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# A Case of Primary HIV Type 1 and Cytomegalovirus Coinfection Presenting With Widespread Clinical Disease

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**Abstract**

Coinfection of HIV-1 and cytomegalovirus (CMV) may occur given the shared routes of transmission, and the clinical presentations of each process overlap. We present a case of acute HIV-1 and CMV coinfection presenting with an acute febrile illness complicated by meningitis, hepatitis, and retinopathy. This and other similar cases demonstrate the need to consider CMV coinfection in acute HIV-1 disease, particularly in situations with significant end-organ damage.

**Keywords**

HIV type 1, human cytomegalovirus, primary coinfection, meningitis, retinitis, hepatitis

## Introduction

Cytomegalovirus (CMV) disease is typically seen in later stages of HIV-1 infection with advanced immunosuppression, when the CD4 counts are less than 50 cells/mm$^3$ and HIV plasma viral loads are greater than 100 000 copies/mL.[1] Most cases occur in previously exposed hosts and result from reactivation of latent infection or possibly reinfection with a novel CMV strain. Much less described is the acute coinfection with CMV during primary HIV-1 infection, although there are several reports of such cases with varying presentations of end-organ damage.[2-8] Here, we present a case of acute HIV-1 with CMV coinfection characterized by widespread clinical disease including meningitis, hepatitis, and retinopathy. This case illustrates the importance of considering acute coinfection with CMV in the setting of primary HIV-1 infection with significant end-organ disease.

## Case

A 25-year-old man presented to our clinic to establish care following a hospitalization for acute (or primary) HIV-1 infection. Five weeks prior to presentation, the patient had sexual contact with a new male partner who was infected with HIV and was not taking antiretroviral therapy (ART). Three weeks prior to presentation, our patient experienced the rapid onset of fatigue, fevers, sweats, and sore throat. That was followed by a diffuse macular rash, loose stool, mild shortness of breath, and dyspnea on exertion. Subsequently, he developed photosensitivity and "floaters" in both eyes. Two weeks prior to presentation, he sought medical care due to symptom progression and was admitted to an outside hospital. He was tested for acute HIV-1 infection and was found to be negative by enzyme-linked immunosorbent assay and Western blot. However, a quantitative plasma HIV-1 viral load showed 1 760 000 copies/mL and his CD4 count was 166 cells/mm$^3$. He was discharged on dapsone for *Pneumocystis jiroveci* pneumonia prophylaxis and referred to our clinic. His past medical history was notable only for depression and an allergy to sulfa.

The patient's physical examination was notable for a temperature of 38.5°C, heart rate of 108 beats/min, and mild diaphoresis. Bilateral lymphadenopathy was noted in the posterior cervical chain and inguinal lymph nodes. The abdomen was soft but there was some tenderness in the right upper quadrant. Bedside retinal examination did not show any abnormalities; however, the slit lamp examination revealed bilateral optic nerve edema, vascular congestion, and tortuosity as well as a cotton wool spot in the left eye (Figure 1).

Peripheral blood laboratory tests are summarized in Table 1. Lumbar puncture was performed and revealed an opening

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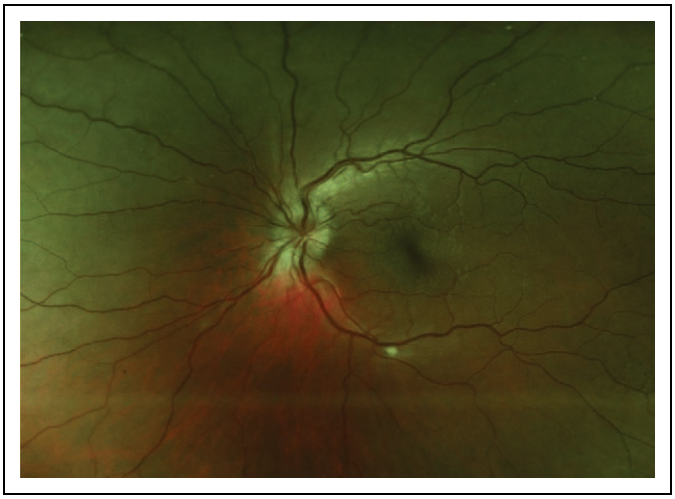

**Figure 1.** Fundus photo of the left eye from the initial slit lamp examination showing a cotton wool spot in the inferior vascular arcade as well as blurred disk margins.

