Extensive ulcerative colitis and extraintestinal manifestations in a patient with HIV infection and significant CD4 T-cell lymphopenia

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ABSTRACT

We report a heterosexual patient with HIV infection and a CD4 T-cell count of 0.45 × 10⁹/L who developed mild ulcerative proctitis, sacroileitis and oligoarthritis. While he was treated with 5-aminosalicylic enemas, the patient rapidly developed severe pancolitis. An emergency colectomy without proctectomy was performed. A few months later, he suffered recurrence of ulcerative proctitis, aggravation of arthritic pain and developed anterior uveitis. All symptoms disappeared after proctectomy. There was no evidence for opportunistic infection or Kaposi’s sarcoma. Antineutrophil cytoplasmic antibodies were positive and the HLA-B27 antigen was present. CD4 counts were lower during the phases of active disease than during remission. This case demonstrates that severe ulcerative colitis can occur in the presence of moderate T-cell defects. In view of a recent report of remission of Crohn’s disease under comparable circumstances, it is possible that the extent of T-cell involvement in both diseases is radically different.

Key words: Ulcerative colitis — Human immunodeficiency virus.

Exacerbation of local T-cell responses has been demonstrated in inflammatory bowel disease (IBD) (1-3). However, it remains to be determined if the disease is due to intrinsic abnormalities of immunoregulatory mechanisms or if T-cell activation is secondary to sustained stimulation due to defects in the mucosal barrier. Furthermore, the respective participation of non-specific inflammatory responses versus T-cell mediated immunity in tissue damage is not precisely established. Therefore, specific features of IBD in patients with selective defects of T-cell mediated immunity are of major interest. We describe the severe course of ulcerative colitis (UC) in a patient with HIV infection and significant drop in CD4 T-cell counts.

CASE HISTORY

A 35-year-old heterosexual man presented to CHBA-Seraing Hospital in January 1992 with rectal bleeding and articular pain. Proctorrhagia without diarrhea had been present since July 1991. Migratory arthralgia involving the left hip, the toes and the back appeared in November 1991. The patient presented with general malaise and fever up to 38°C. Sigmoidoscopy showed ulcerative lesions confined to the rectal mucosa. Rectal biopsy specimen revealed mucosal ulceration, crypt abscess...
formation in the mucosal and submucosal layers and prominent mixed inflammatory reaction with polymorphonuclear neutrophils (PMN) and lymphocytes. There were no granulomas, no viral inclusions and no evidence for mycobacterial infection. Laboratory examination revealed a prominent inflammatory reaction: fibrinogen 6.87 g/L, C-reactive protein (CRP) 67 mg/L, erythrocyte sedimentation rate (ESR) 63 mm/h. Hemoglobin was normal at 13.3 g/100 mL. Because of high risk sexual behavior from 1984 to 1988, antibody testing for HIV was proposed to the patient and revealed positive. The total lymphocyte count was 1.53 × 10^9/L (N : 1.00-4.80 × 10^9/L), the total CD4 T-cells were 0.45 × 10^9/L (N : 0.70-1.10 × 10^9/L) and the total CD8 T-cell count was 0.73 × 10^9/L (N : 0.50-0.90 × 10^9/L). HIV-1 p24 antigen was negative. The patient was classified as having mild ulcerative proctitis (4) and treatment with 5-aminosalicylic enemas (Colitolfalk®) was started. Piroxicam (Feldene®) 20 mg/day was given for the arthralgia. The patient improved and remained stable during several weeks.

In March 1992, he suffered sudden and massive rectal bleeding with severe hypovolemic shock. Emergency colec- tomy without proctectomy was performed. The entire colonic mucosa appeared ulcerated and haemorrhagic with prominent infiltration by PMN. No histological evidence of Kaposi’s sarcoma, lymphoma or opportunistic infection, including cytomegalovirus (CMV) and amoebiasis, was detected. No anti-CMV IgM was found in the serum. The patient progressively improved and was discharged from the hospital in May 1992. When he left the hospital, a significant inflammatory reaction was still present (fibrinogen : 5.55 g/L, ESR : 65 mm/h). The total CD4 T-cell count was 0.62 × 10^9/L and the total CD8 T-cell count was 1.02 × 10^9/L.

