Acute hepatitis C infection after sexual exposure

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Abstract

A case is described of a woman with acute hepatitis C infection whose partner had chronic hepatitis C infection and where heterosexual contact was the only major risk factor. Infection of both partners was confirmed serologically and by the finding of virus RNA by reverse transcription and polymerase chain reaction amplification. Nucleotide sequence analysis of the NS5 region (RNA polymerase) was used to show that both partners were infected with virus of the same genotype (1a). The nucleotide sequence of virus RNA found in the female patient is closest to variants cocirculating in the male contact, consistent with transmission having occurred between the two.

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The role of the sexual route in the transmission of the hepatitis C virus (HCV) remains controversial.[1 2] It is accepted that transmission does occur by the parenteral route, after either blood transfusion, the use of blood derived products or intravenous drug use. However, up to 50% of cases remain unexplained.[3] Evidence for sexual transmission has been conflicting as studies have been confounded by problems associated with first generation serological tests, and other risk factors such as intravenous drug use or coinfection with other viruses (human immunodeficiency virus and hepatitis B virus). Two recent papers using confirmatory demonstration of virus RNA by the polymerase chain reaction have shown no cases of transmission in the sexual partners of HCV infected haemophiliac subjects, in the absence of other risk factors.[4 5] In fact, the authors suggested that there may be no risk of sexual transmission at all and stated that they do not currently recommend protective measures (for example, use of condoms) during intercourse. Other recent reports, however, suggest that transmission may sometimes occur between heterosexual couples where there are no known risk factors.[6–9]

We report on a patient with acute hepatitis C virus infection after sexual exposure of a female partner to a chronic carrier, in the absence of other major risk factors. Nucleotide sequence analysis of virus RNA present in the two subjects is consistent with transmission having occurred between the couple.

Case history

A 29 year old British white woman presented to her general practitioner with pruritus. Physical examination was normal and no initial diagnosis was made. Four days later she returned having developed urinary frequency and dark urine. Screening blood tests were taken. On examination she was slightly tender in the right upper quadrant. Urine analysis showed the presence of protein and bilirubin. Five days later, clinical jaundice was apparent and increased bilirubin was found in her urine. A two week mild illness followed before the jaundice resolved. Further samples were collected for acute serological tests. The patient remained tired with some nausea for the next month before returning to full health. Investigations showed an acute hepatitis (see Table). The rising titre of antibodies to HCV, both in repeated second generation enzyme linked immunosorbent assay (ELISA) (Abbott Laboratories) and the broadening of the response to RIBA-3 (Chiron) suggested acute infection with HCV. Other causes of acute viral hepatitis were excluded by paired serology, autoantibody screening was normal, and she later tested negative for HIV infection.

Nine months before presentation, she had sought advice from her general practitioner about the risk of sexual transmission of hepatitis C virus. She was separated from her husband and starting a new relationship. Her potential partner had previously been diagnosed as having chronic hepatitis C infection after investigation (including liver biopsy) at King's College London. She was advised that any risk was small and therefore declined to use barrier contraception. Over the next nine months before her illness, they had an active physical relationship, which included oral sex by both partners, vaginal, and anal intercourse. She had no history of blood transfusion or intravenous drug use, no tattoos, and no previous contacts with any known cases of hepatitis or jaundice. She had her ears pierced when she was 13 years old and had lived in the

Investigations

Week from onset of symptoms	*0*	*2*	*4*	*6*	*11*	*20*
Full blood count	Normal		Normal		Normal	
Urea and electrolytes	Normal				Normal	
Albumin (g/l)	42	50	38	44	46	
Total bilirubin (μmol/l)	33	16	12	5	6	
Aspartate transferase (IU/l)	660	98	28	16	7	52
Alkaline phosphatase (IU/l)	288	195	115	161	108	
HCV Markers						
ELISA (second generation) optical density	1·13	>2	>2	>2	>2	
RIBA-3 (Chiron)						
c100	1				3	3
c33	3				3	4
c22	4				4	4
NS5	0				0	0
Virus RNA (RT–PCR)	Positive	Positive	Positive	Negative	Negative	Positive

United States for 10 years. The only other admitted risk factor was that the couple shared an electric razor to shave their legs (he is a keen amateur cyclist). Past medical history was unremarkable.

