A Case of Acute Co-infection with Human Immunodeficiency Virus and Cytomegalovirus

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Acute human immunodeficiency virus (HIV) infection refers to the period of primary HIV infection in which there is viral replication, viremia, and variable non-specific symptomatology consistent with an acute viral syndrome. Although HIV infection may occur at the same time as other sexually transmitted infections such as chlamydia, gonorrhea and syphilis, co-infection with HIV and cytomegalovirus (CMV) is however rare. We report a 25-year-old man who presented with fever and headache, and who was diagnosed with concurrent HIV-1 and CMV infection. His condition improved after hospital day 10 without specific treatment.

It is important to understand that a number of viruses can cause an infectious mononucleosis-like syndrome and aseptic meningitis, including HIV.

Keywords: human immunodeficiency virus, cytomegalovirus, acute retroviral syndrome

INTRODUCTION

Acute human immunodeficiency virus (HIV) infection, also known as acute retroviral syndrome refers to a period of primary HIV infection. However, some patients remain asymptomatic, with the acute retroviral syndrome occurring in an estimated 50% to 90% of HIV-infected patients.1 This infection may mimic other illness including infectious mononucleosis (IM), influenza, and may also be a cause of aseptic meningitis. However, co-infection with the causative pathogens of IM, such as Epstein-Barr virus (EBV) and cytomegalovirus (CMV) is rare.2 We report a case of a 25-year-old patient with concurrent acute HIV-1 and CMV infection.

CASE REPORT

A 25-year-old Japanese male was admitted to our hospital with fever and headache. Two weeks prior to admission, he had developed a fever of 38.0°C with chills and a pruritic maculopapular rash over his trunk.
that then spread to his extremities. Acetaminophen was prescribed for presumed rubella infection, and the symptoms subsequently improved within three days. However, his laboratory studies were consistent with previous measles and rubella infection. The patient sought medical attention two days prior to admission with a fever over 38°C, fatigue, headache and nausea. He was again discharged on acetaminophen, but returned two days later with worsening of the headache, nausea and fatigue. The patient was subsequently admitted to another hospital. According to the examination on admission, the results were consistent with previous EBV infection, CMV IgM and IgG were both negative, but the test for HIV antibody was positive. Six days after that admission, the patient was transferred to our hospital for investigation and treatment of acute retroviral syndrome. The patient’s past medical history was notable only for mild atopic dermatitis from the age of seven years. His medications included recently prescribed acetaminophen, which he had been taking for several days. He reported no tobacco or illicit drug use and he rarely drank alcohol. He was sexually active, and was in a same-sex relationship with a new male partner from one month prior to the onset of his symptoms.

On physical examination, the patient appeared acutely ill. His blood pressure was 110/58 mmHg, heart rate was 96 beats per minute and regular, axillary temperature was 39.2°C and respiratory rate was 20 per minute; the pulse oximetry saturation was 98% breathing ambient room air. Neck examination revealed a positive jolt-induced headache. His eyes, nose, oral cavity and throat were normal. There was lymphadenopathy in the anterior triangle of the neck bilaterally, which were one centimeter in size, firm and moderately tender. Cardiorespiratory examinations were normal. The abdomen was soft, non-tender, with normal bowel sounds and no hepatosplenomegaly. His genitalia were grossly normal. Neurologic examination was unremarkable including cranial nerve system.

Laboratory data obtained on admission revealed a white blood cell (WBC) count of 10,400/µL (normal 3590–9640/µL), with 38% neutrophils, 40% lymphocytes, 5% monocytes, and 14% atypical lymphocytes. Hemoglobin was 14.5 g/dL (normal 13.2–17.2 g/dL) with a mean cell volume of 89 fL. The platelet count was 135,000/µL (normal 148000–339000/µL). The erythrocyte sedimentation rate was 36 mm/hour. Serum chemistry evaluation revealed the following: sodium 137 mEq/L (normal 136–147 mEq/L), potassium 4.0 mEq/L (normal 3.6–5.0 mEq/L), chloride 99 mEq/L (normal 98–109 mEq/L); blood urea nitrogen 4.5 mg/dL (normal 8.0–20 mg/dL), creatinine 0.7 mg/dL (normal 0.36–1.06 mg/dL), blood glucose 88 mg/dL (normal 70–109 mg/dL), Ca corr 8.6 mg/dL (normal 8.8–10.2 mg/dL), albumin 3.5 mg/dL (normal 3.9–4.9 g/dL), total protein 6.7 mg/dL (normal 6.7–8.3 g/dL), aspartate transaminase 143 IU/L (normal 8–38 IU/L), alanine transaminase 221 IU/L (normal 4–44 IU/L), total bilirubin 0.9 mg/dL (normal 0.2–1.2 mg/dL), lactate dehydrogenase 489 IU/L (normal 106–211 IU/L), and alkaline phosphatase 982 IU/L (normal 104–338 IU/L). Tests for hepatitis B surface antigen and hepatitis C antibody were negative, while that for HIV antibody was positive. His urinalysis results, chest radiograph and electrocardiogram were normal. An abdominal ultrasound examination was normal, except for mild splenomegaly.

