SEVEN YEARS OF CHRONIC HCV INFECTION IN AN HIV-INFECTED MAN WITHOUT DETECTABLE ANTIBODIES

Published in: AIDS, 2015; Jan 29(3): 389-90.
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DOI: 10.1093/cid/ciu695
Received: 28 February 2014 | Accepted: 5 June 2014

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Presented at the Mid-winter Meeting of the Dutch Association of HIV-Treating Physicians (NVHB), 2015, Rotterdam, NL.
After infection with hepatitis C virus (HCV), in 50% of cases anti-HCV antibodies will be detectable within 5–10 weeks [1–3]. The development of antibodies may be somewhat prolonged in HIV-coinfected individuals: median time from HCV infection to seroconversion has been estimated to be 10–13 weeks among HIV-infected men who have sex with men (MSM) [4,5]. Anecdotal evidence suggests that seroconversion in HIV-infected individuals may be severely delayed: Thomson et al. [4] reported an interval of 3.3 years between the first positive HCV-RNA test and the first positive antibody test in one patient, although testing frequency was not reported. Waning of HCV-specific antibodies (i.e. seroreversion) has been reported among HIV-positive and HIV-negative patients, after spontaneous or treatment-induced clearance of acute [5,6] or chronic [7,8] infection. In an HIV-infected patient with progressive immunosuppression, seroreversion was reported despite continuous HCV replication. However, HCV antibodies became detectable again after antiretroviral therapy (ART) was initiated [9]. Here, we report a case without documented seroconversion and/or hepatitis (reflected by elevated transaminases) despite being infected with HCV for almost 7 years. A 61-year-old bisexual man, known to use noninjecting drugs (amphetamines and cocaine), was diagnosed with HIV in 1997. Possibly related to his drug use, he infrequently visited our outpatient clinic, and was poorly adherent to ART prescribed. In 2010, he presented with onycholysis and blistering of the skin suspect for porphyria cutanea tarda (PCT) but, because of incompliance, no definite diagnosis could be made. After his third clinical admission because of a candida esophagitis in July 2013, he decided to improve his lifestyle, and started taking ART, which resulted in an undetectable HIV viral load. Between 2008 and the last recorded visit in 2014, his CD4 cell count varied between 30–190 cells per mL. Urine analysis showed that he indeed had PCT, which is highly associated with HCV infection [10]. Concurrently, his alanine transaminase (ALT) level was slightly elevated for the first time in years (i.e. 66 U/l), and the patient was tested positive for HCV RNA and negative for HCV antibodies, which is suggestive of an acute infection. Presence of antibodies was tested with the DiaSorin LIAISON XL HCV Ab assay. He denied injecting drug use and did not have sexual intercourse for the past 4 years. Sequence analysis showed infection with HCV genotype 1a. Stored samples were tested and demonstrated that HCV RNA was already detectable from January 2008 onwards. The last HCV RNA negative sample dated from August 2007. All samples were antibody-negative. The slight ALT elevation (from 18 U/l in August 2007 to 41 U/l in January 2008) fits the time frame of infection (Fig. 1). The fact that during 7 years of chronic HCV infection there was never any sign of HCV antibodies (or hepatitis) is remarkable. Several reports already showed that acute HCV infections can easily be missed by using antibody testing only, due to the seroconversion window period [1–5]. Seronegative HCV infection has been reported earlier among immunocompromised patients [11,12], but at least part of these patients probably had an acute infection and antibodies would have been detectable later on. In addition, patients in these studies were tested with second-generation anti-HCV assays, thereby increasing chances of false-negativity [13]. The case we describe shows that chronic HCV infection may also be missed when only third-generation serologic assays are used. Among HIV-infected
MSM, testing for acute HCV is thus ideally performed using HCV RNA testing when there is suspicion of infection, especially since subtle ALT elevations are easily missed when monitored infrequently.

**Figure 1** Graph showing hepatitis C virus (HCV)-RNA status, HIV viral load (solid line), and alanine transaminase (ALT) concentration (dashed line) of a 61-year-old, HIV-infected man with a 7-year documented seronegative chronic HCV infection (from 2005 till present). Poor adherence to antiretroviral therapy until July 2013 is indicated by the fluctuating HIV viral load. The dotted horizontal line shows the upper limit of normal (ULN) ALT concentration (45 U/L).
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