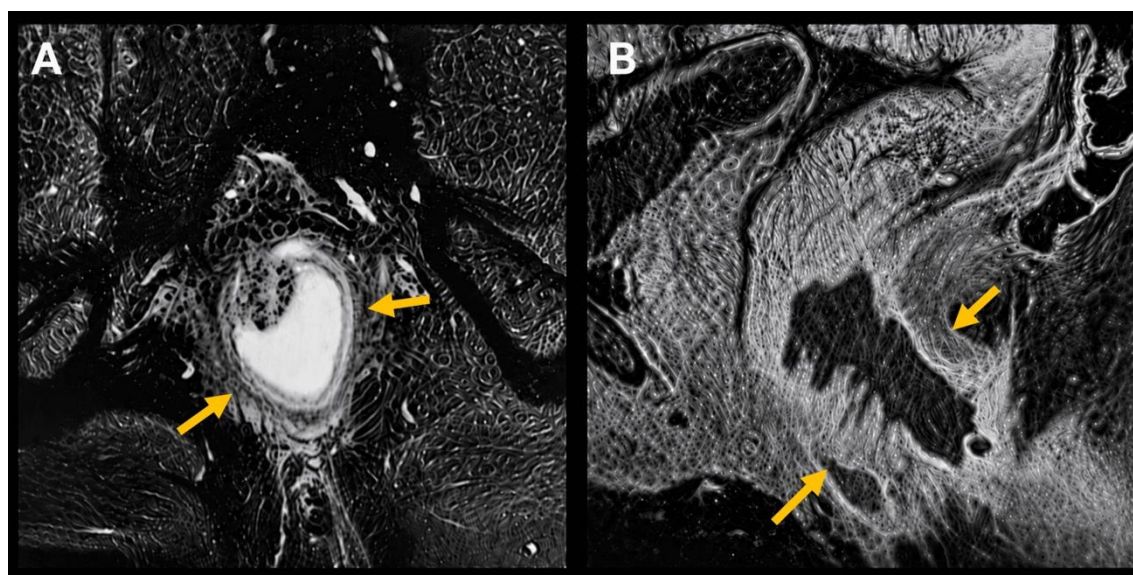
A 23-year-old previously healthy male with a three-dose COVID-19 vaccination (last dose administered in August 2021) presented in June 2022 with odynophagia, cough, fever, myalgia, diarrhea, anosmia, and hypogeusia after contact with a COVID-19-positive individual. Two positive nasopharyngeal reverse transcription-polymerase chain reaction (RT-PCR) swabs for SARS-CoV-2 confirmed infection. He was treated at home with supportive care and initially improved. His past medical, family, genetic, and psychosocial histories were unremarkable, and no relevant previous interventions were reported.

Within two weeks, he developed diffuse abdominal pain involving the periumbilical and right iliac regions and diarrhea. Abdominal ultrasound revealed mesenteric lymphadenopathy. Inflammatory markers, including the erythrocyte sedimentation rate, were mildly elevated, whereas the remaining routine laboratory findings were unremarkable. Available baseline laboratory tests performed in March 2022, approximately three months before the onset of symptoms, were within normal limits.

The glutamate dehydrogenase test, stool culture, and serial examinations for ova and parasites were negative, and routine stool analysis was unremarkable. Multiplex stool PCR testing for additional pathogens and specific testing for cytomegalovirus were not performed. Although serial stool examinations were negative, the patient received empirical antiparasitic treatment with ivermectin for 2 days, albendazole for 3 days, and a single dose of secnidazole, without clinical improvement.

