CLINICAL CASE

Sexually transmitted HCV infection and reinfection in HIV-infected homosexual men

Infections et réinfections d’origine sexuelle par le VHC chez des patients homosexuels infectés par le VIH

L. Cottea,*, b, P. Chevallier Queyronb, c, I. Schliengera, M.-A. Trabaudc, C. Brochiera, P. André, c, e, f, F. Zoulima, b, d

a Service d’hépatologie et de sida, Hôtel-Dieu, hospices civils de Lyon, 1, place de l’Hôpital, 69002 Lyon, France
b Inserm, U871, 69003 Lyon, France
c Laboratoire de virologie Nord, hospices civils de Lyon, 69004 Lyon, France
d IFR62 Lyon Est, université Lyon-1, 69008 Lyon, France
e Inserm, U851, 69007 Lyon, France
f IFR128 biosciences Lyon-Gerland, université Lyon-1, 69007 Lyon, France

Available online 17 September 2009

Summary Multiple, concomitant or successive hepatitis C virus (HCV) infections have been described in injection drug users and following organ transplantation and blood transfusion. However, data on sexual HCV reinfection is scarce. We report sexual HCV reinfection following viral eradication of a first HCV infection in two homosexual HIV-infected men. The first patient acquired HCV genotype 4 infection after resolution of an initial acute HCV genotype 1a infection. The second patient was infected with genotype 1a HCV following remission of an initial acute HCV genotype 4c/d infection. The two subjects were successfully treated with peginterferon alpha-2a and ribavirin for their first and second infection and achieved a sustained virological response on both occasions. Unprotected anal intercourse with multiple partners known to be HIV-positive (serosorting) was the only risk factor for HCV transmission reported by both patients. Therefore, sexual HCV reinfection can occur in homosexual men having unprotected sex and “serosorting” should be considered a risk factor for the sexual transmission of HCV.

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Résumé Les infections multiples, concomitantes ou successives, par le virus de l’hépatite C (VHC) ont été décrites chez les patients utilisateurs de drogues par voie veineuse, et après transplantation d’organe ou transfusion sanguine. Peu de cas de réinfections par le VHC d’origine sexuelle ont été rapportés à ce jour. Nous décrivons le cas de deux patients homosexuels infectés par le VIH, ayant eu une réinfection par le VHC d’origine sexuelle, après guérison d’une première infection par le VHC également d’origine sexuelle. Le premier patient a été réinfecté par un VHC de génotype 4 après guérison d’une infection aiguë par un VHC de génotype 4c/d.

* Corresponding author.
E-mail address: laurent.cotte@chu-lyon.fr (L. Cotte).

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doi:10.1016/j.gcb.2009.06.011
The sexual transmission of hepatitis C virus (HCV) remains a controversial aspect of hepatitis C epidemiology. Evidence of sexual exposure as a risk factor of HCV infection can be found in American and European studies which identified multiple sexual partners as being an independent risk factor associated with sporadic acute hepatitis C [1,2]. On the other hand, no association has been found between male homosexual or heterosexual activity in long-term monogamous relationships and sexual transmission of HCV [1]. Several explanations have been proposed to explain this apparent discrepancy, one which states that high-risk sexual practices might promote transmission of HCV. Here, we report successive infection and reinfection with different HCV genotypes in two homosexual men with none of the classic risk factors for HCV transmission except for unprotected intercourse with multiple partners and a history of multiple sexually transmitted diseases.

