

[CASE REPORT]

An HIV-infected Patient with Confirmed Overlapping Complications of Severe Amebic Colitis and CMV Enteritis

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Abstract:

We herein report a case of simultaneous amebic colitis and cytomegalovirus (CMV) enteritis in an HIV-infected patient. The patient was a 40-year-old man who developed bloody stool and diarrhea. We diagnosed him with severe amebic colitis associated with HIV infection and administered metronidazole. While his symptoms began to improve, the patient then developed CMV enteritis. We administered ganciclovir, and his symptoms improved. However, despite control of the infection, stenosis of the descending colon caused intestinal obstruction, and colostomy was performed. This case shows the importance of considering the possibility of simultaneous infection when gastrointestinal symptoms appear in people infected with HIV.

Key words: HIV, CMV enteritis, amebic colitis, colostomy

(Intern Med 57: 1855-1860, 2018)

(DOI: 10.2169/internalmedicine.0112-17)

Introduction

Human immunodeficiency virus (HIV) infects and destroys CD4-positive T cells (CD4 cells), which control cellular immunity. With the advent of antiretroviral therapy (ART), the prognosis of patients with HIV infection has vastly improved (1). However, HIV infection causes various opportunistic infections, and sexually transmitted diseases occur frequently in Japan among men who have sex with HIV-infected men (2). We herein report the case of an HIV-infected patient with confirmed overlapping complications of severe amebic colitis and cytomegalovirus (CMV) enteritis.

Case Report

The patient was a 40-year-old, previously healthy man. He was admitted to the hospital because of a fever and was diagnosed with hydronephrosis associated with bilateral kid-

ney stones. Antibiotics were administered, and ureteral stents were placed, and the patient's fever improved. However, during treatment, the patient experienced bloody stool, diarrhea and abdominal pain. He was diagnosed with colitis and was treated with fasting, but his symptoms did not improve. At this point, he was transferred to our hospital for colitis treatment. On admission, his temperature was 38.2°C, pulse rate 90 beats/minute, respiratory rate 18 breaths/minute and blood pressure 147/73 mmHg. There was moderate tenderness in the lower abdomen. A peripheral blood examination showed mild anemia, an elevated inflammatory response and hypoalbuminemia. Furthermore, the patient tested positive for HIV antibodies, with a CD4 cell count of just 138.9 cells/ μ l. Accordingly, we diagnosed the patient with HIV infection.

The results for hepatitis B surface antigen (HBs Ag) and hepatitis C virus (HCV) antibody were both negative. Computed tomography (CT) showed edematous changes in the large intestine and part of the ileum (Fig. 1). Colonoscopy

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Received: August 28, 2017; Accepted: November 28, 2017; Advance Publication by J-STAGE: February 28, 2018

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revealed irregular shallow ulcers and verrucous erosions from the sigmoid colon to the rectum, and extensive off-white exudate adhered to the mucosa (Fig. 2). Amebic colitis was suspected based on the endoscopy results, and biopsies were taken from the ulcer base and ulcer margin. A histopathological examination of the large intestine mucosa revealed the presence of *Entamoeba histolytica* trophozoites,

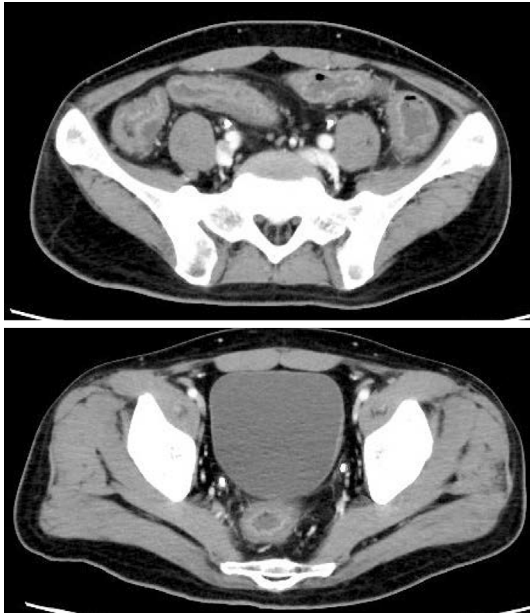


Figure 1. CT findings on admission, showing edematous changes in the colon.

which periodic acid-Schiff (PAS) staining revealed contained ingested erythrocytes (Fig. 3). An indirect immunofluorescence assay confirmed the presence of *E. histolytica* trophozoites, and the serum *Entamoeba* antibody levels were 400 times higher than normal. At this point, the patient was diagnosed with amebic colitis.

