

Acute HIV infection with rapid progression to AIDS

ABSTRACT

Acute HIV infection is rarely recognized as the signs and symptoms are normally unspecific and can persist for days or weeks. The normal HIV course is characterized by a progressive loss of CD4+ cells, which normally leads to severe immunodeficiency after a variable time interval. The mean time from initial infection to development of clinical AIDS is approximately 8-10 years, but it is variable among individuals and depends on a complex interaction between virus and host. Here we describe an extraordinary case of a man who developed *Pneumocystis jiroveci* pneumonia within one month after sexual exposure to HIV-1, and then presented with 3 consecutive CD4 counts below 200 cells/mm³ within 3 months, with no other opportunistic disease. Although antiretroviral therapy (AZT+3TC+ATZ/r) was started, with full adherence of the patient, and genotyping indicating no primary antiretroviral resistance mutations, he required more than six months to have a CD4 restoration to levels above 200 cells/mm³ and 10 months to HIV-RNA to become undetectable.

Keywords: HIV, acute infection, progression, AIDS.

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INTRODUCTION

HIV infection is characterized by a progressive loss of CD4+ cells, which normally leads to severe immunodeficiency after a variable time interval. Following infection with HIV-1, the majority of individuals present with a clinical picture characterized by a mononucleosis-like syndrome, a transient drop in CD4+ cells, and a subsequent recovery of these initially reduced CD4+ T cell counts to near normal levels.¹ The mean time from initial infection to development of clinical AIDS is approximately 8-10 years,²⁻⁵ but can vary among individuals and depends on the complex interaction between virus and host. The strongest predictor for the speed of HIV-1 disease progression is viral load set point, and infected subjects with high levels of viremia usually progress to AIDS faster than those with lower viral load.^{6,7}

Opportunistic infections that occur within the first months after infection with HIV-1 are extremely rare, and are often misdiagnosed or missed. Patients and treating physicians can be misguided by a negative HIV-1 test within the preceding months. Here we describe a case of a homosexual man who developed *Pneumocystis jiroveci* pneumonia within one month of infection by HIV-1.

This case emphasizes that clinicians need to be aware of the possibility of opportunistic infections occurring during early HIV-1 infection.

CASE REPORT

A 28-year-old male patient presented on April 4, 2005, with fever of 38° C, a rash on the upper limbs, which extended to the trunk and face after 2 days, night sweats, headache, myalgia and fatigue. After 7 days, the symptoms spontaneously disappeared. This episode was preceded by a single high-risk sexual exposure to a partner of unknown HIV serostatus, seven days before the onset of symptoms. Apart from this single risk exposure, the subject reported to be in a monogamous relationship with his HIV-1-negative male partner that had no other risk factors for HIV infection (tested HIV-1 negative in March 2005 and still negative at the latest measurement in September 2008). He was also tested negative for HIV-1 on January 17, 2005 (antibody and p24 antigen negative), when an HIV-1 test was performed in a context of an acute episode of diarrhea.

Two weeks after rash onset (on April 22, 2005), the patient was seen at the emergency room of a private hospital complaining of cough and fever. A chest X-Ray showed interstitial

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infiltration and he was prescribed moxifloxacin (400 mg/d, PO). There was no improvement, and after 48 hours he returned to the hospital with persistent symptoms, malaise and shortness of breath. A chest computerized tomography scan revealed an interstitial infiltrate suggestive of *P. jiroveci* pneumonia. His arterial oxygen pressure was 70 mmHg, with an O₂ saturation index of 96%. He was hospitalized, and received prednisone 1mg/kg, and sulphamethoxazole plus thrimethoprim (800/160 mg, qid, 21d). Acid fast bacilloscopy (AFB) and blood pyogenic cultures were negative. Fever disappeared after 48 hours, and clinical symptoms resolved. A new HIV-1 serological test (EIA) performed on April 24, 2005, was positive for HIV (p24 Gag; p 41 Env) antibodies, which was confirmed by Western Blot (p17, p31, p51, p55, p66 = negative, p24 weakly positive, Gp41, Gp120, Gp160 positive).

A CD4+ T cell count performed on May 24, 2005, was 24 cells/mm³, while the CD8+ T cell count was 251 cells/mm³. HIV-1 viral load was quantified using NASBA (NucliSENS, BioMerieux) and was over 7,000,000 copies HIV-1 RNA per mL plasma. At a follow-up visit on June 08, 2007, the HIV-1 viral load had decreased to 3,200,000 copies/mL and CD4+ and CD8+ T cell counts had increased to 61 and 799 cells/mm³, respectively, without the initiation of any antiretroviral therapy. A genotyping test for potential antiretroviral drug resistance mutations performed on May 24, 2005, using the Trugene HIV-1 assay showed no evidence of drug-resistance mutations, mRNA flow cytometric analysis using ViroTect, Invirion Diagnostics Inc.⁸ revealed a dual-tropic virus infection. He was discharged from hospital on May 11, 2005, without any symptoms.