The first patient presented in August 2003 with asymptomatic acute cytolytic hepatitis (aspartate aminotransferase [AST] 189 IU/L, alanine aminotransferase [ALT] 534 IU/L). Human immunodeficiency virus (HIV) infection was known since 1987 and the patient had been taking antiretroviral therapy since 1989. Nadirolipase CD4 cells count was 106/mm³ in 1995. On presentation, he had been taking nevirapine, abacavir and boosted fosamprenavir which was begun on October 2004. CD4 cells count was 1158/mm³ and HIV viral load was <50 copies/mL. Peginterferon alpha-2a 180 µg/week and ribavirin 1000 mg/day were started again in February 2007 but had to be stopped in August 2007 because of psychiatric symptoms. HCV-RNA became undetectable after 4 weeks of therapy and remained undetectable so far. A detailed questionnaire revealed no other risk factors for HCV infection in this patient except for unprotected anal intercourse with multiple HIV-infected partners. Fig. 1 presents the evolution of ALT, AST and HCV-RNA in this patient. The second patient presented in October 2006 with primary HIV infection. His past medical history included rectal gonorrhoea in June 2005 and acute HAV hepatitis in 2004 which was presumed to be sexually transmitted in the absence of other usual risk factors for HAV infection. The patient had been referred to the unit in January 2000, April 2002 and August 2003 for HIV postexposure prophylaxis following unprotected intercourse with anonymous partners. At the time of HIV primary infection, transaminases were normal. HCV antibodies were negative, total HAV antibodies were positive and HBs antibodies were positive following HBV vaccination. No antiretroviral treatment was administered. On the next visit, 4 weeks later, the patient presented with acute hepatitis (AST 233 IU/L, ALT 468 IU/L). HCV-RNA was positive (581 787 IU/L), as was the first sample drawn in October. HCV genotype was determined as 4c/d (InoLipa 2.0). CD4 cells count was 543/mm³ and HIV viral load was 37 000 copies/mL. Peginterferon alpha-2a 180 µg/week and ribavirin 1200 mg/day were given from December 2006 to July 2007 with a good overall tolerance. HCV-RNA became undetectable from January 2007 to January 2008 and met the criteria for a sustained viral response. Despite counselling and psychotherapy, the patient continued to have unprotected sex and was diagnosed with acute syphilis in June 2007, rectal gonorrhoea in December 2007 and rectal lymphogranuloma venereum in March 2008. In April 2008, a systematic blood test revealed asymptomatic acute hepatitis (AST 1438 IU/L, ALT 2395 IU/L). HCV-RNA was again positive in serum (6 136 470 IU/mL) and HCV genotype was determined as being type 1a (InoLipa 2.0). CD4 cells count was 543/mm³ and HIV viral load was 11 580 copies/mL. Peginterferon alpha-2a 180 µg/week and ribavirin 1200 mg/day were given from December 2006 to November 2007 with a good overall tolerance. A detailed questionnaire revealed no other risk factors for HCV infection in this patient except for unprotected anal intercourse with multiple HIV-infected partners.
Sexual HCV reinfections

undetectable at week 2 and is still negative so far. Like the former patient, no other risk factors for HCV infection were found except for unprotected anal intercourse with multiple HIV-infected partners. Fig. 2 presents the evolution of ALT, AST and HCV-RNA in this patient.

Several clusters of acute HCV infections have been described in homosexual, mostly HIV-infected, men [3—6]. High-risk sexual practices, including unprotected anal intercourse as well as unprotected active and passive fisting and group sex, have been associated with acute HCV infections, along with sharing drugs via the nasal or anal route and being involved in multiple high-risk activities [3—6]. "Serosorting", meaning that people with "known" HIV status voluntarily decide to have unprotected sex with persons of the same status, has been associated with an increase in syphilis and other sexually transmitted diseases [7,8] and with HIV transmission from patients during the primo-infection stage [9]. Multiple, concomitant or successive HCV infections have been well-described in patient populations where multiple exposures are common such as intravenous drug users or following organ transplantation or blood transfusion [10]. A recent cross-sectional study in HIV-infected

Figure 1  Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and HCV-RNA evolution for patient 1 (non proportional time scale). Peg-IFN: pegylated interferon; RBV: ribavirin.

Figure 2  Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and HCV-RNA evolution for patient 2 (non proportional time scale). Peg-IFN: pegylated interferon; RBV: ribavirin.
patients showed that patients who were presumed to be infected by injection drug use spontaneously cleared HCV infection less frequently (11.6%) than patients in whom sexual transmission of HCV was suspected (21.9%) [11]. However, this difference was mainly due to a higher clearance rate in heterosexual patients (26%) than in homosexual patients (13.5%). The authors hypothesized that smaller viral inoculums in case of sexual transmission might explain the ability of the immune system to clear HCV. An editorial in the same issue of the Journal of Hepatology suggested that this phenomenon could be related to less frequent HCV reinfections in case of sexual transmission [12]. Regarding the high frequency and the severity of chronic HCV infection in HIV-infected patients, HCV treatment is systematically started in our unit as soon as HCV acute infection is confirmed, which precludes analysis of spontaneous clearance in such cases. However, our observation, in addition to two other similar cases recently reported in the literature [13], further suggest that HCV reinfections following viral eradication of an acute infection with a different HCV genotype may be quite frequent in homosexual men who engage in unprotected anal intercourse. Other patterns of multiple HCV infections in homosexual HIV-infected men have been recently reported by Ghosn et al. [13], who described the case of a HCV type 3 superinfection in a patient with chronic HCV type 4d infection, and the case of a HCV type 1a reinfection with a different HCV type 1 strain following eradication of the first strain in another patient. As no immune protection can be expected from a previous HCV infection, HCV should be added to the list of sexually transmitted infections than may repeatedly occur, as long as high-risk practices continue. Serosorting and associated unprotected intercourse alone should be considered a major risk factor for transmission of HCV and other sexually transmitted diseases. Regular screening of transaminases and HCV-RNA should be considered in this high-risk population. In case of unexpected recurrence of HCV-RNA following virological response, HCV genotype should be determined to distinguish relapse of HCV infection from reinfection.

Conflicts of interest

None.

References