A Case Report of Severe Ulcerative Colitis in an HIV Patient

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Abstract

We present the case of a patient with severe de novo ulcerative colitis (CU) and a simultaneous diagnosis of Human Immunodeficiency Virus (HIV) infection. These two immunologically and pathophysiologically opposing diseases are rarely found in association, and it has even been suggested that inflammatory bowel disease (IAS) may be less aggressive in HIV infections. The diagnosis is challenging, given the spectrum of diseases that can affect the colon in the context of an HIV infection. Treatment is similarly controversial considering that the use of immunomodulators or biological block another component of the immune system that could enhance the state of immunosuppression in this group of patients. Natural history, treatment and prognosis remain a challenge for currently available evidence.

Keywords

Inflammatory bowel disease, ulcerative colitis, human immunodeficiency virus.

INTRODUCTION

Inflammatory bowel disease (IBD) is thought to be a persistent and an aggressive immune response mediated by cells in response to an unknown environmental antigen in a genetically susceptible host. (1, 2) In contrast, HIV infections result in diminished immune response in the gastrointestinal tract secondary to an early and profound loss of CD4 + T cells which makes the digestive tract susceptible to opportunistic infections. (3, 4)

In IBD, macrophages are prepared for inflammation and produce a variety of chemokines and cytokines, some of which may decrease expression of CCR5 and CD4 thereby limiting the ability of HIV to infect intestinal microphages. On the other hand, some proinflammatory cytokines produced by macrophages in IBD may also increase the susceptibility of CD4 + lymphocytes to HIV due to cellular activation. The effect of HIV-infected macrophages on the pathogenesis of IBD is not yet clear because of these countervailing tendencies to produce both proinflammatory (TNFα) and anti-inflammatory cytokines (IL-10). Other pathophysiological mechanisms show that, in IBD, intestinal dendritic cells produce high levels of Th1 cytokines, such as IL-2 and IL-23, which may increase HIV's infectivity, Nevertheless, in the mucosa of patients with HIV, the loss of CD4+ T cells can attenuate the pathogenesis of IBD due to loss of the function of these cells. Finally, Natural Killer T Cells (NK) may also play a proinflammatory role in the pathogenesis of UC, but when there is also an HIV infection, there is a decrease in CD4 expressing NK. Thus, through these mechanisms, HIV could diminish the UC phenotype. (4, 5)

The clinical combination of HIV and IBD also has implications for the therapeutic approach. The role of biologics for treatment of IBD is well established, but their effects

on HIV infections are poorly understood. The objective of presenting this clinical case is to review the pathophysiological, clinical and therapeutic issues in cases of concomitant presentation of these two diseases.

CLINICAL CASE

The patient was a 53-year-old unmarried male economist who was an active smoker. He was admitted to the Emergency Department after two months of changes in bowel movements and episodes of rectal bleeding. In the week prior to admission, he had had bowel movements five to eight times a day with visible mucus and blood. At admission, he presented abundant rectal bleeding, asthenia, adynamia and lipothymia. Physical examination showed dehydrated, generalized mucocutaneous pallor, somnolence, tachycardia and hypotension. Patient did not respond to crystalloid liquids, presented hemodynamic instability and required vasopressor support with noradrenaline and transfusion of two units of packed red blood cells (PRBC).

Initially, a diagnosis of mixed hypovolemic and septic shock of gastrointestinal origin was considered. Treatment with intravenous ampicillin-sulbactam and metronidazole was begun and the patient was admitted to the intensive care unit (ICU). Computed tomography of the abdomen showed thickening of the walls of the colon and rectum, with abnormal enhancement of the mucosa. These findings are compatible with pancolitis (Figure 1).

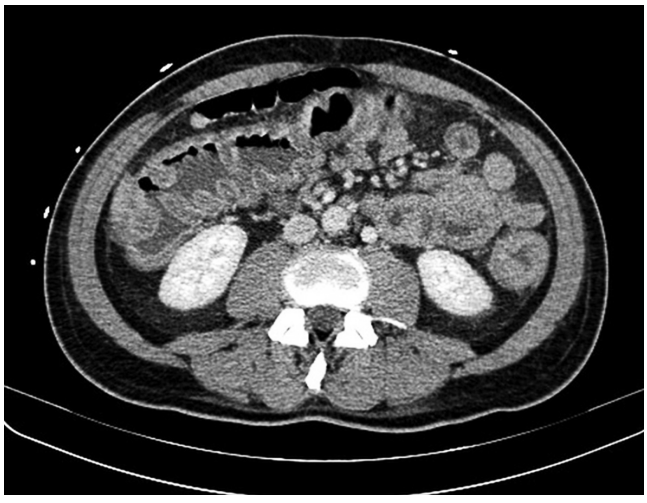

Figure 1. Abdominal contrast CT scan showing thickening of the walls of the colon without pericolonic inflammatory changes. Findings suggest pancolitis.