CMV inclusion bodies were not observed in the pathology specimens. Blood tests for CMV-C7HRP and CMV-IgM antibodies were both negative, but the CMV-IgG test was positive. Therefore, CMV was diagnosed as an existing infection.

We started the administration of metronidazole at 2,250 mg/day for amebic colitis. The symptoms and inflammatory markers showed some improvement, but recurrence of abdominal pain and an increase in stool frequency were observed from hospital day 17. Colonoscopy was performed again on hospital day 20 (Fig. 4). Extensive shallow ulcers were observed from the sigmoid colon to the rectum, and some were accompanied by punched-out ulcers. We performed biopsies of the ulcer bases and margins. Histopathology showed inflammatory cell infiltration, mainly neutrophils and giant cells, with nuclear inclusions in the large intestine mucosa. CMV-infected cells were identified by immunohistochemical staining using anti-CMV monoclonal antibodies (Fig. 5). Blood samples were CMV antigen-positive (C10-/C11-positive cell ratio: 49/38).

CMV enteritis was diagnosed based on the clinical symptoms, characteristic colonoscopy findings, CMV antigenemia and detection of nuclear inclusion bodies and CMV cells

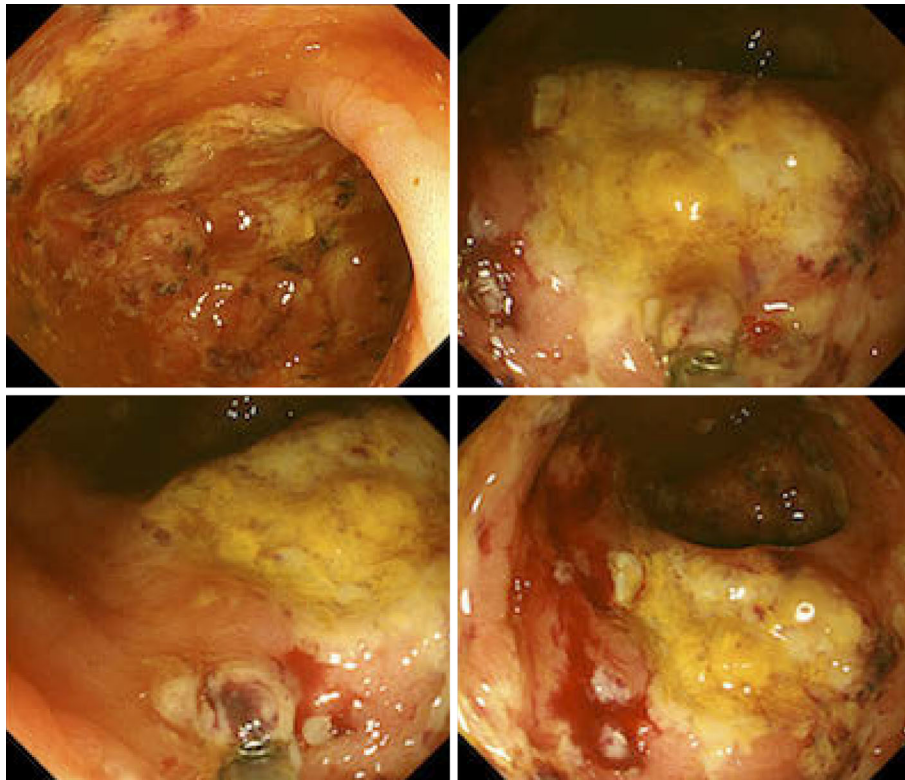


Figure 2. Colonoscopy on admission, showing irregular shallow ulcers from the rectum to the sigmoid colon and extensive white exudate adhering to the mucosa.