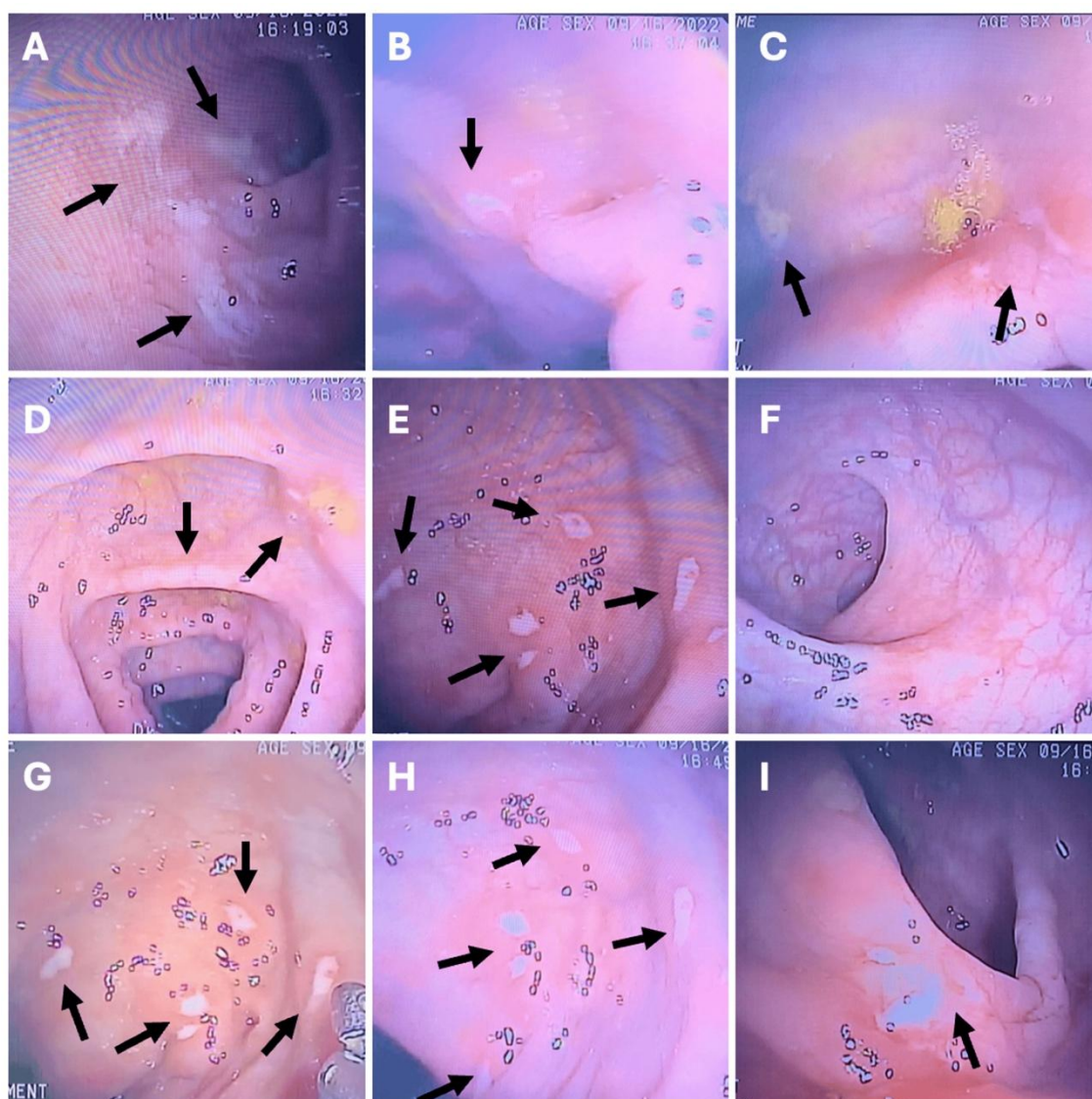
As his flu-like symptoms progressed, a single empirical dose of intramuscular corticosteroid was administered, resulting in partial improvement. Two weeks later, his symptoms recurred, with perianal pain, profuse watery diarrhea with mucus, bloody diarrhea, oral ulcers, lactose intolerance and syncope. By that time, he had lost 22 kg in less than two months. Physical examination revealed left-sided perianal swelling and an internal anal fissure, and pelvic MRI showed an intersphincteric perianal abscess (Figure 1). Surgical drainage was performed, and antibiotics (ciprofloxacin/metronidazole) were prescribed.

Figure 1. Pelvic MRI demonstrating a left-sided intersphincteric perianal abscess. Left-sided perianal intersphincteric abscess extending from the external anal ridge to the anorectal junction, mildly displacing the anal canal to the right and measuring 5 × 3 × 2.4 cm.



At the 1-month follow-up, he had developed an anterior anal fissure and a complex fistula. Fecal calprotectin exceeded 3,000 $\mu\text{g/g}$, and colonoscopy revealed multiple scattered circular erosions and small aphthous ulcers extending from the transverse colon to the rectum, with more pronounced involvement of the sigmoid colon and rectum and preservation of the intervening mucosa and vascular pattern (Figure 2). Approximately 15 cm of the terminal ileum was examined and appeared macroscopically normal, as did the ileocecal valve, cecum, and ascending colon.