An ELISA test for clostridium difficile toxin and a colonoscopy were performed once the patient had been stabilized. Total mucosal involvement was found in the rectum with loss of vascular pattern, small ulcerations in the rectum, and larger, deeper ulcerations in the left colon, and loss of haustra on the pathway examined. The procedure was suspended in the distal descending colon because of severe inflammatory involvement of the mucosa (Figure 2).

Multiple biopsy samples confirmed severe UC, with structural distortion of the intestinal crypts, decreased branching and numbers of goblet cells, mixed with dense lymphoplasmacytic inflammatory infiltrate associated with very characteristic cryptic microabscesses (Figure 3).

All findings confirmed severe UC type IBD according to the Mayo Clinic classification (11 points) and the Truelove and Witts' severity index (number of bowel movements, rectal bleeding, anemia, hypoalbuminemia and hypokalemia). Treatment was begun with 400 mg/day intravenous hydrocortisone and two grams of mesalazine granules every 12 hours. The patient was given intestinal rest and peripheral parenteral nutrition was initiated. By the third day an improvement in clinical status had been achieved, but multiple liquid bowel movements with red blood persisted. The patient had up to 18 bowel movements in one day despite treatment. A diagnosis of toxic megacolon was discarded with a simple abdominal x-ray which was normal. A Ho score of 5 was calculated which indicated a high risk of steroid failure and a high probability that the patient would require additional treatment with cyclosporine or biologics. A chest x-ray, tuberculus test (PPD), blood tests for hepatitis B and C, and ELISA for human immunodeficiency virus (HIV) were requested.

On the fourth day of hospitalization, the report from the ELISA HIV test was reactive. A Western Blot was requested for confirmation. In addition, the patient's viral load for CMV was tested and histology with special staining was requested. Both were negative. The patient's behavior continued to be torpid with multiple episodes of rectal bleeding. In addition, it was clear that the patient now had a condition of HIV immunosuppression even though UC rescue therapy with immunosuppressants was being considered. Fortunately, it was not needed and on the fifth day the patient presented clinical improvement with a decrease in the number of stools and less rectal bleeding. Intravenous administration of steroids was replaced with 40 mg/day of oral prednisolone. The patient's clinical evolution was appropriate which allowed progressive decreases of prednisolone doses. Dosages were decreased 5 mg each week until the dosage arrived at 20 mg/day. After that, the dosage was decreased by 2.5 mg/week until suspension. The patient continued to receive two grams of mesalazine every 12 hours which maintained UC under good control.

The patient was assessed by the Infectious Diseases Department which confirmed the HIV infection by Western Blot and an absolute CD4 + count at 445 cells/mm^3. Intestinal infections by other opportunistic germs were

