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Case Report

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Acute Hepatitis and Esophageal Candidiasis During Primary Human Immunodeficiency Virus Infection

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Abstract

Primary human immunodeficiency virus infection (PHI) may take place without symptoms or may be associated with mononucleosis-like illness. Sometimes, the clinical presentation includes aseptic meningitis, mucocutaneous ulcers, oropharyngeal candidiasis and elevated aminotransferases. We describe the case of a 25-year-old male, who had sex with other men, and presented to the emergency department with elevated aminotransferases levels and esophageal candidiasis. Acute hepatitis markers (hepatitis A, B, C, Epstein-Barr virus and cytomegalovirus) were performed and all were negative. Repeated testes revealed 3 consecutive negative HIV antibody tests with a strongly high HIV-1 RNA plasma concentration (> 500,000 copies /mL) and a loss of $CD4^+$ T cells (347 cells/μL), characterizing an acute hepatitis occurring during a course of an acute retroviral syndrome. Antiretroviral therapy was started while waiting a genotyping test performed to assess the presence of potential drug resistance mutations, and the patient recovered uneventfully, with normalization of aminotransferases, CD4 restoration and viral load become undetectable. Genotyping test indicated primary antiretroviral mutations, and appropriate changes in antiretroviral therapy were performed. Our case like other reports suggested that a diagnosis of PHI needs to be considered in patients who presented with acute hepatitis.

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Introduction

The presentation of primary human immunodeficiency virus infection (PHI) is highly variable, and may have a variety of symptoms, including flulike syndrome, lymphadenopathy, gastrointestinal symptoms, headache, cutaneous lesions, aseptic meningitis, meningoencephalitis and hepatitis [1, 2]. The nonspecific presentation and a lack of suspicion among clinicians often delay the diagnosis of PHI.

Case Report

In June 2009, a 25-year-old white male presented to the emergency department of the Instituto de Infectologia Emilio Ribas in Sao Paulo, Brazil, with 4 days of headache, fever and vomiting. He also complained of malaise for 10 days. The patient had taken two days before admission levofloxacin under medical supervision, without improvement. He denied cough, diarrhea or rash. On the morning of presentation, he had presented one episode of vomiting blood. The patient had no significant medical history, including sexually transmitted diseases, and denied tobacco or intravenous drug abuse. He had no drug allergies and reported social drinking. The patient was sexually active with men (MSM), and experienced unprotect contact with multiple partners. He also reported business trip to the Caribbean three weeks before the onset of symptoms. Currently living in Sao Paulo and works as a dancer.

On examination, he was afebrile with a temperature of 36.2 °C, the weight was 59 kg, heart rate of 78 beats/min, respiratory rate of 20/min, blood pressure of 120/68 mmHg, and oxygen saturation of 97% in room air. The most significant findings on physical examination included conjunctival hyperemia, eyelid edema and palpable lymph nodes, about 1 cm in diameter, in submandibular region bilaterally. There was also diffuse abdominal tenderness to palpation without

peritoneal signs. No rash was present. No other abnormalities were observed at the physical examination.

Admission labs were significant for a platelet count of 64 $\times 10^3/\mu L$, otherwise normal, with a hemoglobin level of 15.7 g/dL and a white blood cell count of 5.2 $\times 10^3$ cells/μL (neutrophils were 70%). Coagulation parameters revealed international normalized ratio (INR) of 1.18 and partial thromboplastim time (PTT) of 54.9 sec (normal range 25 - 37 sec). C-reactive protein was 2.6 mg/dL (normal range < 0.5 mg/dL).

Biochemical tests revealed the following: aspartate aminotransferase (AST) level was 4,410 U/L (normal range < 37 U/L); alanine aminotransferase (ALT) level was 4,450 U/L (normal range < 41 U/L); lactic dehydrogenase was 2,406 U/L (normal range 240 - 480 U/L); alkaline phosphatase was 182 U/L (normal range 40-129 U/L); gamma glutamyil transferase was 386 U/L (normal range 10 - 66 U/L); and total bilirubin was 1.43 mg/dL (normal range 0.20 -1.00 mg/dL).

