Acute Cytomegalovirus Colitis Presenting during Primary HIV Infection: An Unusual Case of an Immune Reconstitution Inflammatory Syndrome

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Severe ulcerous cytomegalovirus pancolitis developed during primary human immunodeficiency virus (HIV) infection in a patient who underwent early combination antiretroviral treatment. This massive inflammatory process led to acute colon perforation. Serological testing demonstrated cytomegalovirus reactivation. Severe immunosuppression caused by primary HIV infection resulted in cytomegalovirus colitis, and initiation of early combination antiretroviral therapy triggered an immune reconstitution inflammatory syndrome potentially leading to colonic perforation.

Acute retroviral syndrome is defined by unspecific symptoms that can vary greatly, and it occurs in 40%–90% of HIV-infected individuals [1, 2]. On rare occasions, opportunistic infections present simultaneously with acute retroviral syndrome [1], and only 2 reports mentioning acute cytomegalovirus (CMV) disease in primary HIV infection were found in the literature [3, 4]. To date, no case of immune reconstitution inflammatory syndrome during primary HIV infection has been reported.

CMV is one of the most common causes of opportunistic infections in persons with AIDS, and clinical CMV disease has been reported in up to 40% of these patients [5, 6]. Similar to other common herpesvirus infections in HIV-infected patients, CMV disease almost exclusively occurs as a result of reactivation of the latent virus in a previously infected host. Clinically manifested CMV disease in HIV-infected patients usually presents in severely immunocompromised patients with CD4 cell counts <100 cells/µL, with 85% of patients showing retinitis. Esophagitis and colitis have been observed in 2.7% and 7.3% of these patients, respectively [6, 7]. Colitis is the most common extraocular manifestation of CMV disease in HIV-infected patients, although only a few anecdotal reports of CMV colitis in immunocompetent hosts are found in the literature [8, 9]. Most patients with CMV colitis present with diarrhea, abdominal pain, fever, weight loss, and cachexia. Extensive gastrointestinal hemorrhage and perforation have also been reported.

Case report. A 40-year-old man who had sex with men presented in July 2005 at our tertiary care hospital with a 3-week history of weight loss, frequent diarrhea, nausea, and vomiting, accompanied by fevers and oral candidiasis. Furthermore, the patient reported having had flu-like symptoms without exanthema for 7 days. Clinical examination revealed tachycardia, tachypnea, a temperature of 38.3°C, and diffuse abdominal pain, combined with massive pain on rectal examination. Initial blood counts revealed anemia (hemoglobin level, 10.6 g/dL), leukocytosis (leukocyte count, 11.66 × 10³ leukocytes/µL), and a massively elevated C-reactive protein level (387 mg/L). The result of an HIV screening test was positive, and a subsequent Western blot assay confirmed the result. The result of a p24 antigen test was negative, the patient’s plasma HIV RNA level was 3,080,000 copies/mL, and his CD4 cell count was 164 cells/µL (with 22% neutrophils). Primary HIV infection was suspected on the basis of clinical findings at presentation, anamnestic sexual risk exposure, and a previous negative HIV test result (in July 2004) and was later confirmed by an anti-gp120 avidity assay [10]. Following initiation of early antiretroviral treatment (ART; lopinavir plus ritonavir, zidovudine, and lamivudine) and cotrimoxazole prophylaxis, the patient's clinical condition aggravated, and colonoscopy and subsequent biopsy findings led to the diagnosis of a severe, ulcerous acute colitis. The patient began to receive empirical intravenous antibiotic therapy with ciprofloxacin and amoxicillin–clavulanic acid; later, therapy was switched to ciprofloxacin and metronidazol. Antibiotic therapy was stopped after numerous tests yielded results negative for diverse bacterial, viral, and parasitic pathogens. During the following days, the patient improved clinically. Twenty days after hospital admission and 14 days after initiation of early combination ART, he suddenly developed high fevers, combined with an acute abdomen and elevated inflammation parameters. Abdominal CT
showed a pneumoperitoneum, indicating perforation of the colon (figure 1A), and the patient underwent emergency subtotal colectomy. Histopathological examination revealed severe ulcerous colitis with acute inflammation and granulation tissue on hematoxylin-eosin staining (figure 1B and 1C). Subsequent immunohistochemical examination for immediate early antigen and early antigen revealed multiple cells with cytomegalovirus inclusions, thus confirming the diagnosis of CMV pancolitis (figure 1D). The patient immediately started receiving gancyclovir therapy, and a perioperatively installed course of intravenous piperacillin-tazobactam was continued for 14 days. Serological and virological examinations 7 days after hospital admission revealed a negative CMV PCR result, a negative CMV IgM test result, and a CMV IgG titer of 98 IE/mL. On the day of histopathological diagnosis of CMV pancolitis (27 days after hospital admission), the CMV PCR result was positive (plasma CMV RNA level, 1327 copies/mL). Twelve days later, the patient had a positive CMV IgM test result and an IgG titer >400 IE/mL. These results unambiguously confirmed reactivation of CMV disease presenting as severe ulcerous pancolitis during primary HIV infection.

Because of the development of severe neutropenia (neutrophil level, 370 cells/µL) and worsening anaemia (hemoglobin level, 8.0 g/dL), gancyclovir and zidovudine were replaced with valgancyclovir and abacavir, respectively. Furthermore, trimethoprim plus sulfamethoxazole prophylaxis was replaced with pentamidine inhalation. Again, intravenous antibiotics (ciprofloxacin and metronidazol) were initiated until the neutropenia resolved after 14 days.

Following this period, CMV disease and HIV infection were

Figure 1. A, Abdominal CT showing a pneumoperitoneum indicating perforation of the colon. B, Hematoxylin-eosin stain revealing severe ulcerous colitis (original magnification, ×15). C, Hematoxylin-eosin stain revealing ulcerous colitis with acute inflammation and granulation tissue (original magnification, ×40). D, Immunohistochemical stain for detection of immediate early antigen and early antigen, revealing cells with cytomegalic inclusions (original magnification, ×200).
have been described in the context of primary HIV infection. The patient had a normal CD4 cell count and did not initiate combination ART at that time. Smith et al. [4] reported a case of CMV colitis during early HIV infection, with their patient only retrospectively receiving a diagnosis of HIV infection. This patient had received combination ART, and HIV seroconversion was suspected to have occurred ∼4 months prior to diagnosis of CMV colitis.

In general, even though diarrhea is frequently associated with primary HIV infection, our case demonstrates that severe CMV colitis can present during primary HIV infection, and in rare cases, early combination ART may result in an immune reconstitution inflammatory syndrome.

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References