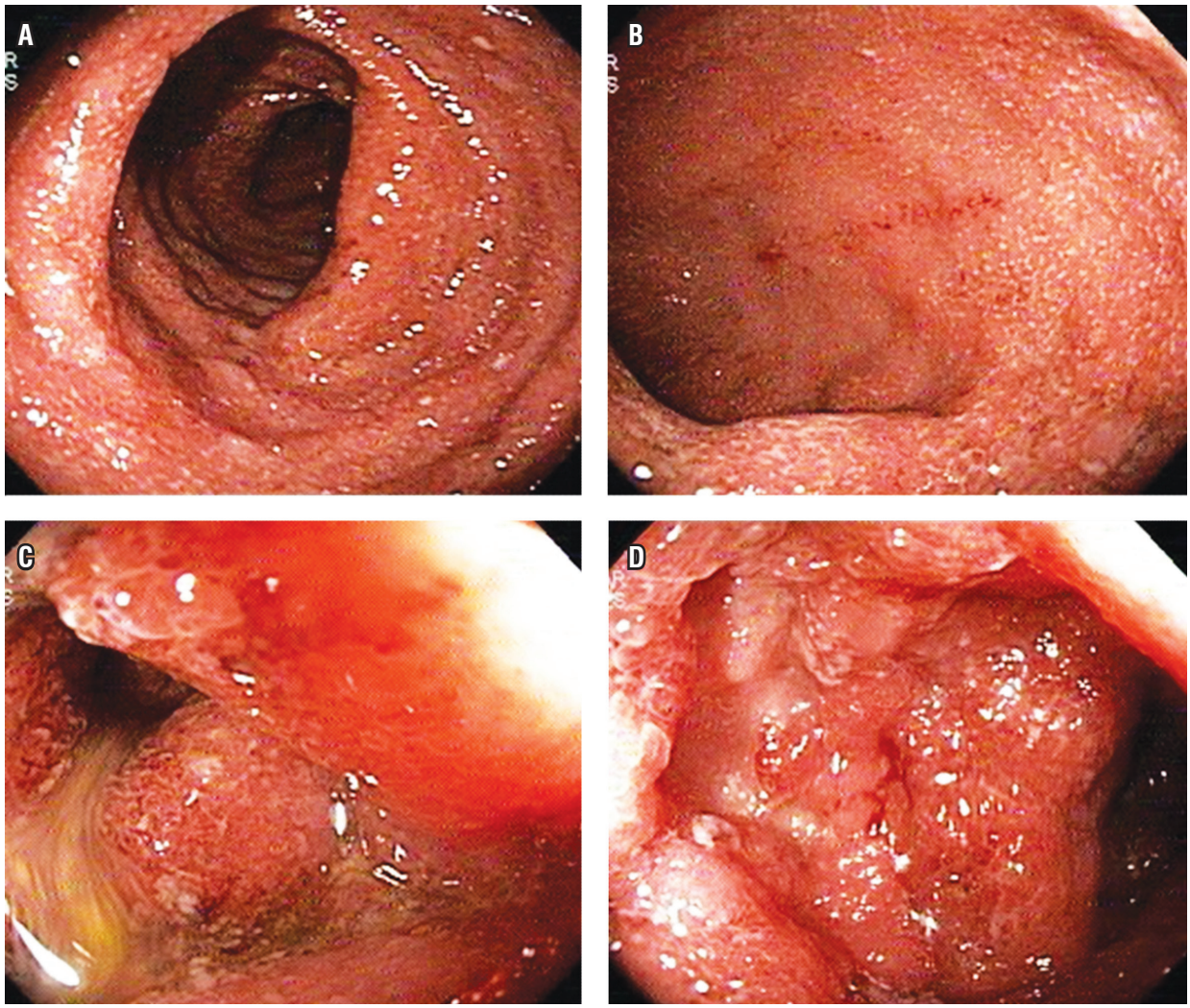

Figure 2. A and B. Colonoscopy showing total involvement of the rectal mucosa with loss of vascular pattern and small ulcerations. **C and D**. Larger and deeper ulcerations in the sigmoid colon with severe involvement of the mucosa.

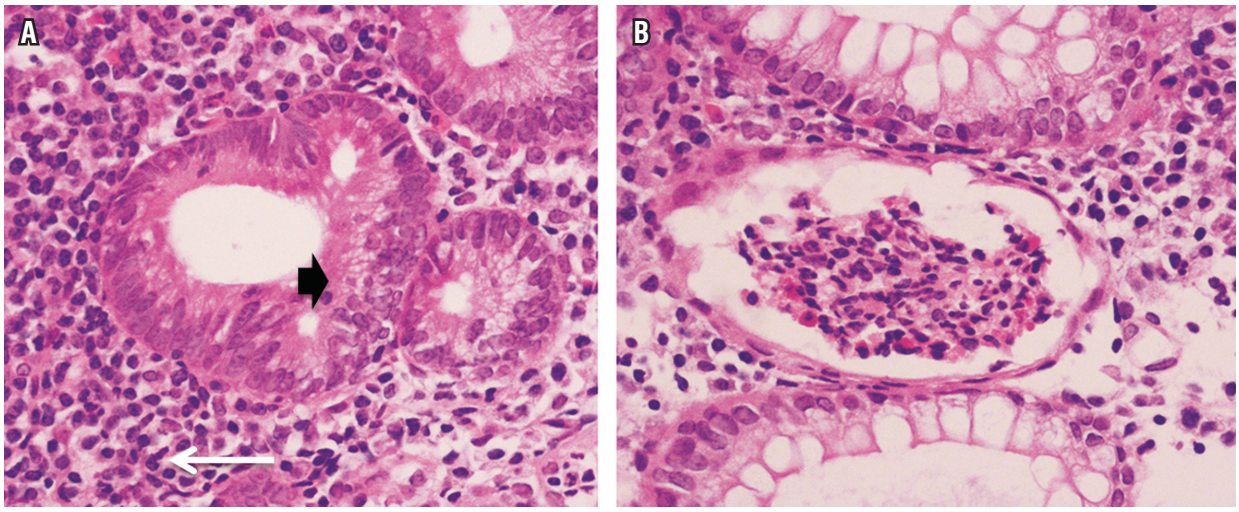

Figure 3. A. Histopathology showing marked loss of glandular architecture (arrowhead) with dense lymphoplasmacytic inflammatory infiltrate (arrow). **B.** Cryptic microabscesses.

ruled out. Outpatient treatment for HIV using antiretroviral therapy with efavirenz, lamivudine and abacavir was initiated along with continuous follow-up and monitoring.