Several serologic studies were performed to rule out infectious diseases from different etiologies. Quick test for dengue was negative. Enzyme-linked immunosorbent assay (ELISA) immunoglobulin M (IgM) for leptospirosis was negative. Acute hepatitis markers, including immunoglobulin M to hepatitis A virus (HAV-IgM), hepatitis B surface antigen (HBsAg), anti-hepatitis C virus antibody (anti-HCV), Epstein-Barr virus (EBV) IgM and immunoglobulin M to cytomegalovirus (CMV-IgM) were also all negative. The patient's epidemiological history suggested that he might have acquired the HIV infection recently. As part of an acute HIV infection study, our patient performed several HIV-1 screening tests with an interval of 1 week (one rapid test and two HIV enzyme immunoassay-EIA) with negative results, a negative HIV-1 Western blot analysis, and a indeterminate indirect immunofluorescence test. Primary infection was confirmed 8 days later from admission by a very high viremia (> 500,000 copies /mL HIV-1 RNA tested by b-DNA), which suggest that this patient was in the process of HIV seroconversion. Subsequently, a CD4 cell count was found to be 347 cells/μL and CD8 cell count was 2,165 cells/μL. The patient underwent endoscopy due to vomiting blood, which revealed esophageal candidiasis, which was treated with fluconazole 200 mg/day. A genotyping test for potential antiretroviral drug resistance mutations was conducted at this time using the Trugene HIV-1 assay, and showed a subtype B virus with the presence of polymorphisms in the protease region (L10I, I62V, L63P, A71T, V77I) and a principal RT mutation (K103N). While awaiting the results of resistance testing and after discussion with the patient about benefits (and disadvantages) of early antiretroviral treatment (ART), we initiated treatment with zidovudine, lamivudine and efavirenz on July 9, 2009. About a week later the patient was discharged from hospital, with progressive and rapid improvement of liver function: levels of ALT were 315 U/L and AST was 105 U/L. Adjustment was made to this initial regimen once resistance results were available (switch for IP/r). On follow-up six months later, patient's clinical and laboratorial condition progressively improved, with his viral load decreasing to less than 50 copies/mL and his CD4 count increased to 953 cells/μL.

Discussion

PHI is a critical phase of infection when irreparable damage to the immune system occurs and individuals are highly infectious [3]. The nonspecific signs and symptoms of acute HIV infection are often not recognized. It has been previously published that 21% of patients with PHI presented abnormal liver function tests [1, 4].

We described the case of a young man who had sex with men and presented acute hepatitis in the setting of confirmed acute HIV infection. The most common infectious causes of hepatitis were negative: hepatitis A, B, C, Epstein-Barr virus and cytomegalovirus. There are reports describing the association between elevated aminotransferases and PHI. However, there was previously only one retrospective case report of acute hepatitis associated with acute HIV infection [5].

It has been clearly established that individuals with PHI have an increase in activated $CD8^+$ T cells, which could result in a state of immune activation as seen in this patient. Clonal expansions of T cells have been reported in the early phase of HIV infection [6], and can be attributed to massive response of the patient's immune system against the virus. On the other hand, acute HIV infection can occasionally result in a rapid and extensive loss of intestinal mucosal $CD4^+$ T cells associated with the increase of cytotoxic $CD8^+$ T cells. Treatment of the patient's recently infected is controversial and still under discussion, particularly with regard to long-term benefits of ART. Clinicians must be aware that opportunistic infections can occur during this early phase of infection, and early ART has benefits for both public health reasons (reducing the transmission of the virus) and for individual reasons (improving prognosis by slowing the rate of disease progression). This case also raises questions about whether acute HIV infection can be considered as a possible etiology of hepatitis in patient with HIV risk factors. In these cases, HIV viral load should be performed in addition to HIV antibody testing.

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Conflict of Interest

All authors report no conflicts of interest to declare.

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Ethical Approval

This study was approved by the Research Ethics Committee of the Instituto de Infectologia Emilio Ribas, Sao Paulo, Brazil.

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