**Table 1.** Baseline Clinical Laboratory Test Results.

| Test | Result | Normal Range |
|---|---|---|
| Alanine transaminase (ALT) | 180 U/L | 4-45 U/L |
| Aspartate aminotransferase | 112 U/L | 7-36 U/L |
| Alkaline phosphatase | 176 U/L | 31-103 U/L |
| Total bilirubin | 0.7 mg/dL | 0.2-1.1 mg/dL |
| Albumin | 4.4 g/dL | 3.7-5.1 g/dL |
| Hepatitis B surface antigen | Negative | N/A |
| Core antibody | Negative | N/A |
| Surface antibody | >750 IU/L | N/A |
| Hepatitis C antibody screen | Negative | N/A |
| Hepatitis A | Negative | N/A |
| Rapid plasma reagin (RPR) | Nonreactive | Nonreactive |
| Fluorescent treponemal antibody absorption (FTA-ABS) | Nonreactive | Nonreactive |
| Cytomegalovirus (CMV) IgG and IgM antibodies | Not detected | N/A |
| Blood bacterial and mycobacterial cultures | Negative | Negative |

Abbreviation: Ig, immunoglobulin; N/A, not available.

pressure of 230 mm Hg (normal 60-200 mm Hg). Cerebrospinal fluid examination showed clear fluid with a white blood cell count of 31 cells/mm$^3$ (93% lymphocytes and 7% monocytes), red blood cell count of 1 cell/mm$^3$, glucose level of 59 mg/dL (normal range 43-73 mg/dL), protein level of 50 mg/dL (normal range 15-45 mg/dL), and a cryptococcal antigen titer of less than 1:1. At that time, the absolute CD4 count was 801 cells/mm$^3$, and the HIV plasma viral load was 386 000 copies/mL. A brain magnetic resonance imaging showed no contrast enhancement or structural abnormalities.

The patient was started on an ART regimen of tenofovir (TDF), emcitritabine, elvitegravir, and cobicistat. His fatigue, fevers, sweats, and dyspnea improved following initiation of ART.

At 9 weeks after the onset of symptoms, the patient developed intermittent numbness and weakness of his upper and lower extremities with associated paresthesias, as well as some mild right temporal headaches. On repeat examination, there was slightly diminished motor tone and bulk throughout, with diminished left dorsal interosseous grip and left iliopsoas muscle strength. The patient also showed numbness in the lower extremities bilaterally when his neck was flexed. There was diminished pinprick in the forearms and calves bilaterally, brisk reflexes in the upper and lower extremities bilaterally, and a positive Kernig sign. A CMV quantitative polymerase chain reaction plasma level was 690 copies/mL (linear detection range 500-100 000 copies/mL) and CMV immunoglobulin (Ig) M and IgG antibodies were detected at 10 weeks. Magnetic resonance imaging of the thoracic and cervical spine showed no significant abnormalities.

With continued use of ART, the patient's symptoms improved with eventual resolution of his neurologic complaints. His visual complaints of floaters resolved after several months. Five months following the onset of the patient's illness, the repeat retinal examination was normal.

## Discussion

Here, we present a case of a 25-year-old previously healthy man with acute onset of a febrile illness progressing with ophthalmologic and neurologic complaints. He was found to have hepatitis, retinopathy, meningitis as well as some clinical findings suggestive of myelitis. Further evaluation revealed acute HIV-1 infection as evidenced by the high HIV-1 viral load with negative HIV-1 antibody testing, as well as concomitant acute primary CMV infection indicated by a positive CMV blood DNA level and the development of new serum CMV IgM and IgG antibodies 10 weeks from illness onset. To our knowledge, this is the first presentation of coinfection involving widespread end-organ damage of the neurologic, hepatic, and ophthalmologic systems.

