ACTA SCIENTIFIC CLINICAL CASE REPORTS

Volume 5 Issue 7 July 2024

Case Report

Case Report: Hidden Truth – Patient with Ulcerative Colitis and Systemic Lupus Erythematosus with Secondary Antiphospholipid Syndrome

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Received: June 07, 2024

Published: June 16, 2024

Abstract

Background: It is well known that some viruses can modify and even induce autoimmune diseases. There are several data that suggest association of COVID19 with onset of different autoimmune diseases.

Case Presentation: Therefore, we report a case of a female patient with the diagnosis of ulcerative colitis, initially presented as acute severe form in February 2021 when she was hospitalized as COVID19 negative. Flexible sigmoidoscopy revealed severely active ulcerative colitis (Mayo subscore 3), confirmed on histopathology. Therapy according to ECCO guidelines was initiated. Since optimal response after three days was achieved, maintenance therapy, Azathioprine with Infliximab, was planned because of the initial severe presentation. However, patient reported recurrence of symptoms with fever, abdominal pain, and increased C-reactive protein. After abdominal CT scan, in lower parts of the lung, ground glass opacities were seen, and rapid antigen test on COVID19 was positive. Since patient refused admission in COVID hospital, she was sent home. Anti-TNFα therapy (Infliximab) was started two weeks from full recovery from COVID19. Endoscopic remission was achieved at week 24. However, arthralgia and constant pain under the left rib cage persisted even after successful treatment of colitis. After rheumatologists' examination, diagnosis of systemic lupus erythematosus was made in February 2022.

Conclusion: Two weeks after the resolution of symptoms in mild COVID19 cases, it is safe to start or continue with anti-TNFα therapy. IBD patients are susceptible individuals, hence regular follow up is recommended. There is a strong belief that in genetically predisposed patients, COVID19 can trigger autoimmune disease.

Keywords: Inflammatory Bowel Disease; Systemic Lupus Erythematosus; COVID-19; Gastroenterology

Background

Inflammatory Bowel Disease (IBD) is a group of chronic inflammatory conditions of the gastrointestinal tract, primarily including Crohn's disease and ulcerative colitis. IBD is characterized by periods of relapse and remission, and its etiology is thought to involve a complex interplay of genetic, environmental, immunological, and microbial factors. Patients with IBD often experience a significant impact on their quality of life due to the chronic and relapsing nature of the disease, which can lead to various complications and require long-term medical treatment [1,2].

Ulcerative colitis (UC) is a major form of IBD that specifically affects the colon and rectum. It is characterized by continuous mucosal inflammation starting from the rectum and extending proximally in a continuous manner through parts of or the entire colon [3]. The exact cause of ulcerative colitis is unknown, but it is believed to result from an inappropriate immune response in genetically predisposed individuals, triggered by environmental factors [4].

The inflammation in UC is typically limited to the mucosal layer of the colon and rectum. Histologically, it is marked by the presence

of crypt abscesses, goblet cell depletion, and mucosal ulceration. The inflammation leads to symptoms such as abdominal pain, bloody diarrhea, and an urgent need to defecate. In severe cases, complications can include toxic megacolon, perforation, and an increased risk of colorectal cancer [5,6].

Diagnosis of ulcerative colitis is based on clinical presentation, endoscopic findings, and histopathological examination [7]. The Mayo Clinic scoring system is commonly used to assess the severity of UC, which ranges from mild to severe based on stool frequency, rectal bleeding, endoscopic findings, and physician's global assessment [8].

Management of UC involves both induction and maintenance of remission. The treatment approach varies depending on the severity and extent of the disease. First-line treatments often include aminosalicylates for mild to moderate disease and corticosteroids for more severe flare-ups. Immunomodulators (e.g., azathioprine) and biologic agents (e.g., anti-TNFα therapies such as infliximab) are used for maintaining remission and in cases where patients are refractory to conventional therapies [9,10].

The COVID-19 pandemic has posed additional challenges for managing patients with ulcerative colitis. There is growing evidence suggesting that viral infections, including SARS-CoV-2, can exacerbate autoimmune conditions or trigger new onset autoimmune diseases. This interplay complicates the therapeutic strategy, especially regarding the use of immunosuppressive and biologic therapies during and after COVID-19 infection [11,12].

