

Acute human immunodeficiency virus infection

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Received: March 15, 2004 Revised: June 1, 2004 Accepted: June 10, 2004

Human immunodeficiency virus type 1 (HIV-1) infection has a broad spectrum of clinical manifestations, ranging from asymptomatic seroconversion to a severe symptomatic illness resembling infectious mononucleosis or other medical conditions including hepatitis, meningoencephalitis, or pneumonitis. Without clinical alertness, the illness is usually misdiagnosed or even not considered. Here we report 3 cases of acute HIV-1 infection with either a negative HIV-1 antibody assay or an indeterminate Western blot result, but high plasma levels of HIV-1 RNA. The initial presentations included fever, skin rash, sore throat, neck lymphadenopathy, cough and headache. One patient presented with infectious mononucleosis-like illness, 1 with aseptic meningitis, and 1 with acute tonsillitis. Physicians should be alert to the possibility of acute HIV-1 infection, especially in cases with unexplained fever, lymphadenopathy or rash.

Key words: Acute disease, case reports, HIV infections, HIV seronegativity, signs and symptoms

The clinical spectrum of acute infection caused by human immunodeficiency virus type 1 (HIV-1), which is also referred to as acute HIV infection, acute retroviral syndrome, HIV seroconversion syndrome, or primary HIV infection, ranges from asymptomatic seroconversion to a severe symptomatic illness resembling infectious mononucleosis, and may present with a wide range of symptoms or signs. The incidence of symptomatic acute infections among patients recently infected with HIV-1 has been reported in the range from 40-90% [1]. A similar collection of clinical features of primary infection has been described in all populations at risk of HIV-1 infection, including homosexual men and women, intravenous drug users, recipients of contaminated blood products, recipients of organs from infected donors, and accidentally infected workers in the health care sector [2]. Early recognition and diagnosis of acute HIV-1 infection is imperative for patients and for public health, as it allows for early initiation of antiviral therapy and prevention of subsequent transmission. We report 3 cases of acute HIV-1 infection with a focus on the clinical clues for early detection.

Case Report

Case 1

A previously healthy 24-year-old man presented with fever and sore throat in September 2002. He also

complained of chills, cough, bone pain, headache, odynophagia, and general weakness. He had been hospitalized for 2 weeks and treated for acute tonsillitis in a local hospital. He reported having intercourse with a sex worker without using a condom about 2 months before this admission. He was treated with clindamycin and gentamicin, but fever persisted. He was transferred to our hospital and was noted to have generalized erythematous maculopapular skin rash over the neck, trunk, and 4 extremities. On admission, his consciousness was clear, body temperature was 38.2°C, pulse rate 102/min, respiratory rate 20/min, and blood pressure 146/77 mm Hg. The chest film was clear. Serum biochemistry showed aspartate aminotransferase 147 U/L (normal range, 16-40 U/L), alanine aminotransferase 433 U/L (normal range, 8-54 U/L), and neither hepatitis B surface antigen (HBsAg) nor hepatitis C virus antibody was detected (Table 1). Enzyme-linked immunosorbent assay (ELISA; AxSYM HIV 1/2 gO, Abbott GmbH & Co. KG, Wiesbaden, Germany) test to screen for HIV was negative, but a high HIV-1 viral load in plasma (>750,000 copies/mL) was found by Amplicor assay (Roche Diagnostics, Branchburg, New Jersey, USA). Analysis by using monoclonal antibodies (Immunotech Company, Marseille, France) and flow cytometry (Beckman Coulter EPICS XL, Florida, USA) revealed a reversal of the CD4⁺:CD8⁺ ratio (194/891).