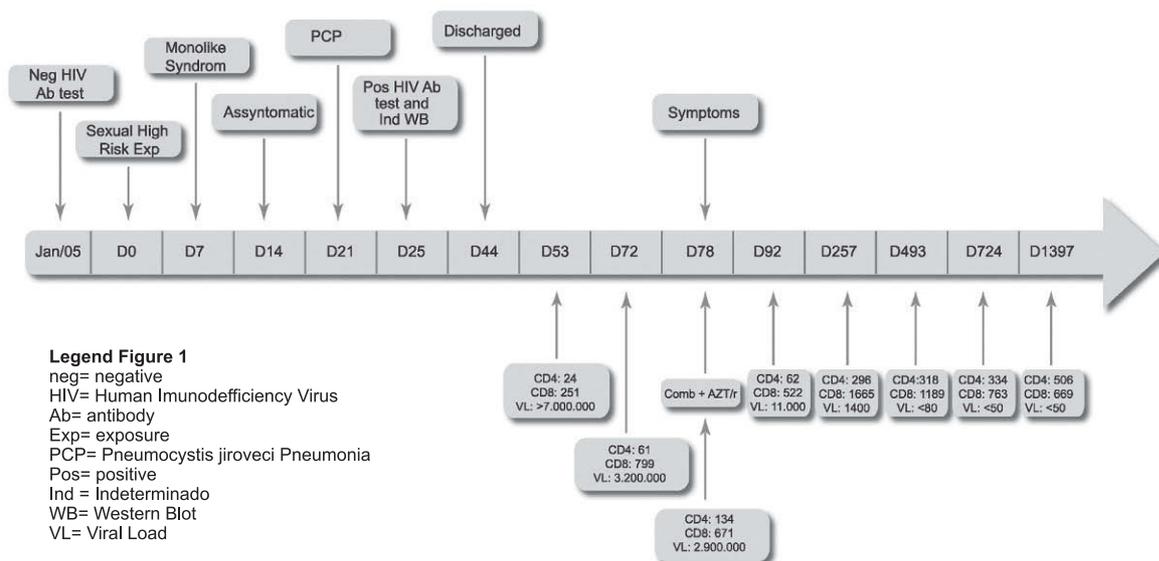
He returned to hospital on June 11, 2005, with a clinical picture suggestive of upper respiratory tract infection (fever,

headache, nasal congestion). An X-Ray of his face showed sinusitis, which was successfully treated with amoxicillin-clavulanate (500/125 mg, tid, 14d). His plasma viral load was 2,900,000 copies/mL; CD4+ cells count had increased to 136 cells/mm³ (June 14, 2005). The patient was started on antiretroviral (ARV) therapy using AZT + 3TC + ATV/r on June 14, 2005, and then discharged. After 2 weeks of therapy (June 28, 2005), his viral load decreased to 11,000 copies/mL and CD4 count was 62 cells/mm³. Four weeks after (July 12, 2005), his plasma viral load was 320 copies/mL, while his CD4+ cells count has increased to 196 cells/mm³. Besides report of full adherence to ARV therapy, measures 3 and 5 months after initiation of viral load were 210 and 1400 copies/mL, respectively; he only became undetectable 9 months after and remained as such since then (36 months) (Figure 1). The patient's HLA type was Locus A*23, 24 B*1503, 35 Cw*02, 04.

DISCUSSION

The natural history of HIV infection is highly variable.^{2,9} However, most infected individuals remain free of symptoms for 6-10 years after initial infection, and a subset of infected individuals do not progress to AIDS after being infected for more than 25 years (so called "long-term non-progressors"). Differences in the speed of HIV-1 disease progression have been linked to several factors; most consistently to genetic factors, including chemokine polymorphisms and the expression of specific HLA class I or KIR alleles.^{10,11} On the other hand, there are rare individuals who progress to AIDS in a very short time after initial exposure to HIV. In MACS cohort a rate < 1% of rapid progression to AIDS within 12

Figure 1: Timeline



months of infection was reported with 0.007% of individuals reaching a CD4+ cell count less than 200 cells/ mm³ within 6 months of infection, and 0.045% within one year.^{12,13} The factors that are responsible for the rapid progression of disease in these individuals are not known.

Recently, a case of a man who developed AIDS, including the need for ARV therapy within 4-5 months after acute infection, was reported, and potential co-factors, such as life-style, use of drugs, or even an exceptionally virulent resistant strain of HIV have been discussed in this context.¹⁴ There are some cases of *P. jiroveci* in literature, but all recovered CD4 levels without ARV therapy within four months after symptoms.¹⁵ In the present case, the study subject did not report any drug use and he had stable HIV negative sex-partner. It was previously reported that HLA-B*35, Cw*04 and A*68 were associated with increased risk of fast progression to AIDS;¹⁶⁻¹⁹ of these, our patient has the first two antigens. In addition, the HIV-1 strain isolated was sensitive to all current antiretroviral drugs, and belonged to subtype B, the most frequent viral subtype circulating in Bahia and associated with non-aggressive progression,²⁰ however, the dual tropic viral profile was related to a increased risk of fast progression.¹⁴ Most importantly, this case emphasizes that physicians must be aware that life threatening opportunistic infections can occur during this early phase of infection. Acute HIV-1 infection can occasionally result in a rapid and dramatic loss of CD4+ T cells.

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