Case significance

This case report highlights the complexities involved in managing ulcerative colitis, especially in the context of concurrent COVID-19 infection and subsequent development of systemic lupus erythematosus (SLE). It underscores the need for a multidisciplinary approach and careful monitoring of IBD patients who develop new autoimmune conditions or contract viral infections. This case report aims to contribute to the understanding of the intricate relationship between viral infections and autoimmune diseases, particularly in genetically predisposed individuals [13,14].

Case Presentation

We report the case report of a 45-year-old female with a history of ulcerative colitis, initially presenting as an acute severe form in February 2021. The patient was hospitalized COVID-19 negative, in the time of highest pandemic rate of COVID19 infection. Flexible sigmoidoscopy revealed severely active ulcerative colitis (Mayo subscore 3), first diagnosis confirmed on histopathology. Laboratory results on admission are shown in table 1. Therapy according to ECCO guidelines was initiated, such as:

White blood cells	7,7 x 10^9/L
Red blood cells	3,84 x 10^{12}/L
Hemoglobin	10.0 g/dl
MCV (Mean Corpuscular Volume)	86,3 fL
Hematocrit	29,5%
Platelets	661 x 10^9/L
C-reactive protein	51,8 mg/L
Potassium	2,8 mmol/L
Magnesium	0,97 mmol/L
Albumin	26 g/L

Table 1: Laboratory results on admission.

- Metilprednisolon 60mg i.v. (intravenous), x1
- Metronidazole 500mg i.v. x3,
- Nadroparin 0,6mL s.c. (subcutaneous) x1
- Pantoprasole 40mg p.o. (per os) x1
- Mesalazine 4g p.o.x1
- Multi-straine high potency probiotic
- Intravenous fluid

And optimal response was achieved within three days, leading to planned maintenance therapy with Azathioprine and Infliximab. However, the patient experienced a recurrence of symptoms including fever, abdominal pain, and increased C-reactive protein. An abdominal CT scan revealed ground glass opacities (Figure 1) in the lower parts of the lungs, and a rapid antigen test for COVID-19 was positive. The patient refused admission to a COVID hospital and was sent home.

Anti-TNFα therapy (Infliximab) was started two weeks after full recovery from COVID-19 in combination with Azathioprine.

Both endoscopic and patohistological remission was achieved at week 24. Patient was on standard dosing regimen of Infliximab.

Despite this, arthralgia and persistent pain under the left rib cage continued. Initially, due to a decrease in Infliximab trough levels (trough level at 1.1 µg/mL) with no detectable antibodies, we optimized the therapy by shortening the administration interval to 4 weeks. Despite therapy optimisation, there was no clinical

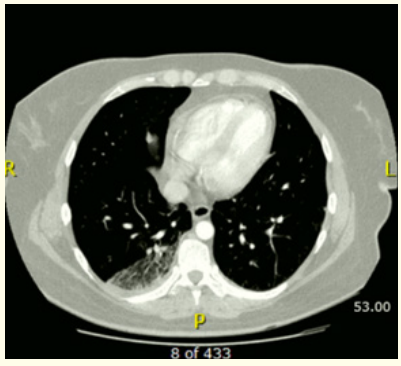

Figure 1: Ground glass opacities on CT scan.

improvement. Due to that fact, we have started rheumatological examination. Following a rheumatological examination, systemic lupus erythematosus (SLE) was diagnosed in February 2022. On table 2, we have presented antibodies that led to establishing diagnosis of systemic lupus erythematosus with secondary antifosfolipid syndrome. However, following the diagnosis of systemic lupus erythematosus (SLE), anti-TNF therapy was discontinued, and azathioprine was also withdrawn from the treatment regimen.

RF	25/cut off <30/
ACPA antibodies	4,8/cut off <20,0/
Hep-2,IIF	Positive
ANA	1:640
Anti-dsDNA antibodies	238,3/cut off <55/
Anti-histone antibodies	4,4/cut off <20/
Anti-Sm antibodies	Negative
Anti-U1RNP antibodies	
Anti-Ro/SSA antibodies	8,9/cut off <20/
Anti-Lo/SSB antibodies	Negative
Lupus anticoagulants(dRVVT)	LA nije prisutan
APTT	27, 4/25-38/
LA1	42.5/cut off <45/
Anticardiolipin antibody IgG	0, 2/cut off <48/
Anticardiolipin antibody IgM	63/cut off <44/
Anti-beta-2-glycoproteins IgG	0.9/cut off <7.0/
Anti-beta-2-glycoproteins IgM	58, 9/cut off <7.0/
C3	1,54/0,90-1,80/
C4	0, 20/0,10-0,40/
PEG	0, 240/cut off<0, 500/

Table 2: Autoantibodies that led to SLE diagnosis.

