INTERNAL MEDICINE

□ CASE REPORT □

Severe Thrombocytopenia and Acute Cytomegalovirus Colitis during Primary Human Immunodeficiency Virus Infection

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Abstract

We herein report the case of a 25-year-old man who was referred to our hospital due to acute cytomegalovirus (CMV) colitis. The initial blood tests showed that the patient had concurrent primary human immunodeficiency virus (HIV) infection and severe thrombocytopenia. Raltegravir-based antiretroviral therapy (ART) was initiated without the use of ganciclovir or corticosteroids and resulted in a rapid clinical improvement. Platelet transfusions were only necessary for a short period, and subsequent colonoscopy revealed a completely healed ulcer. This case implies that ART alone could be effective for treating severe thrombocytopenia during primary HIV and CMV coinfection.

Key words: antiretroviral therapy, CMV, HIV, thrombocytopenia

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Introduction

Human immunodeficiency virus (HIV)-infected patients with CD4 cell counts below 50/μL are at high risk of cytomegalovirus (CMV)-induced end-organ damage (1). CMV disease mainly occurs as a result of the reactivation of the latent virus in an immunocompromised host. However, in rare occasions, it may occur during primary HIV infection as well, either as a consequence of transient CD4 lymphopenia or primary CMV coinfection (2-9). Furthermore, primary CMV coinfection may increase the severity of primary HIV infection (8-10). We herein present a case of primary acute CMV colitis in conjunction with primary HIV infection that was complicated by severe thrombocytopenia.

Case Report

A 25-year-old man was transferred to our hospital for the management of acute CMV colitis. Three weeks prior to admission, he developed a high fever that was accompanied by throat pain, cervical lymph node swelling, and malaise. He was diagnosed with acute tonsillitis and antibiotics were prescribed at a nearby clinic. Since his symptoms persisted for the 2 following weeks, he visited the emergency department of a university hospital. Blood tests demonstrated a slight increase in liver enzymes and atypical lymphocytes, but the results, including the platelet count, were otherwise unremarkable. Computed tomography revealed generalized lymphadenopathy and thickening of the rectal wall. Although the patient denied any abdominal symptoms, colonoscopy revealed multiple ulcers of the rectum, which was later confirmed, from the pathological results, to be CMV colitis (Fig. 1, 2). On the initial examination, the patient was negative for immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to CMV. The patient reported having had unprotected homosexual intercourse 2 weeks before the onset of fever and was therefore transferred to our hospital to undergo further examinations.

On admission, his vital signs were as follows: blood pressure, 120/66 mmHg; pulse rate, 105 beats per minute; temperature, 38.5℃; and oxygen saturation, 97% (ambient air).

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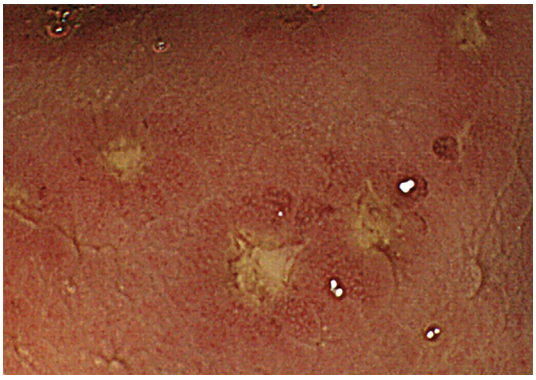

Figure 1. The clinical appearance of the rectum. Colonoscopy revealed multiple ulcers.

A physical examination revealed petechiae on his soft palate, with no other rash observed on any of his skin, including the genital area. Soft, tender cervical lymphadenopathy was noted. The chest and abdominal examinations revealed a palpable spleen but were otherwise essentially normal. Table shows the laboratory data on admission. The white cell count was elevated to 17,100/μL, and the platelet count was markedly decreased to 9,000/μL. Liver and kidney dysfunction was noted, along with a prominent increase in the lactate dehydrogenase and alkaline phosphatase levels. He tested negative for hepatitis A, B, C, and syphilis, but was positive for HIV. His CD4 cell count and HIV RNA level were 866 cells/μL and 400,000 copies/mL, respectively. However, a Western blot assay for HIV antibody was indeterminate. The patient's CMV-IgG and IgM antibody titers were both positive. CMV antigenemia was also detected using the C7HRP method (422/50,000). Bone marrow aspiration demonstrated normocellular marrow without any evidence of hemophagocytosis or malignancy. Abdominal ultrasound demonstrated an enlarged spleen. Based on these results, we diagnosed the patient with primary HIV and CMV infections, accompanied by severe thrombocytopenia. Genotypic testing for HIV drug resistance showed no drug-resistant mutations.