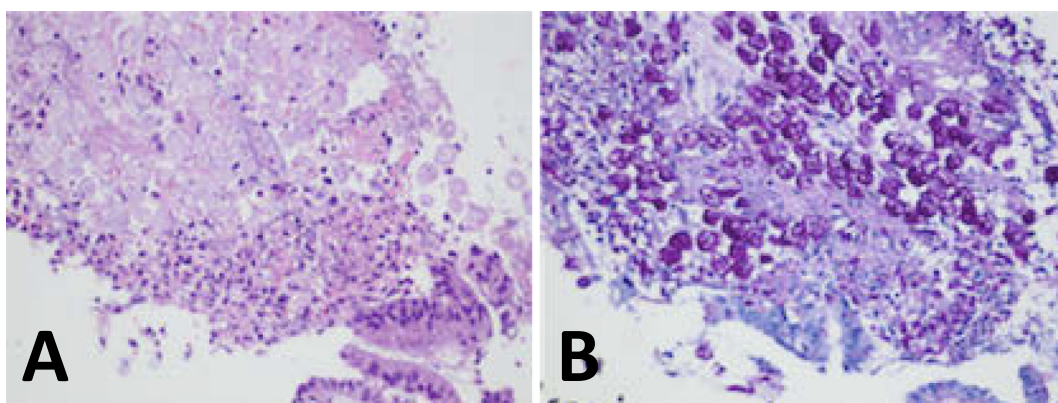


Figure 3. Histological findings of the sigmoid colon biopsy: A) *Entamoeba histolytica* trophozoites present in the mucosa (Hematoxylin and Eosin staining, 100× original magnification) and B) *E. histolytica* trophozoites containing ingested erythrocytes in the mucosa (periodic acid-Schiff stain, 100× original magnification).

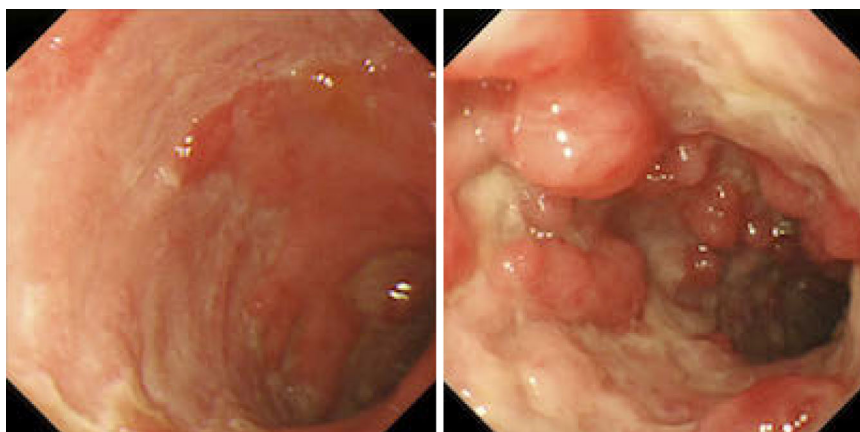


Figure 4. Colonoscopy performed on hospital day 20, showing extensive shallow ulcers from the sigmoid colon to the rectum, some accompanied by punched-out ulcers.

from biopsies of lesion sites. Ganciclovir at 500 mg/day was started, and the symptoms improved. ART (dolutegravir and tenofovir/emtricitabine) was started on hospital day 62. Abdominal bloating then appeared on hospital day 75. CT revealed stenosis of the descending colon and dilation of the oral side of the intestinal tract (Fig. 6). Colonoscopy revealed such a high degree of stenosis that the colonoscope could not be passed through the descending colon. Active ulcers were not found in the stricture region, and a biopsy showed that neither amebic colitis nor CMV enteritis were present. The stenosis was considered to have been caused by scarring during the healing of enteritis. Colostomy was performed on hospital day 86.

Discussion

For people living with HIV infection, a diagnosis with one or more indicator diseases leads to a diagnosis of acquired immunodeficiency syndrome (AIDS). AIDS-defining illnesses include various opportunistic infections and opportunistic tumors, including CMV enteritis. Furthermore, in Ja-

pan, a marked increase in the incidence of amebic colitis as a sexually transmitted disease has been noted (2). Rates of amebic colitis are reportedly as high as 37-50% among those infected with HIV (3). Amebic colitis is an intestinal infection caused by the amebae of the *Entamoeba* group, and it manifests as diarrhea, viscid stools and abdominal pain. In many cases, amebic colitis presents with a chronic course. The rectum and cecum are predilection sites, but *Entamoeba* are sometimes present throughout the colon (2). Typically, endoscopic investigation reveals amebic colitis as red aphthoid lesions with irregular white exudate at the top. The ulcer base is shallow, with extensive white exudate adhering to the mucosa. Amebic colitis is diagnosed by detecting *E. histolytica* trophoblasts or cysts in fecal samples or by detecting trophoblasts in biopsy tissue collected by colonoscopy. The measurement of serum ameba antibody levels can also aid in the diagnosis. In the present case, the endoscopic results were typical of those for amebic colitis. Additional evidence by way of ameba detection in biopsy tissue and positive serum ameba antibody results helped us reach a diagnosis of amebic colitis.