She was subsequently treated with low doses of steroids along with an antimalarial. The patient had been on long-term steroid therapy, which helped stabilize her ulcerative colitis, but this led to the development of Cushing's syndrome. From a gastroenterological perspective, the patient is on 4g of mesalamine orally, as well as mesalamine suppositories, daily. Clinical, endoscopic, and histopathological remission of ulcerative colitis is maintained. As for the systemic lupus erythematosus (SLE), arthralgia persists, but on the other hand, the disease has not progressed to involve other organs.

Discussion

Ulcerative colitis is a chronic inflammatory condition primarily affecting the colon and rectum, characterized by episodes of relapse and remission [15]. Systemic lupus erythematosus, on the other hand, is a systemic autoimmune disease with diverse clinical manifestations, including arthritis, skin rashes, and renal involvement [16]. The coexistence of UC and SLE in the same patient is relatively rare but not unprecedented. Some studies suggest that patients with IBD may have an increased risk of developing other autoimmune diseases, including SLE [1,17].

A study by Narváez., *et al*. reported an association between IBD and SLE, indicating that the immunological mechanisms underlying both diseases might share common pathways [19]. Similarly, Oliveira., *et al*. documented cases where patients with IBD developed SLE, suggesting a potential link between the two conditions [20]. The pathogenesis might involve genetic predisposition, immune dysregulation, and environmental triggers. This case reinforces the need for vigilance in monitoring IBD patients for signs of other autoimmune diseases.

Viral infections and autoimmune diseases

Viral infections are known to trigger autoimmune diseases in susceptible individuals. The molecular mimicry hypothesis suggests that viral antigens can resemble self-antigens, leading to an autoimmune response [21]. Various viruses have been implicated in the onset of autoimmune diseases, including Epstein-Barr virus, hepatitis C virus, and SARS-CoV-2 [22].

COVID-19 and autoimmunity

The COVID-19 pandemic has highlighted the potential of SARS-CoV-2 to induce autoimmune phenomena. Several studies have reported the onset of autoimmune diseases, including Guillain-Barré syndrome, Kawasaki-like disease, and SLE, following COVID-19 infection [23,24]. The virus's ability to trigger an exaggerated immune response, characterized by a cytokine storm, may contribute to the development of autoimmunity [25].

A case series by Galeotti and Bayry reviewed instances where COVID-19 was associated with new-onset autoimmune diseases, including SLE. They hypothesized that the severe inflammatory response induced by SARS-CoV-2 might unmask or trigger latent autoimmune conditions in predisposed individuals [26]. Additionally, Anaya., *et al*. discussed the mechanisms by which COVID-19 could lead to autoimmunity, emphasizing the role of viral persistence and immune dysregulation.

Implications for management

The management of UC in the context of concurrent autoimmune diseases and COVID-19 poses significant challenges. Immunosuppressive therapies, essential for controlling UC, can increase susceptibility to infections, complicating treatment strategies during a pandemic. In this case, the patient developed SLE and secondary antiphospholipid syndrome following UC treatment with biologics and steroids. This necessitated a shift in therapeutic approach, balancing the need for immunosuppression with the risk of exacerbating SLE and susceptibility to infections.

The European Crohn's and Colitis Organisation (ECCO) has provided guidance on managing IBD during the COVID-19 pandemic, recommending the continuation of necessary treatments while closely monitoring for infections. Studies have shown that anti-TNFα therapy, such as Infliximab, can be safely resumed after COVID-19 recovery, provided there is careful monitoring. This case supports these recommendations, demonstrating successful management of UC with anti-TNFα therapy post-COVID-19, albeit with subsequent autoimmune complications.

Conclusion

The interplay between UC, SLE, and COVID-19 in this case underscores the complexity of managing autoimmune diseases in the context of viral infections. It highlights the importance of a multidisciplinary approach and the need for ongoing research into the mechanisms by which viral infections can trigger autoimmune diseases. Regular follow-up and personalized treatment strategies are crucial for optimizing outcomes in such complex clinical scenarios.

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