Her partner, a 33 year old man was first noticed to have an increase in transaminase activities in 1987 after an episode of jaundice. He had first become unwell during a world tour. He had received a full course of recommended vaccinations before leaving the United Kingdom including anti-hepatitis A virus gammaglobulin. After six months of travel, he received a further vaccination with anti-hepatitis A gammaglobulin in Australia. Six weeks later in South America, he developed mild jaundice and could not tolerate alcohol. Subsequently on returning to the United Kingdom, his symptoms resolved and after negative serological tests, he was diagnosed as a case of non-A, non-B hepatitis. His liver function was then monitored regularly and he was told it remained 'mildly abnormal'. In 1990 anti-HCV antibodies were found in his serum and he was referred to King's College London. Liver biopsy examination showed chronic hepatitis. He was offered treatment with interferon but declined. He had no past history of contacts with either hepatitis or jaundice and had not received blood transfusions. In 1976 he had briefly experimented with intravenous drugs. Although the woman is HIV negative, his status remains unknown as he has declined testing.

To find out if the virus had been transmitted between the couple, nucleotide sequence analysis was performed on virus RNA extracted from the serum of both subjects. Virus RNA was copied into cDNA by reverse transcription and amplified by the polymerase chain reaction (PCR) using oligonucleotides specific for the NS5 (RNA polymerase) region of the virus genome. Oligonucleotides were 1203 (5'-ATGGGGTTCTCGTATGATAC-CCGCTGCTTTGACTC-3') and 1204 (5'-GGAGGGGCGGAATACCTGGTCATAG CCTCCGTGAA-3') for primary PCR and 122,123[10] for the secondary PCR, and permit nucleotide sequence analysis between positions 8000 and 8196 (numbering as in[11]). This region of the virus genome can be used to distinguish between the six different virus genotypes and further subtypes that have been described to date.[10]

The nucleotide sequence of virus from the female patient at presentation corresponds to virus of genotype 1a[10] and was unchanged five months later. Analysis of virus RNA isolated from the male contact showed a closely related NS5 nucleotide sequence except that nucleotide polymorphisms were present at several positions. Further analysis of this RNA at limiting dilution produced eight independent nucleotide sequences that differed from each other by 0–7 nucleotide substitutions. They differ by 4–7 substitutions from the sequence present in the female patient, which itself differs by 7 or more substitutions from other published HCV NS5 sequences. This is consistent with the virus in the female patient having derived from one of the cocirculating variants present in the male contact.

Discussion

Evidence of sexual transmission of HCV is inconclusive with varying results as to the degree of risk, although overall this is thought to be low.[1 2] Even before the identification of the aetiological agent, an epidemiological study of clinical non-A, non-B hepatitis cases suggested that multiple sexual partners or household contacts accounted for a further 11% of cases[3] that were not explained by the parenteral route. Subsequently, studies continued to suggest the possibility of sexual transmission,[12–15] although one study of sexual and household contacts showed no cases of transmission.[16] These studies were based on serological tests for HCV with the possibility of error due to lack of sensitivity and specificity. Haemophiliac subjects have frequently been infected with HCV through the use of contaminated blood products and have been used in several case controlled studies[4 5 17 18] as the predominant group. Two early papers showed a low incidence of probable sexual transmission to the partners of infected haemophiliac subjects.[17 18] In Eyster's study all cases where the partner was infected were associated with coinfection with the HIV virus in the carrier. These studies were based on serological testing and the low risk has not been confirmed by two more recent studies using detection of virus RNA.[4 5] These last studies have shown no cases of sexual transmission except where there were additional important risk factors. These case control studies, however, have used predominately haemophiliac populations and as there is no evidence to suggest that such groups are representative of the normal population in terms of sexual behaviour or risk of transmission, we should be cautious in using them as a model for the general population.

We have shown the infection of HCV in both partners is by virus of the same genotype (1a) and that the nucleotide sequence of virus from the female patient is closest to those of variants cocirculating in the male contact. These data provide evidence for transmission of the virus from the chronically infected male contact to his female partner and further shows the use of genotyping in the investigation of the epidemiology of HCV. In this case, sexual transmission seems to be the only important risk factor (which included anal intercourse), although a source of possible bloodborne transmission is their occasional shared use of an electric razor. Other case reports of heterosexual transmission have recently been published,[6–8] all of which support the need for continued caution during sexual contact between infected subjects and their partners. Therefore our current practice is to advise HCV infected cases and their partners that there is a small risk of transmission of the virus during sex and we continue to recommend barrier contraception.

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