Acute HIV-1 infection was diagnosed, and anti-retroviral therapy with nelfinavir 1250 mg and lamivudine/zidovudine 150/300 mg twice daily was

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Table 1. Clinical characteristics and laboratory findings of 3 cases of acute human immunodeficiency virus type 1 (HIV-1) infection

	Case 1	Case 2	Case 3
Gender	Male	Male	Male
Age (years)	24	24	35
Sexual orientation	Heterosexual	Homosexual	Homosexual
White blood cell (/mm ³)	6000	6300	7500
Hemoglobin (g/dL)	14.4	14.7	13.2
Platelet (/mm ³)	286,000	326,000	163,000
Lymphocyte (/mm ³)	1260	3175	5325
CD4 ⁺ :CD8 ⁺ (cells/ μ L)	194/891	346/2394	382/1887
GOT/GPT (U/L)	147/433	181/243	134/214
Hepatitis B surface antigen	—	—	—
Hepatitis C virus antibody	—	—	—
Initial HIV-1 antibody			
ELISA	—	+	+
Western blot	^a	—	—
Initial HIV-1 viral load (copies/mL)	>750,000	2,510,000	118,273
Follow-up HIV-1 antibody			
ELISA	+	+	+
Western blot	+	+	+
Outcome	Survival at 22nd month	Survival at 24th month	Survival at 36th month

Abbreviations: GOT = aspartate aminotransferase; GPT = alanine aminotransferase; ELISA = enzyme-linked immunosorbent assay

^aNot done.

initiated. He became afebrile before the initialization of antiretroviral therapy. At 1 month after initiation of therapy, CD4⁺ cell count increased to 483 cells/mm³, HIV-1 viral load decreased to 410 copies/mL, and serum aminotransferase levels returned to the normal range. ELISA and Western blot (NEW LAV BLOT 1 BIO-RAD, Steenvoorde, France) of serum HIV-1 antibodies were both positive at 3 months after discharge.

Case 2

A 24-year-old soldier complained of fever and chills, accompanied by headache and night sweats, for more than 10 days. He was admitted to our hospital in July 2002. On admission, his consciousness was clear, blood pressure was 130/70 mm Hg, body temperature 38.6°C, pulse rate 100/min and respiratory rate 20/min. Physical examination showed generalized maculopapular rash, and enlargement of bilateral inguinal and right axillary lymph nodes. Laboratory study revealed aspartate aminotransferase 181 U/L, alanine aminotransferase 243 U/L, and undetectable HBsAg or anti-hepatitis C virus (HCV) antibodies (Table 1). Initial HIV-1 antibody was positive by ELISA but could not be confirmed by Western blot method, as shown in Table 1. In addition, his HIV-1 viral load was 2,510,000 copies/mL, and reversal of CD4⁺:CD8⁺ ratio (181/243) was also noted (Table 1). Due to persistent headache, lumbar puncture was performed, and mild lymphocytic pleocytosis

(23/mm³, 94% lymphocyte), decreased glucose level (58 mg/dL; serum glucose, 96 mg/dL), and elevated protein level (126 mg/dL) were found in the cerebrospinal fluid. After the prescription of nelfinavir 1250 mg twice daily and lamivudine/zidovudine 150/300 mg twice daily, his symptoms quickly abated. After 3 days of antiviral therapy, HIV-1 RNA viral load decreased to 2130 copies/mL, CD4⁺ cell count increased to 564 cells/mm³, and serum aminotransferase returned to the normal range (aspartate aminotransferase 12 U/L, alanine aminotransferase 17 U/L). ELISA and Western blot for serum HIV-1 antibodies were positive at 1 month after discharge.

Case 3

A 35-year-old previously healthy man presented with intermittent fever for 1 month and productive cough with yellow sputum in June 2001. Physical examinations showed bilateral neck lymphadenopathy. His consciousness was clear, blood pressure was 140/69 mm Hg, pulse rate 68/min, respiratory rate 17/min, and body temperature 36.5°C. Spontaneous resolution of the symptoms occurred within 2 days. At first, laboratory study showed serum aspartate aminotransferase 134 U/L, alanine aminotransferase 214 U/L, and negative on HBsAg or anti-HCV antibody testing (Table 1). HIV-1 antibodies were positive by ELISA, but could not be confirmed by Western blot (Table 1).

One-and-a-half months later, serum HIV-1 antibodies were detected by ELISA and Western blot and the HIV-1 viral load was 118,273 copies/mL. Efavirenz 600 mg daily and lamivudine/zidovudine 150/300 mg twice daily were started. Serum HIV-1 RNA level became undetectable and CD4⁺ cell count increased to 858 cells/mm³ 4 months later.