DISCUSSION

The diagnosis of HIV in a patient with UC changes the management scenario and approach to the case. The relevance of diagnosing HIV early in UC is a matter of discussion, with screening being conducted only for those at risk rather than more sensitive and universal systematic screening for all patients with UC which would allow more timely diagnosis and decrease the likelihood that a late diagnosis may lead to worse outcomes. (6)

The prevalence of IBD in patients with HIV infections has not been established, but it is not a pathophysiologically frequent association. Classically, profound and selective losses of CD4+T lymphocytes are described in patients with HIV infections. This leaves the intestinal tract in a state of immune vulnerability. In contrast, IBD is related to several genetic, environmental and immunological factors that are characterized overly active immune responses. (4)

Several case reports have described a tendency toward symptomatic remission of IBD directly proportional to decreases in CD4 cell counts. (7) Modulation of IBD has been observed in patients with diseases such as HIV that impair the immune system, as would be expected, Nevertheless, it is striking that control can be maintained or easily achieved, including when there are high CD4 counts, such as in the case of the patient described here, or when immune reconstitution occurs with initiation of antiretroviral therapy. (4)

One of the most complete descriptions of these outcome is found in a prospective study of 20 patients with IBD and HIV who were compared with 40 control patients who had IBD but who did not have HIV. In the HIV-positive group, the relapse rate was 0.016 episodes per year compared to 0.053 episodes in the control group, a difference that did not achieve statistical significance. (2)

Regarding treatment of IBD with biologics, it is easy to suppose that this should lead to greater immunosuppression in patients with HIV. However, there is evidence that the TNFα in HIV infections contributes to pathogenesis, promotes viral replication and is related to the activation of apoptotic T cells in the HIV process. In turn, HIV seems to induce the expression of TNF, either directly or indirectly by increasing TNF receptor activation through molecular mimicry. (8, 9) Thus, anti-TNFα agents may have a beneficial potential for HIV patients and may be relatively safe for patients with concomitant IBD and HIV infections. The only series of HIV patients treated with anti-TNFα agents to date included mostly patients treated for rheumatic diseases, but there was no evidence of opportunistic infectious complications or increased viral loads.

The use of anti-TNF agents in any patient with high CD4 counts, whether or not the patient is receiving antiretroviral therapy, has been examined. It was confirmed that anti-TNF agents such as adalimumab, infliximab and etanercept have minimal impact on HIV viral load and CD4 counts and are therefore relatively safe. However, the use of anti-TNF agents remains limited for patients with low CD4 counts and high viral loads. (4, 10)

Recently, antiα4β7 agents including natalizumab, vedolizumab and ertolizumab have begun to be used to treat IBD. This makes it important to remember that HIV binds to the α4β7 integrin through the envelope glycoprotein GP120 which serves as a receptor for intestinal lymphocytes. Coupling of α4β7 to HIV may result in increased infection and contribute to the decrease of CD4 + T cells in the intestinal mucosa. (11) This suggests a potential benefit of anti-4β7 therapy in HIV, but since there are only a few recent studies performed in vitro in Rhesus macaques with conflicting results, further studies are required. At present, pathophysiological considerations support the use of selective α4β7 inhibitors such as vedolizumab, which could become first-line tools for the treatment of IBD patients who have HIV. (4)

As for the use of immunomodulators, such as azathioprine, data are also limited. One recent case series has been published. It included seven patients treated with azathioprine for different pathologies who were simultaneously receiving antiretroviral therapy. Average treatment time was 12 months with 6 months of follow-up after suspension. No serious opportunistic infections or malignancies were reported. Two deaths were reported but were not associated with the use of azathioprine. Data were compared with control patients without significant differences in cell counts or viral loads. (12) However, studies with a larger number of patients are required before this treatment can be recommended for use.

CONCLUSION

In conclusion, this case report highlights the need to develop research to establish the relationship between the pathogenesis of HIV and the pathogenesis of UC, antiretroviral therapy, biologics and immunomodulators. The scarcity of current evidence prevents recommendation of appropriate therapy for these patients.

Presentation

Leadership Seedbed Contest, organized by ABBVIE on August 27, 2015.

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