

Cytomegalovirus Hepatitis in HIV Infection

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Abstract

Human immunodeficiency virus (HIV) is a virus spread through certain body fluids that attacks the body's immune system, specifically the CD4 cells, often called T cells. This damage to the immune system makes it harder and harder for the body to fight off infections. acquired immunodeficiency virus (AIDS) is the stage of infection that occurs when the immune system is badly damaged and becomes more vulnerable to opportunistic infections. Cytomegalovirus (CMV) infection is one of the major causes of morbidity and mortality in patients with AIDS, mainly at very low CD4 count of < 50 cells/mm³ with particular involvement of the retina causing chorioretinitis. Nevertheless, the involvement of other organs is unusual in AIDS patients. Here we present a case of HIV with CMV-related hepatitis which is considered a very rare presentation.

Keywords: CMV hepatitis; AIDS; HIV

Introduction

Cytomegalovirus (CMV) is a known opportunistic pathogen among immune-compromised patients with various spectra of manifestations which most of the time depend on the underlying immune suppression status. In solid organ or hematopoietic stem cell transplant, CMV has a predilection to invade the allograft leading to graft rejection or invasive disease such as pneumonitis, colitis or bone marrow suppression [1]. On the other hand, CMV is a manifestation of advanced retroviral disease with predominant involvement of the retina causing retinitis. We describe a case of CMV hepatitis as immune reconstitution inflammatory syndrome (IRIS) in a retroviral human immunodeficiency virus (HIV) patient.

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Case Report

A 43-year-old gentleman known to have HIV, hypothyroidism, type 1 DM and vitiligo presented with poor oral intake and generalized fatigability 2 weeks before presentation. He had no history of fever, night sweats, chills, cough, chest pain, shortness of breath, vomiting, abdominal or genitourinary symptoms.

He was diagnosed recently with HIV when he was admitted to another hospital as a case of chest infection and discovered to have acquired immunodeficiency virus (AIDS) with very low CD4 counts of 4. He was started on truvada and efavirenz with pneumocystis (PCP) prophylaxis. Later on, after discharge, patient became more depressed, and neglected himself living alone till he was brought by one relative to us.

Examination

He was conscious, alert, and oriented but looked dehydrated, pale and jaundice, and cachectic with hypopigmented patches over his face, hand, and trunk. There was no lymphadenopathy but with extensive oral thrush. Vital signs showed temperature 37.6 °C, BP 99/65 mm Hg, HR 80 bpm, and RR 20 bpm. Chest was clear. Cardiovascular system was unremarkable. Abdomen was soft, lax with mild hepatosplenomegaly but no stigmata of liver disease. Funduscopic examination showed no evidence of retinitis.

Laboratory results

WBC was $2.9 \times 10^9/L$ (4.0 - 11.0), Hb was 9 g/dL (12.5 - 18.0), and platelet was $232 \times 10^9/L$ (150 - 450). Baseline liver profile showed total bilirubin 72 (2 - 21), ALT 54 (0 - 42), alkaline phosphatase 619 (40 - 129) U/L, GGT 952 (8 - 61), LDH 247 (135 - 225) U/L, albumin 26 (35 - 52) g/L, direct bilirubin 95 $\mu\text{mol/L}$ (0 - 5), NA 128 mmol/L (136 - 145), K 4.5 mmol/L (3.5 - 5.1), urea 3.7 mmol/L (2.8 - 8.1), creatinine 45 $\mu\text{mol/L}$ (59 - 104), CRP 35, CMV IgG positive/IgM negative, CD4 41 cells/mm³ (29 - 59), and HIV PCR quantitative 9,974 copies. Toxoplasma IgG was negative, syphilis screening was negative, and hepatitis A, B, C was negative. No infiltration was seen in chest X-ray. CT CAP (chest, abdomen and pelvis) showed generalized mediastinal, subcarinal lymphadenopathy, right upper lobe ground glass opacity with mild hepatosplenomegaly. Based on these findings, the patient was worked up to rule out opportunistic infection (TB-*Mycobacterium avium* complex) or lymphoma. ART had been continued with switching of efa-

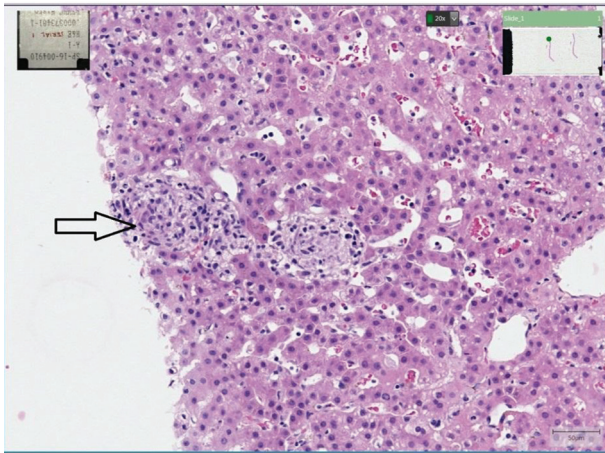


Figure 1. Liver tissue showing multiple granulomas (arrow), composed of aggregates of histiocytes, lymphocytes and plasma cells.