From May to December 1992, the general condition kept improving slowly. Occasional rectal bleeding was still present. The patient described the persistence of moderate pain in the knees, the ankles and the back. Inflammatory reaction never subsided. CD4 T-cell counts remained between 0.50 and 0.60 × 10^9/L. In January 1993, rectal bleeding and articular pain rapidly worsened and the patient was admitted at CHU Sart-Tilman Hospital. Rectoscopy showed a fragile and inflamed mucosa with pseudopolyps. Biopsy confirmed typical histology without evidence of opportunistic infection, lymphoma or Kaposi’s sarcoma. There was also a large ulceration in the anal canal which was thought to be infectious, but serology for Treponema pallidum was negative and biopsies showed non specific features. That ulceration healed spontaneously. Radiology demonstrated left sacroileitis. Juxta- articular osteopenia without erosion was observed at the level of the left knee and of the left ankle. Effusion was also present in the left knee. Soon after, the patient developed ocular discomfort and was diagnosed by the mitogen BMA030 : 12 790 cpm compared to 21 752 cpm (95 % confidence interval : 14 547-28 955) in controls. The patient is currently free of any rectal bleeding or articular pain. His general condition is improving.

**DISCUSSION**

We have described the course of an ulcerative colitis in an HLA-B27 positive patient infected with the HIV-1 virus and presenting with a significant decrease of CD4 T-cells. Few cases of inflammatory bowel disease in HIV-infected subjects have been reported so far (5-8). In several cases, homosexual patients with chronic HIV-infection were initially diagnosed as having UC and were ultimately found to present Kaposi’s sarcoma of the bowel (9, 10). James (5) described the complete remission of a long-standing Crohn’s disease (CD) in an HIV-infected patient when his CD4 T-cell counts reached 0.41 × 10^9/L. This was further confirmed by other case reports from France (8). Franke et al. (6) reported severe UC in a homosexual patient with chronic HIV-1 infection and CD4 T-cells at 0.50 × 10^9/L. Although the diagnosis was not histologically established in Franke’s report, there was a strong clinical presumption given the rapid response to prednisone and mesalazine. In another report, an heterosexual patient with lower CD4 T-cell counts (0.22 × 10^9/L) developed acute UC after amoebic dysentery. The diagnosis was confirmed by the biopsy and the response to prednisone and mesalazine (7).

In the present case, the diagnosis of ulcerative colitis has been firmly established by typical histological findings, absence of evidence for CMV infection, amoebiasis and Kaposi’s sarcoma and negativity of stool cultures. Several non-specific abnormalities often associated with UC such as the positivity for antineutrophil cytoplasmic antibodies (11), increased serum IgG1 (12), increased proportion of circulating CD8 T-cells expressing CD57 (13) and increased level of sIL-2R (14) were also found in our patient. However, the diagnostic value of these non-specific features is low in the present case because several of them have also been described in HIV patients or infectious colitis. Moreover, this patient had a rather severe disease. First, the disease, initially localized to the rectum, rapidly involved the entire colonic mucosa. Classically, such a rapid extension of the disease is found only in 5 to 10 % of the cases (15). Second, he had a
severe manifestation of this extensive colitis with major bleeding leading to an emergency colectomy. The use of a classical treatment of severe UC with IV steroids could have been considered in such a situation. However the life-threatening bleeding with hypovolemic shock motivated the gastroenterological team to perform a colectomy. Third, the extent of extraintestinal manifestations was unusually severe with anterior uveitis and major limitation of motion due to sacroileitis and migratory oligoarthritis. Ocular manifestations are found in only 5% of patients with IBD and are associated with particular severity (16).

Our patient did not develop any opportunistic infection before the diagnosis of IBD, however it is important to note that his CD4 T-cell counts were in the same order of magnitude than those associated with remission of CD in James’ study (5). Furthermore, it is well established that striking functional defects of CD4 T-cells can be observed in asymptomatic HIV-infected patients before the collapse of CD4 counts (17, 18). Indeed our patient presented a mild defect in lymphocyte proliferation to the mitogen BMA030. This suggests that a moderate CD4 T-cell defect does not inhibit the course of UC and indicates that the involvement of T-cell mediated immunity in CD and UC might be fundamentally different. This hypothesis is also supported by studies on T-cells characteristics and activity in IBD. Phenotypic signs of T-cell activation in situ are less prominent in UC than in CD (14), furthermore stimulated-interleukin-2 (IL-2) secretion by intestinal T-cells is more impaired in UC than in CD (19, 20). A recent study of the lymphokine production by CD4 + lamina propria lymphocytes in CD and UC showed significant differences (21). There was an increased production of IFN-γ in CD and of Interleukin-10 (IL-10) is described in HIV infection (24) and could be related with HIV infection since the association of this infection with other musculo-skeletal syndromes such as Reiter’s syndrome has been well established, especially in HLA-B27 patients (25).

The influence of UC on the course of HIV infection has to be addressed. It is interesting to note that the CD4 T-cell counts were significantly lower when the disease was diagnosed, rose after colectomy, and decreased again during the recurrence of the symptoms in December 1992. Furthermore, the appearance of circulating HIV p24 antigen in this patient was unusual given the absence of major immunodeficiency. It may indicate that the immune activation associated with UC (as reflected in this patient by the increased levels of sIL-2R) might enhance HIV replication and accelerate the course of the disease.

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REFERENCES