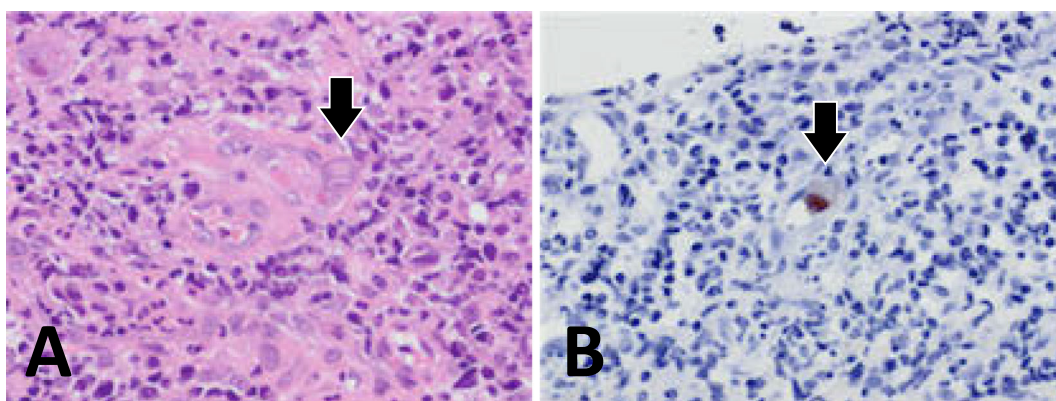


Figure 5. Histology of the sigmoid colon biopsy: A) inflammatory cell infiltration, mainly of neutrophils and giant cells, with nuclear inclusion in the colonic mucosa (black arrow, Hematoxylin and Eosin staining, 400× original magnification); B) CMV-infected cells with nuclear inclusion (black arrow) (immunohistochemical stain using anti-CMV monoclonal antibody, 100× original magnification). CMV: cytomegalovirus

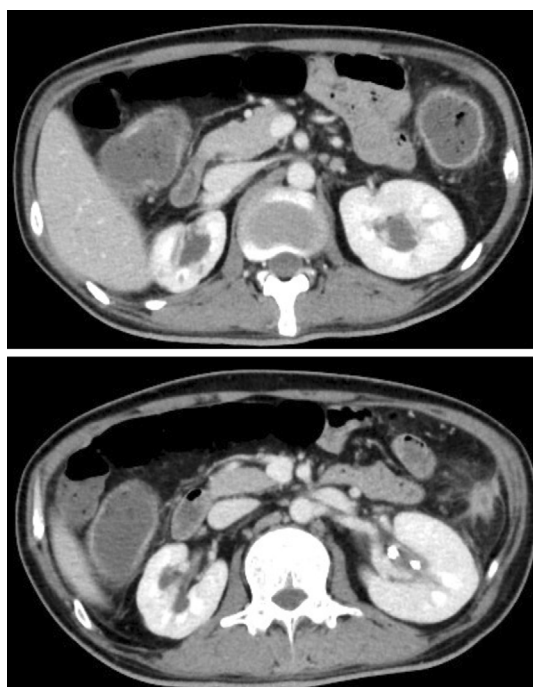


Figure 6. CT findings on hospital day 75, showing stenosis of the descending colon and dilation of the oral side of the intestinal tract.

CMV is a DNA virus belonging to the family Herpesviridae. After primary infection, CMV remains latent in infected cells, leading to subclinical infection. In Japan, the anti-CMV antibody prevalence is estimated to be 60% to 80% (4), and many CMV enteritis cases are diagnosed as opportunistic infections. Endoscopic findings typically show circular punched-out or irregular-shaped ulcers. The diagnostic criteria are as follows: 1) clinical symptoms, which may include diarrhea, bloody stool and abdominal pain; 2) the presence of organ lesions and 3) the detection of CMV in lesion tissue. In addition, immunostaining and the proof of inclusion bodies in endoscopic biopsy samples are useful for

Table 1. The Relationship between HIV Infection Activity and Gastrointestinal Disease (5).

	Disease	CD4 positive cells
1	CMV enteritis	>100/μL
2	Amebic colitis	-
3	Condylomata Acuminata	-
4	Kaposi's sarcoma	>500/μL
5	Malignant Lymphoma	>100/μL

CMV: cytomegalovirus

a diagnosis (4). In our case, CMV enteritis was diagnosed because of characteristic endoscopic findings, detection of CMV in biopsy tissue and CMV antigenemia.

In general, after a diagnosis of AIDS, it is recommended that ART be started as soon as possible (5). However, there is a case report of small bowel perforation secondary to CMV-related immune reconstitution inflammatory syndrome in an AIDS patient (6). There is no conclusive indication regarding the timing for the initiation of ART in patients complicated by CMV infection. In our hospital, if obvious organ symptoms of CMV infection are found in a patient, we generally schedule ART initiation for after the improvement in the CMV symptoms. In the present case, we waited to initiate ART until the gastrointestinal symptoms induced by ganciclovir administration for CMV were resolved.