Figure 2. Initial ileocolonoscopy demonstrating patchy erosive colitis with predominant rectosigmoid involvement. Ileocolonoscopy showing scattered circular erosions with fibrinous centers and small aphthous ulcers extending from the transverse colon to the rectum. The lesions were more numerous in the sigmoid colon and rectum, with preservation of the intervening mucosa and vascular pattern. The terminal ileum appeared macroscopically normal, although histological examination demonstrated chronic active granulomatous ileitis.

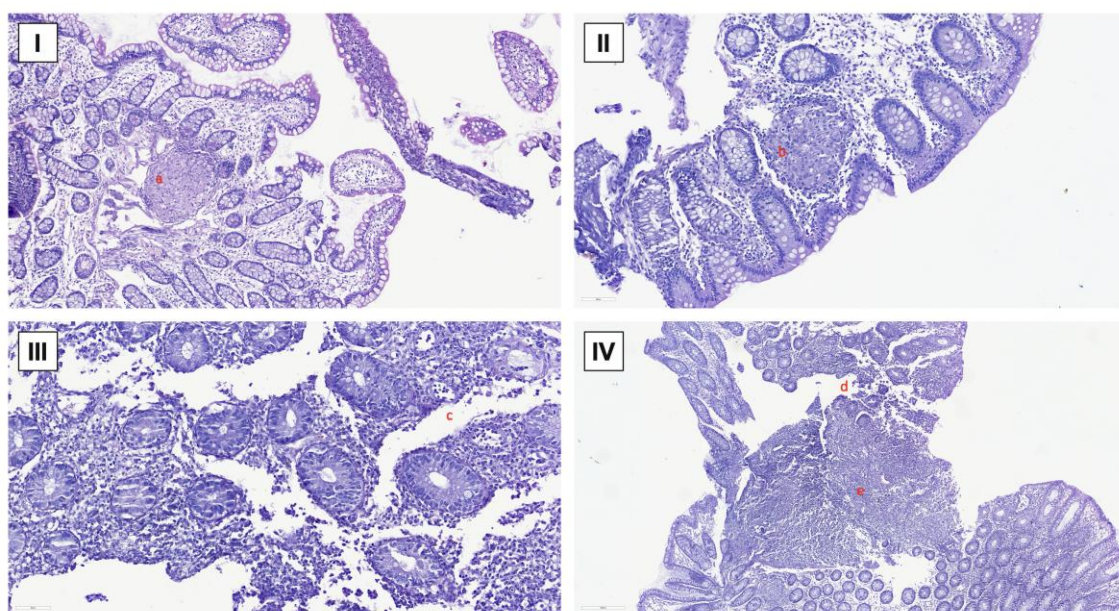


Histology demonstrated chronic active ileocolitis, with focal sarcoid-like granulomas in the terminal ileum and multiple colonic segments, multinucleated giant cells, acute cryptitis, and focal crypt microabscesses. No architectural distortion or dysplasia was

identified, and PAS and Wade stains were negative for fungi and bacilli, respectively (Figure 3). Together with the patchy endoscopic pattern and fistulizing perianal disease, these findings supported the diagnosis of Crohn's disease.

High-dose prednisone and azathioprine were initiated, with a planned transition to infliximab because of the severe fistulizing perianal disease and the patient's young age at disease onset. Magnetic resonance enterography showed no abnormal small-bowel mural thickening or enhancement and no intra-abdominal collections or fistulous tracts; however, it confirmed a persistent left intersphincteric fistulous tract with surrounding inflammatory and granulation tissue. Patient initially declined further surgical management and opted for conservative management of the fistula.

Figure 3. Histopathological findings supporting the diagnosis of Crohn's disease. I. Terminal ileum showing chronic active ileitis with a well-formed granuloma (a). II. Colonic biopsy demonstrating a sarcoid-like granuloma with multinucleated giant cells (b). III. Acute cryptitis with active chronic inflammation and reduced mucin production (c). IV. Focal mucosal erosion/ulceration (d) associated with chronic active granulomatous colitis (e).



During steroid taper, he developed arthralgias, episcleritis, and mild diarrhea. After infliximab was started (5 mg/kg at weeks 0, 2, and 6, then every 8 weeks), his symptoms, fistula, and inflammation resolved completely before the third dose. Fecal calprotectin normalized, and follow-up colonoscopy at one year showed complete mucosal healing. He remained adherent to scheduled infliximab infusions, and no infusion reactions, treatment-related adverse effects, or unanticipated complications were documented during follow-up.

