

Spontaneous Clearance of Hepatitis C Virus in a Patient Co-Infected with Hepatitis C Virus and Human Immunodeficiency Virus: a Case Report

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ABSTRACT

The effect of highly active antiretroviral therapy (HAART) on hepatitis C virus (HCV) infection remains unclear. Spontaneous HCV clearance with initiation of HAART in non-cirrhotic HCV patients co-infected with human immunodeficiency virus (HIV) has been reported. We describe an HIV/HCV patient with decompensated cirrhosis, who had spontaneous HCV clearance after an episode of elevated liver enzymes and a change in HAART regimen. His HCV RNA level remained undetectable for six months by quantitative and qualitative polymerase chain reaction (PCR) tests. The disappearance of HCV RNA may be due to a combination of host immune recovery, genetic polymorphism and direct effect of HAART against HCV.

Key words: Hepatitis C virus – HIV infection – HCV/HIV co-infection – HCV resolution – HAART.

INTRODUCTION

Hepatitis C virus (HCV) co-infection is estimated to affect 15-30% of the HIV-positive population [1]. HCV infection is a significant cause of morbidity, and liver disease is the leading non-HIV related cause of death in HIV/HCV co-infected patients [2]. Spontaneous HCV resolution usually occurs within the first 6 months after onset of infection [3]. However, spontaneous clearance of chronic HCV infection is rare. Few have described HCV clearance in association with cessation of immunosuppression, liver transplantation, other acute viral infections or change in HAART regimen [3-13]. To our knowledge, spontaneous HCV clearance in HIV/HCV patients with decompensated cirrhosis has not been reported in the literature. The mechanism

of spontaneous HCV resolution in HIV/HCV patients and the effect of HAART on HCV infection are not very well understood. We report a patient with HIV/HCV co-infection and decompensated cirrhosis, who had spontaneous HCV clearance after an episode of elevated liver enzymes and a change in his HAART regimen.

CASE REPORT

A 45-year-old man with treatment-naïve genotype 1a chronic hepatitis C and HIV on HAART was admitted in May 2013 for worsening jaundice. He had decompensated cirrhosis complicated with lower extremity edema, variceal bleeding and encephalopathy. He was diagnosed with HIV in 2002. His most recent viral load was 173 copies/mL and CD4+ T cells count was 90/mm³. He had been on stable HAART regimen of darunavir and emtricitabine-tenofovir for years. His alanine aminotransferase (ALT) was 69 U/L, aspartate aminotransferase (AST) 139 U/L, alkaline phosphatase (ALP) 154 U/L and total bilirubin 14.8 mg/dL up from baseline of 2 mg/dL (Table I). His most recent HCV-RNA level was 1.3 x 10⁶ copies/mL. Work-up comprising abdominal ultrasound, magnetic resonance imaging/magnetic resonance cholangiopancreatography (MRI/MRCP) and viral etiologies including Cytomegalovirus, Epstein - Barr virus serologies were unrevealing. Liver biopsy showed chronic active hepatitis, cirrhosis and cholestasis without any evidence of lymphoproliferative disorder. No clear etiology for

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Table 1. Clinical course of the patient. Liver enzymes, HIV, HCV viral loads and CD4(+) counts. His HAART regimen was changed after his hospitalization in May 2013.

Dates	ALT (U/L)	AST (U/L)	ALP (U/L)	Total Bilirubin (mg/dL)	HCV RNA (Copies/mL)	Qualitative HCV RNA	HCV Genotype	HIV RNA (Copies/mL)	CD4 count (Cells/mL)
Jan-12	119	323	220	1.6				4310	
Jul-12	113	326	276	2.3					
Apr-13	136	425	183	11.8	1,319,670	Positive	1a	173	90
May-13	69	194	154	14.8					
Aug-13	94	175	131	2.9					
Sep-13	50	117	129	2.1	<20	Negative			
Oct-13	50	113	134	1.3				<20	69
Nov-13	41	100	155	1.2	<20	Negative		<20	72
Mar-14	35	83	245	1.5	970	Positive	1a		97
Apr-14	28	71	213	1.6	4870	Positive			

his elevated liver enzymes was found, and he was discharged from the hospital. Following discharge, his HAART regimen was changed to a combination of elvitegravir, cobicistat, emtricitabine and tenofovir. His jaundice subsequently resolved and his total bilirubin level returned to the baseline. In follow up visit to our liver clinic in September 2013, his HCV RNA by PCR was found to be negative when checked in the anticipation of HCV treatment. After both quantitative and qualitative HCV-RNA tests remained undetectable for 6 months, repeat PCR in March 2014 showed 970 copies/mL. The genotype was found to be 1a.

DISCUSSION

HCV co-infection in HIV patients is associated with more rapid progression of liver disease to cirrhosis, increased liver-related morbidity and higher HCV loads [14]. Several studies suggested that HIV/HCV co-infected patients may mount a less vigorous T-cell response to HCV than mono-infected patients contributing to high rates of disease progression [15-17]. On the other hand, there were reports on spontaneous HCV clearance in HIV/HCV co-infected patients being treated with HAART. Several mechanisms of viral clearance have been hypothesized. Previous studies described that immune restoration and higher humoral response with increase in CD4+ and CD8+ T lymphocytes from HAART was central to the control of HCV viremia [7, 8, 11, 12, 18]. Falconer et al reported that a low level of chronic T cell activation and a high level of T cell function contributed to increased chances of HCV clearance in HIV patients [19]. Elevated transaminases were also observed preceding HCV clearance, and considered as hepatitis flare-ups from immune restoration [7, 12].

Direct or indirect effect of HAART on HCV replication has been proposed to play a role in spontaneous resolution of HCV infection [9, 13]. Neau et al reported that serum HCV-RNA levels increased during the first months of HIV treatment with protease inhibitors, and thus, HCV viral load suppression was likely due to host immune recovery from long-term HAART therapy [20]. Furthermore, genetic factors may contribute to HCV clearance. Some studies have suggested that IL28B-CC

genotype is associated with lower levels of HCV viral load compared to other genotypes and may promote HCV clearance in HCV/HIV co-infected patients [21, 22].

Our patient had an episode of elevated liver enzymes with marked jaundice of unknown etiology preceding his HCV clearance. We propose that the host immune response to the inciting cause may have cross-cleared his HCV. In addition, his newer HAART regimen may have a direct effect on HCV replication as well as promote his immune restoration contributing to HCV suppression. Although his IL28B genotype is unknown, genetic polymorphism may also play a critical role in spontaneous HCV clearance. Lastly, decompensated cirrhosis may contribute to the complex interaction among host immunogenetic factors and drug effects in this HIV/HCV co-infected patient.

CONCLUSION

We report a case of a HIV/HCV patient with decompensated cirrhosis, who had spontaneous HCV clearance after an episode of elevated liver enzymes and a change in antiretroviral therapy. The mechanism of HCV clearance is likely to be multifactorial. Further studies are needed to fully understand this rare phenomenon.

Conflicts of interest: There is no potential conflict of interest that is relevant to the manuscript.

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