We diagnosed the present patient first with amebic colitis and then with CMV enteritis during the same hospitalization period. For gastrointestinal infections in people infected with HIV, CMV enteritis is regarded as an opportunistic infection, although the onset of amebic colitis is not considered to be related to HIV infection (7). Table 1 shows the relationship between HIV infection and gastrointestinal disease. In our patient, the CD4 count at the onset of amebic colitis was 138.9 cells/μL, suggesting advanced HIV infection and immunodeficiency. Although CMV enteritis was not suspected at this time, CMV-IgG was positive, confirming a

Table 2. The Breakdown of the Patients with HIV Infection Complicated with Lower Gastrointestinal Disease at Our Hospital.

	Age	Gender	CD4 (μL)	Diagnosis	Site of lesion	Endoscopic finding	Treatment
1	29	M	22.4	CMV enteritis	Colon	Punched-out ulcer	Ganciclovir
2	40	M	64.3	Amebic colitis CMV colitis	Colon	Extensive dirty white moss adhering Punched-out ulcer	Metronidazole Ganciclovir
3	65	M	5.4	Malignant Lymphoma	Ileum	Extensive irregular ulcer Irregular elevated lesion	Surgery
4	44	M	414.5	Squamous papilloma	Anal canal	Irregular elevated lesion	Surgery
5	47	M	138.9	Amebic colitis CMV colitis	Colon	Extensive irregular ulcer Extensive dirty white moss adhering Punched-out ulcer	Metronidazole Ganciclovir

Table 3. Data on Two Previously Reported Cases of Intestinal Stenosis due to Amebic Colitis and One Case at Our Hospital (9, 10).

	Reference	Age	Gender	Site of lesion	Treatment
1	(9)	34	F	Terminal ileum	Partial resection of ileum
2	(10)	62	M	Sigmoid colon	Colostomy
3	Our case	40	M	Descending colon	Colostomy

previous CMV infection. The CD4 count at the onset of CMV enteritis was 142.9 cells/ μL , showing that the degree of immunodeficiency had not significantly changed since the onset of amebic colitis. We suspect that this persistent immunodeficiency allowed for the reactivation of CMV and the onset of CMV enteritis. Thus, amebic colitis and CMV enteritis may appear simultaneously in patients with HIV infection. In our case, it was thought that the patient's immunocompetence upon hospitalization was compromised to the degree that CMV enteritis was able to develop simultaneously with amebic enteritis.

Nebiki et al. (8) reviewed the initial colonoscopy findings for patients infected with HIV and reported that the incidence of both amebic colitis and CMV enteritis was high. Regarding co-infection, as occurred in our case, Matsumoto et al. (3) reported that, in HIV-infected patients, 31.5% of those with CMV enteritis also had amebic colitis. A breakdown of the clinical summary of HIV-infected patients complicated by lower gastrointestinal disease at our hospital is shown in Table 2. We have treated two cases of co-infection with CMV enteritis and amebic colitis, and symptomatic improvement was observed after the administration of metronidazole and ganciclovir in both patients. The stenosis of the descending colon, which caused intestinal obstruction that developed during the course of treatment, may have been caused by scars that developed after ulcer healing. There have been previous reports of amebic colitis with stenosis after enteritis healing (9, 10). As in our case, amebic colitis with extensive deep ulcer lesions may heal with intense scarring stenosis (11, 12). Surgery may be necessary in such cases.

Endoscopic dilatation for colon stenosis has been reported mainly in patients with Crohn's disease (13). Even in cases of stenosis caused by amebic colitis, endoscopic dilatation may be indicated, but this has never been reported. In our case, dilatation was not considered because the patient had an active ulcer in the stricture. In another case of amebic colitis-induced stenosis experienced at our hospital, also associated with HIV infection, the stenosis was found in the descending colon, and surgery was required. Data on these two previously reported cases of stenosis due to amebic colitis and one case at our hospital are shown in Table 3.

Patients with HIV infection may develop a variety of opportunistic infections and opportunistic tumors. It is important to understand the spectrum of gastrointestinal diseases that affect HIV-infected patients. We recommend that patients presenting with these gastrointestinal diseases always be screened for HIV infection. In addition, there is risk of overlapping conditions for all gastrointestinal diseases, so it is necessary to screen for other infectious diseases in cases in which the response to treatment or the treatment course is poor.

The authors state that they have no Conflict of Interest (COI).

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