3. Discussion

In this case, we describe a patient with histopathologically confirmed Crohn's disease diagnosed after SARS-CoV-2 infection. Recent studies suggest a pathophysiological overlap between IBD and COVID-19, providing biological plausibility for a possible association, although a definitive relationship has not been established yet. Both conditions involve upregulation of innate immune signaling genes and increased expression of ACE2 in the gastrointestinal epithelium [2]. Viral binding to ACE2, aided by transmembrane serine protease 2 (TMPRSS2), can disrupt the gut barrier, induce local inflammation, and promote dysbiosis resembling that seen in IBD [3,4]. These alterations may persist after

acute infection, even in patients naïve to antibiotic therapy. Moreover, SARS-CoV-2 can trigger autoimmune phenomena via molecular mimicry, bystander activation, and loss of self-tolerance, especially during post-infectious immune reconstitution [5]. Similar autoimmune flares are known to occur after transient immunosuppression, such as postpartum or after withdrawal of immunosuppressive therapy.

Although isolated case reports have described new-onset IBD following SARS-CoV-2 vaccination [6], available studies have not demonstrated an increased risk of IBD relapse or exacerbation after vaccination, which appears to be generally safe and well tolerated in these patients [7,8]. Vaccine-induced immune activation has been considered as a possible mechanism in some individual reports, but such events appear to be rare, and a causal relationship has not been established. In the present case, there was no relevant temporal association between vaccination and disease onset, since the patient had received his last vaccine dose in August 2021, almost one year before the onset of gastrointestinal symptoms in June 2022.

Similar cases have increasingly been reported. A literature review identified 15 case reports comprising 19 patients with newly diagnosed IBD following COVID-19 (Supplementary File 1). Most patients (79%) developed ulcerative colitis, while only four were diagnosed with CD. Ages ranged from 9 to 84 years, and fever and diarrhea were the most common initial manifestations of COVID-19. Most patients experienced mild COVID-19. Notably, none of the previously reported CD cases presented with perianal disease or required anti-TNF therapy, indicating a more severe phenotype in the present case.

In the present case, CD was diagnosed shortly after COVID-19 in an individual without previously recognized disease, providing temporal support for a possible association. However, a single case report cannot establish causality, and this temporal sequence may represent coincidence rather than a direct causal relationship. Furthermore, the possibility that previously subclinical CD was unmasked or exacerbated by SARS-CoV-2 infection cannot be excluded.

4. Conclusion

This report describes a rare case of newly diagnosed Crohn's disease presenting with severe fistulizing perianal involvement shortly after COVID-19. While the temporal sequence and clinicopathological findings support a possible association, causality cannot be established from a single case. Persistent or worsening gastrointestinal symptoms after COVID-19, especially when accompanied by alarm features such as bloody diarrhea, weight loss, perianal pain, or fistulizing disease, should prompt timely evaluation for IBD. Further prospective studies are warranted to clarify the long-term impact of COVID-19 on intestinal immune homeostasis and its possible role in the onset, exacerbation, or unmasking of IBD.

5. Patient's perspective

The patient reported that the most difficult aspect of the initial course was the intensity, persistence, and discomfort of his symptoms. The marked weight loss was particularly concerning to his family and was the main factor that prompted further diagnostic investigation. He described the fistula and diarrhea as having the greatest impact on his daily life, mainly because of pain, hygiene difficulties, and dependence on family members for daily support. He initially declined further surgical management of the fistula because he was preparing for an important examination that year and was concerned that another intervention could interfere with his studies and delay his academic progression. The indication for surgery and the risks of conservative management were explained to him, and this decision was made consciously and in agreement with the treating medical team.

Although he noticed some improvement with corticosteroid therapy, he reported that he only felt truly well after the initiation of biologic therapy. He also expressed deep

gratitude to the medical team and emphasized the essential support provided by his family, who helped him during these difficult moments. He reported no major difficulties in accessing the requested examinations or prescribed medications, as most were covered by his health insurance, and those not covered he was able to obtain privately without significant delay.

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Research Ethics Committee Approval: This case report was submitted to and approved by the Research Ethics Committee of the Pedro Ernesto University Hospital, State University of Rio de Janeiro (HUPE-UERJ), under approval number 8.425.132 and CAAE number 97945426.9.0000.5259. Written informed consent was obtained from the patient for the publication of this case report and the accompanying images. All clinical information and images were appropriately anonymized to protect patient confidentiality, with the removal of both direct and indirect identifiers. No additional interventions, procedures, or diagnostic examinations were performed beyond those required for routine clinical care. This manuscript was prepared in accordance with the CARE Guidelines for Case Reports.

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Conflicts of Interest: The authors declare no conflicts of interest.

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