On hospital day 1, the patient was suspected as having an infectious mononucleosis-like syndrome or viral meningitis acute retroviral syndrome. Lumbar puncture was subsequently performed and the cerebrospinal fluid (CSF) examination showed a WBC count of 34/µL with 88% polymorphonuclear leukocytes, a protein level of 129 mg/dL and a glucose level of 62 mg/dL. Gram stain, pneumococcal antigen and herpes simplex virus (HSV) polymerase chain reaction (PCR) of the CSF, India ink staining and the test for cryptococcus antigen were negative, as were cultures for bacteria, mycobacteria and fungi. Although the test results were consistent with previous infection with measles, rubella, and Epstein-Barr virus (EBV), the cytomegalovirus (CMV) IgM index was 7.38 (normal <0.8), and the CMV IgG index was 3.5 (normal <2.0). The results of additional tests were as follows; serum HIV-1 RNA level 4.4 × 10^5 copies/mL, HIV-1 RNA level in the CSF 5.4 × 10^5 copies/mL, HIV western blotting indeterminate, CD4 lymphocyte count 910/µL, serum CMV DNA level 2.1 × 10^2 copies/mL, and CMV DNA level in the CSF negative. The results of serologic tests for
syphilis, cryptococcal antigen, toxoplasma, and hepatitis A were negative. The patient was diagnosed with concurrent acute HIV-1 and CMV infection. The patient’s condition began to improve spontaneously with conservative therapy, including his liver function test parameters after hospital day 10. Acetoaminophen was prescribed as needed. On hospital day 14, the cytomegalovirus (CMV) IgM index was 5.4, the CMV IgG index was 8.5, and the serum CMV DNA level was $3 \times 10^3$ copies/mL. He was discharged back to his home on hospital day 21. Although the patient was advised to inform his partner about his HIV infection, he refused to do so. As a result, we were unable to offer his partner HIV testing because to do so might have breached doctor-patient confidentiality.

The patient was well and active without recurrence problems as an outpatient, but his CD4 lymphocyte count decreased to 410/µL one month later, 370/µL two months later, and 270/µL three months later, respectively. As a result, he was prescribed antiretroviral treatment (ART) with emtricitabin-tenofovir and darunavir with ritonavir three months later.

**DISCUSSION**

Acute retroviral syndrome was first described in 1985, and the timing and duration of symptoms are variable. In symptomatic cases, acute HIV syndrome develops within 1 to 4 weeks after primary infection, and the symptoms persist for 2 to 4 weeks. The most frequent symptoms are fever (80% to 90%), fatigue (70% to 90%), and rash (40% to 80%). IM is a frequently encountered illness in adults, and HIV-1 and CMV are among the causative pathogens of this syndrome. According to a study of the infectious mononucleosis-like syndrome in adult patients in Japan, the syndrome was caused by EBV in 57.5% of cases, by CMV in 27.5% of cases and HIV-1 in 2.5% of cases, respectively. Like the present case, there have been some reported cases of HIV-1 and CMV co-infection, characterized by a mononucleosis-like illness with prolonged fever and severe symptoms, although this is rare. Our patient demonstrated seroconversion to both HIV-1 and CMV and it is likely that the two viruses were acquired from unprotected sexual intercourse. The reason for HIV and CMV co-infection predict that one of the possible sources of transmission were from saliva; deep kissing, is a known mode of transmission and is consistent with risky sexual behavior. Another possibility is sexual transmitted infection by semen. Although semen contains HIV, conversely it rarely contains CMV, but when present, it has the potential of initiating a primary infection. Although CMV disease may cause opportunistic infections such as retinitis, pneumonia, and colitis in advanced acquired immune deficiency syndrome (AIDS), there are some reports in the literature of acute CMV disease in cases of acute retroviral syndrome, such as colitis and esophagitis, when the CD4 lymphocyte count reaches a nadir prior to the formation of an immunological response. In this case, the patient demonstrated a simple co-infection, and not acute CMV disease because the patient’s CD4 lymphocyte was not critically low. The role of ART in cases of acute retroviral syndrome remains uncertain and treatment during this phase is not clearly defined. Like the present case, treatment seems to be often supportive, because the symptoms of acute infection are usually self-limiting. Although the patient was newly diagnosed with HIV infection, he had minimal knowledge about HIV and AIDS and he initially refused to commence ART. He was also poorly motivated and there were concerns about whether it was appropriate to commence such treatment. Because he was otherwise clinically stable and without opportunistic infections, our initial choice was to wait until his CD4 lymphocyte count became stable. However, his CD4 lymphocyte count continued to decrease after the acute phase of HIV infection and as a result, he was commenced on ART. This progressive fall in lymphocytes is unusual and it is possible that acute CMV infection caused activated and apoptosis-vulnerable T cells to increase HIV-1 disease progression. Moreover, neurologic manifestations of primary HIV infection are associated with accelerated progression of disease. In this case, we speculate that rapid disease progression might have been caused by a high HIV-1 viral load, co-infection with CMV, the presence of neurological manifestation, or the possibility of an already established chronic HIV infection with the acquisition of acute CMV infection prior to admission.
thereby resulting in a viral syndrome mimicking an acute retroviral syndrome including the manifestation of a maculopapular rash.

In this case, physicians could have easily missed the diagnosis of HIV. Therefore, physicians must always bear in mind the possibility of HIV infection in patients presenting with an IM-like syndrome and aseptic meningitis, especially in those with a history of high-risk sexual behaviors. Moreover, an early diagnosis of HIV infection is beneficial not only to individual patient management but also to preventing further transmission in the community. Although partner notification should be addressed when the infection is first diagnosed and revisited for subsequent partners, this system is not in operation in Japan. Partner notification needs to be considered by the Japanese clinician from a public health perspective.

In conclusion, we report a case of primary co-infection with HIV and CMV. This case highlights that appropriate patient interview including a sexual history, physical examination including that of the genitalia, and formulating a wide differential diagnosis that includes HIV infection is essential in such patients presenting with an IM-like syndrome and aseptic meningitis, who have high-risk sexual practices.

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References