Many of the aspects of this patient's syndrome, such as the fevers, fatigue, rash, and diarrhea, can be explained by primary HIV-1 infection. Meningitis as well as myelitis can be seen in HIV-1 infection,[9] and although much less frequently described, HIV-associated hepatitis has also been reported.[10] Cotton wool spots like the one seen in this patient are typical of HIV-related retinal microvasculopathy; however, this is described in individuals with AIDS and not acute infection.[11] CMV infection can also cause a febrile illness and similarly cause the various complications seen in this patient. Elevations in transaminase level without significant increases in bilirubin levels are frequently seen in CMV infection.[12] CMV encephaloradiculomyelitis can occur in HIV disease as well; however, this has been described in more advanced disease (absolute CD4 less than 50 cells/mm$^3$).[9] CMV retinopathy may be a consideration in this patient; however, this complication would also be typical of more advanced disease, and retinal lesions are more often described as fluffy, yellow-white, with possible areas of intraretinal hemorrhage.[13] Altogether, however, the overlap in the clinical manifestations of acute HIV-1 and CMV infection makes it difficult to determine how each contributed to this patient's presentation.

As noted earlier, CMV disease is typically seen as an opportunistic infection (OI) during advanced immunosuppression in HIV-1 disease. However, reports of acute CMV have previously been described in primary HIV-1 infection.[2-8] The clinical manifestations of CMV disease varied among those cases and included a new or persistent febrile illness, encephalitis, colitis, hepatitis with pneumonitis, and in 1 case multiple system involvement with pancytopenia, hepatitis, nephritis, perimyocarditis, myositis, and alopecia totalis. Most cases were able to show evidence of acute CMV infection by demonstrating the presence of IgM antibodies to CMV with prior negative IgG. In fact, the clinical history of 2 reports suggested that CMV and HIV-1 were acquired simultaneously from the same exposure. The CD4 count in 3 cases ranged from 242 to 458 cells/mL$^3$, suggesting that the timing of CMV infection was coincident with the expected drop in CD4 count that occurs in primary HIV-1 infection. Two cases showed clinical improvement after initial treatment with intravenous (IV) ganciclovir and transition to either IV foscarnet or oral valganciclovir.

Other types of OIs occurring in the setting of acute HIV-1 infection have also been reported, including *P jiroveci* pneumonia[14,15] and esophageal candidiasis.[16] As in the CMV cases, those OIs occurred in the setting of low CD4 counts. In Ungprasert et al,[15] a review of cases with *P jiroveci* pneumonia showed CD4 counts in the range of 32 cells/mL to 420 cells/mL. In 2 of the 3 cases of esophageal candidiasis, resolution was seen by endoscopy as the T cell counts increased. Those reports suggest there is an increased risk of OIs due to the severe and usually transient immunosuppression during primary HIV-1 infection.

The clinical presentation of our patient suggested possible simultaneous infection with CMV and HIV-1. Indeed, CMV coinfection may play a role HIV-1 transmission. HIV-1-infected women with CMV DNA detected in cervicovaginal lavage specimens also showed higher levels of HIV-1 RNA in the same fluid compartment.[17] A quantitative correlation was shown between HIV-1 and CMV levels in semen samples of HIV-1-infected, untreated men.[18] High seminal levels of CMV were also associated with HIV-1 seminal shedding in men taking ART and with low plasma HIV-1 viral load levels (<50 copies/mL).[19] These findings suggest that coinfection could lead to a higher likelihood of transmission of HIV-1 infection.

In conclusion, our report and other similar reports highlight the need to consider CMV and other OIs during primary HIV-1 infection in the presence of unusually prolonged or recurrent symptoms or otherwise unexplained end-organ damage. Because of the potential for severe CMV disease resulting from infection during the significant immune dysfunction of primary HIV-1, as well as the possible enhanced rate of transmission during coinfection, a reasonable therapeutic approach would be to start ART immediately. In instances with significant end-organ damage, targeted antiviral therapy for CMV infection should also be considered. Based on prior reports of successful treatment regimens,[2,3] initial therapy with IV ganciclovir followed by oral valganciclovir or foscarnet would be the suitable choice.

## Declaration of Conflicting Interests

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