On hospital day 1, platelet transfusions were started immediately. However, the increase in the platelets was minimal, which mandated daily platelet transfusion. On day 2, raltegravir-based antiretroviral therapy (ART) was initiated. Ganciclovir was not administered because the symptoms of CMV colitis were mild, and the risk of bone marrow toxicity was thought to outweigh the benefits. Likewise, corticosteroids were not used because there was no evidence of hemophagocytosis and because of the fear of exacerbating the CMV colitis. On day 5, the patient's platelet count was 24,000/μL. Thereafter, it increased steadily without further transfusions. His general condition improved, and he became completely afebrile by day 14. During the clinical course, he denied any abdominal symptoms or adverse effects from the antiviral therapy. On day 16, colonoscopy was performed, and the complete resolution of the ulcers was observed. On day 24, the platelet count was found to have increased to

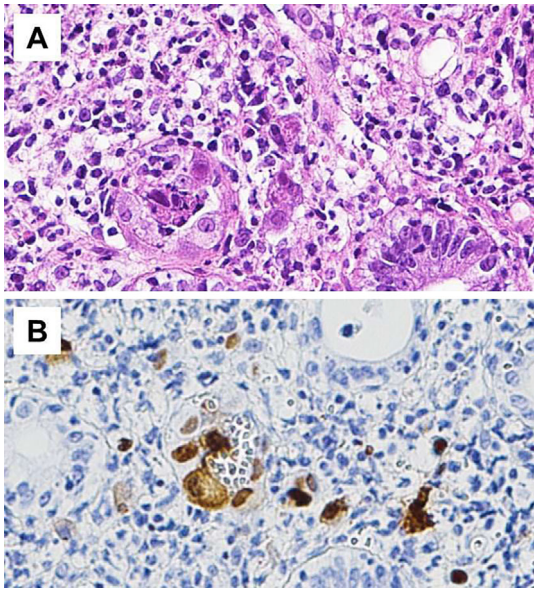

Figure 2. Photomicrographs of the colon biopsy sections taken from a lesion. A: The intranuclear inclusion bodies were seen in the rectum mucosa (Hematoxylin and Eosin staining). B: Anti-cytomegalovirus antibodies were observed (immunohistochemical staining).

131,000/μL and the patient's liver enzymes were within the normal limits. Three months after initiating ART, his CD4 cell count was 597 cells/μL, and HIV RNA was undetectable. The platelet count plateaued at around 250,000/μL and remained stable thereafter. One year later, a Western blot assay was positive for HIV antibodies.

Discussion

We encountered a case of primary HIV and CMV infections accompanied by severe thrombocytopenia in which ART alone resulted in the complete resolution of the clinical symptoms. To the best of our knowledge, among the reports of primary coinfection with both viruses, this is the first case to be complicated by severe thrombocytopenia.

Severe thrombocytopenia was presumed to have resulted from coinfection with the two viruses. Thrombocytopenia is not uncommon during primary HIV infection. A recent prospective study, including 290 primary HIV-infected patients showed that 37% of the patients presented with thrombocytopenia (7). In addition, reports from the pre-ART era demonstrated that the incidence of thrombocytopenia ranged from 45-74% (11, 12). However, few cases of severe thrombocytopenia have been reported. Aoki et al. reported a case with a platelet count of 17,000/μL (13), which was slightly higher than the present case (9,000/μL). Acute CMV infection may also result in thrombocytopenia (14, 15), which may have had a negative impact on the patient's degree of thrombocytopenia.

The present case was successfully treated with ART alone, without the concomitant use of systemic steroids. The symptoms of acute HIV infection are thought to be related

Table. The Laboratory Data on Admission.