Discussion

Acute HIV-1 infection is defined as the period from initial infection with HIV-1 to complete seroconversion [3]. Most patients (40-90%) present with mononucleosis-like symptoms in the first week of acute HIV-1 infection [1]. They may visit emergency department physicians, dermatologists, primary care physicians, and ear, nose and throat specialists, but more than 90% of cases of acute HIV infection go undiagnosed at the initial medical encounter [4,5]. The most commonly reported symptoms and signs of acute HIV infection are non-specific, e.g., fever, fatigue, rash (especially maculopapular), headache, photophobia, stiff neck, lymphadenopathy, vaginal candidiasis, pharyngitis, myalgia, arthralgia, retro-orbital pain, weight loss, depression, gastrointestinal distress, night sweats, oral or genital ulcer [5-10], and fever and skin rash, many of which occurred in our patients. Acute tonsillitis was diagnosed in patient 1 at the initial visit for medical care and he was not screened for HIV-1 infection. Detailed history taking and physical examination are important. Misdiagnosed cases will lose the chance for early treatment. The 3 patients in this report were previously healthy young men, and the clinical characteristics and laboratory findings are shown in Table 1. The initial presentations of the other 2 patients were similar to those of common cold. The exact timing of the exposure to HIV-1 in these 3 patients in relation to the onset of symptoms was not clear, except patient 1, who reported unprotected intercourse with a sex worker 2 months prior to symptom onset.

All 3 patients had a reverse ratio of CD4⁺:CD8⁺, elevation of serum transaminases, and a negative or indeterminate result of HIV-1 antibody determined by Western blot. The diagnoses of acute HIV-1 infection for the 3 cases were confirmed by the results of high plasma titers of HIV-1 RNA, and the seroconversion within 3 months' follow-up. Initiation of potent antiretroviral therapy was associated with decreases in plasma HIV-1 viral load, normalization of serum transaminases, and increases in CD4⁺ cell counts.

Laboratory abnormalities in cases of acute HIV-1 infection may include elevation of serum transaminases [7,9], as in our 3 patients who had recovery of serum levels of liver enzymes within 2 months after initiation of highly active antiretroviral therapy (HAART). This laboratory abnormality may be a clinical clue for acute HIV-1 infection. When physicians encounter a patient with unexplained fever and abnormal liver function, evaluation of risk factor for HIV and ordering of HIV antibody tests may be indicated for differential diagnosis.

From the individual and public health views, early diagnosis of acute HIV-1 infection can be enormously beneficial. Patients who receive appropriate consultation may reduce risky sexual behavior leading to a decreased risk of HIV-1 transmission. It has been demonstrated that administration of antiretroviral therapy during acute HIV-1 infection may improve the subsequent clinical course and increase the CD4⁺ cell count [11]. Therefore, HAART for acute HIV-1 infection will result in rapid remission of relevant symptoms and signs, and also has a beneficial effect on laboratory markers of disease progression and long-term clinical impact [12,13]. Patients receiving HAART were observed to have an increment of CD4⁺ cell count and improvement of HIV-1 RNA viral load, and a resulting decrease in the risk of opportunistic infections.

Physicians are generally unable to diagnose acute HIV infection at the initial patient examination for several reasons. First, such patients are not adequately assessed for the risk factors for acquisition of HIV-1. Second, physicians may be unaware of current information about methods to diagnose acute HIV-1 infection. As in these 3 cases, the presentations of acute viral infection is typically nonspecific and the differential diagnosis should at least include many infectious diseases, such as primary CMV infection, Epstein-Barr virus mononucleosis, viral hepatitis, primary herpes simplex virus infection, influenza, severe streptococcal pharyngitis, secondary syphilis, toxoplasmosis, rubella, brucellosis, or malaria [14].

Primary care physicians remain the key health care professionals for detecting acute HIV-1 infection. This report has illustrated several clinical clues to the diagnosis of acute HIV-1 infection, such as fever lasting for more than 1 week, presence of generalized maculopapular rash, sore throat, lymphadenopathy, elevation of serum aminotransferases, and a reversal of the CD4⁺:CD8⁺ ratio, especially in an initially healthy young man. Similar cases should receive appropriate

counseling, a complete history taking, physical examinations, and appropriate HIV laboratory tests.

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