virenz to raltegravir along with prophylactic daily dose septrin. At the same time, given his liver derangement, he was put empirically in modified anti-tuberculosis (anti-TB) drugs covering both possibilities of MTB and NTB mainly ethambutol, moxifloxacin, amikacin and clarithromycin. Shortly after the patient underwent US-guided liver biopsy, he was sent for AFB stain, TB and fungal culture, TB PCR and histopathology. During the hospital stay, the patient experienced episode of shortness of breath which then improved on antibiotics coverage (piperacillin-tazobactam) and anti-TB.

Later on, the histopathology result of liver biopsy had shown multiple non-necrotizing granuloma with intranuclear inclusion bodies characteristics of CMV hepatitis (Figs. 1 and 2). Furthermore, CMV PCR viral load was 14,714. Based on that, he was put on intravenous ganciclovir 5 mg/kg q12h for 3 weeks with follow-up CMV viremia of 2,874, then he was switched to oral valganciclovir 900 mg q12h until his viremia was undetectable, and then he was switched to secondary prophylaxis 900 mg oral q24h which had to be till the improvement of CD4 to be more than 100 cells/mm³ for consecutive 6 months. The patient was discharged in good condition and improved liver functions on valganciclovir and septrin along with ART. However, anti-TB had been discontinued awaiting the further microbiological results. Interestingly, his liver biopsy culture after 1 month showed non-tuberculous mycobacteria for which he was started on rifampicin, ethambutol and clarithromycin.

Discussion

CMV is one of the herpes viruses that can stay dormant in the human body after the primary infection, and then will reactivate when the immune system is suppressed secondary to any reason including retroviral infection. Usually, it manifests at a very low level of CD4 < 50 cells/mm³ with predominant retinal involvement. After introducing ART, the rate had declined to be approximately 0.75 - 3.2 cases per 100 person-years [2]. However, some case reports had described other organ damag-

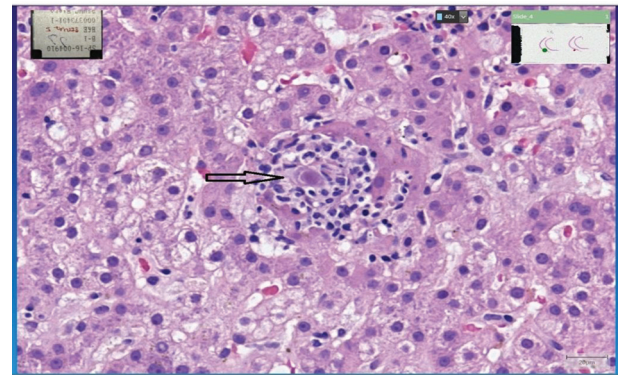


Figure 2. Deeper levels show cells of characteristic intranuclear and intracytoplasmic inclusions (CMV).

es such as pneumonia, hepatitis, myocarditis and meningitis in the setting of primary HIV and CMV coinfection [3, 4]. CMV hepatitis is a frequent feature in liver transplant recipients. However, it is uncommon in HIV-infected patients [5]. Our patient is seropositive for CMV which considered him previously infected and, thus, his presentation represents either reactivation of latent infection or reinfection with a novel strain.

Interestingly, our patient was diagnosed to have retroviral disease and started on ART about 1 month prior to the occurrence of CMV diseases which had made the IRIS strongly possible. It is worthy to mention that similar reaction had been reported in a primary HIV patient who had been started on ART then complicated with unusual CMV colitis with colonic perforation [6].

The presence of CMV viremia is known to have little positive predictive value in patients with HIV and does not mandate presence of invasive disease, even at low CD4 T-lymphocyte counts [7]. In our patient CMV hepatitis was detected by hepatic histopathological examination. As reported from the previous studies, the detection of CMV infection by PCR is correlated with the development of CMV disease and death in the future [8]. Ganciclovir had been started at baseline CMV viral load of 14,714, and then was continued till his plasma CMV level had decreased to the reference level.

Our case highlights the importance of CMV as a potential pathogen causing extraretinal disease in a patient with HIV infection.

Abbreviations

CMV: cytomegalovirus; HIV: human immunodeficiency virus; AIDS: acquired immunodeficiency virus; anti-TB: anti-tuberculosis

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