<Hematology>			<Biochemistry>			<Infection>		
WBC	17,100	/μL	TP	6.7	g/dL	HA-Ab	-	
Neu	51.5	%	BUN	12	mg/dL	HBs-Ag	-	
Lym	34.5	%	Cre	1.3	mg/dL	HBs-Ab	-	
A-Lym	12.5	%	Na	137	mEq/L	HCV-Ab	-	
Mono	1.0	%	K	4.1	mEq/L	RPR	-	
RBC	546	× 10^4/μL	T-Bil	1.3	mg/dL	TPLA	-	
Hb	16.4	g/dL	AST	201	IU/L	HIV-Ab	+	
Plt	9,000	/μL	ALT	305	IU/L	HIV-RNA	400,000	copies/mL
<Coagulation>			ALP	1,299	IU/L	WB	Indeterminate	
PT	75	%	γGTP	290	IU/L	CD4	866	cells/mL
APTT	45.5	sec	LDH	878	IU/L	CMV-IgG	+	
Fib	139	mg/dL	β2MG	9.2	mg/L	CMV-IgM	+	
			CRP	1.9	mg/dL	C7HRP	422/50,000	

Abbreviations: RPR: rapid plasma regain, TPLA: *Treponema pallidum* latex agglutination, CMV: cytomegalovirus

to the high level of virus in the circulation, either through a direct effect or indirectly through the immune response to the viral infection. Early treatment with ART may attenuate the severity of the symptoms through a rapid reduction in the HIV RNA level. However, there are no clinical data that clearly demonstrate this theoretical effect; thus, the initiation of ART must be decided on a case-by-case basis. In this context, an integrase-based regimen rather than a protease-based regimen was chosen, since the former reduces the HIV RNA level much faster than the latter (16, 17). In addition, raltegravir was chosen because Gentile et al. reported a case in which the platelet count appeared to be independent of the suppression of the viral load (18). Raltegravir may possess a positive effect on autoimmune disease due to its inhibition of herpes virus. The use of systemic corticosteroids is an alternative choice for the treatment of thrombocytopenia induced by either HIV or CMV. However, there have been reports that demonstrate only a partial response or no response (13, 14). In addition, steroid use is reported to be independently associated with the development of CMV colitis in immunocompetent hosts (19). In the present case, there was concern that the use of corticosteroids might exacerbate the patient's CMV colitis. We therefore decided to only administer specific treatments for the patient's HIV infection, which was successful.

The present case was diagnosed as primary CMV infection rather than reactivation. Previous reports have diagnosed primary CMV infection based on CMV IgG seroconversion (3, 6). Our case demonstrated the positive conversion of both CMV IgM and IgG antibodies as well as pathological evidence of CMV, suggesting acute primary CMV colitis. We were not able to perform a CMV IgG antibody avidity test. One must be careful when interpreting antibody results, since IgM assays against common herpesviridae including CMV, may demonstrate false-positive results during primary HIV infection (20). While the majority of acute CMV colitis cases occur secondary to the reactivation of latent infection in immunosuppressed patients, it can also occur in the setting of primary infection in immunocompetent patients. In general, primary CMV infection in immunocompetent hosts is asymptomatic or may present as a mononucleosis-like syndrome and recover without intervention (1). However, there are cases that demonstrate organ-specific complications with significant morbidity and mortality. Klauber et al. reported that the mortality rate among 15 immunocompetent patients with CMV colitis was 26.7% (21). Fifty-three percent of the patients presented with diarrhea with grossly bloody stools, fever, and abdominal pain. They concluded that the efficacy of antiviral medication, which was given to eight patients (53.3%), was unknown. It is difficult to prove that antiviral therapy against CMV has a significant impact on the clinical outcome. It's use must therefore be balanced against the risk of medication toxicity. In the present case, the patient denied any abdominal symptoms, which would be suggestive of mild CMV colitis, leading us to avoid the use of ganciclovir, which could have exacerbated the underlying thrombocytopenia.

In summary, we described a case of severe thrombocytopenia and acute CMV colitis in a patient with primary HIV. The course of the present case implies that ART alone may be effective in treating severe thrombocytopenia in patients with untreated primary HIV.

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

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