Hepatitis C infection: the quest for new treatment strategies
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A physician with a positive HCV-RNA test after a needle stick injury.

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Summary

Needle stick accidents continue to be a hazard for healthcare workers. We report the development of acute hepatitis C infection in a physician after needle stick injury. Hepatitis C virus (HCV)-RNA, seroconversion and a raised plasma alanine aminotransferase (ALAT) level were found in plasma 3 months after the accident. Treatment with interferon-α and ribavirin was started. While the physician was on treatment, HCV-RNA test results from plasma taken the day the treatment was started became available. HCV-RNA was undetectable by quantitative bDNA assay, undetectable by qualitative polymerase chain reaction (PCR) and undetectable by transcription mediated amplification (TMA). A dilemma arose at this point: should the patient stop the treatment or continue the planned therapy? The physician decided to continue a 24 week course of treatment. Six months after the end of treatment, the physician was still HCV-RNA negative and with a normal plasma ALAT level. The rationale of the decision to continue therapy is discussed. This information may be useful for clinicians confronted with a similar dilemma.
Introduction

The overall rate of HCV transmission after a needlestick accident with hepatitis C virus (HCV) positive blood ranges from zero to about 10%. If an acute hepatitis C infection is established, only 15-40% of persons will clear the HCV-RNA spontaneous and thus a substantial number will become chronically infected (1). There have been several reports of acute hepatitis C infection after HCV contaminated needle stick injuries in healthcare workers (2-4). So far there is no effective method, (no post exposure prophylaxis, and no vaccin), to prevent HCV infection in anyone who experiences a HCV contaminated needle stick accident (5). A recent study showed that early treatment of acute HCV infection, with induction therapy of 5 MU interferon-α (IFN) daily for the first 4 weeks, followed by 5 MU IFN three times a week for another 20 weeks induced a sustained virological response (SVR) in 98% of patients, with the remarkable finding that the response to treatment was not influenced by the viral genotype (6). In the treatment of chronic hepatitis C infection, only genotype 2 and 3 patients achieve a SVR of 80% after 1 year of treatment with Peg-IFN and ribavirin, whereas about 40% of patients with genotype 1 and 4 will achieve a SVR (7). We report a case of an acute HCV infection following a needle stick injury in a physician who decided to give himself maximal chances to clear the virus.

Case report

A 28 year-old physician sustained a needle stick injury on 27 February 2000 with a needle contaminated by blood from a 49 year-old, HIV negative, haemophilia patient. This patient was chronically infected with HCV and had never received antiviral treatment. He was infected with HCV genotype 1a (TruGene™ HCV Genotyping Assay, Visible Genetics Inc., Toronto, Canada) and had a viral load of \( 7 \times 10^5 \) IU/mL (VERSANT™ bDNA 3.0 assay [linear range 520-8.3 \( \times 10^6 \) IU/mL], Bayer Diagnostics, Berkeley, CA) in a blood sample drawn at the time of the accident. While the physician, who sustained the needle stick injury, had a normal plasma ALAT level (upper limit of normal (ULN) 45 U/L) and his plasma was negative for antibodies to HCV (third generation assay EIA 3.0, Abbott Laboratories, Chicago, Ill) and negative for HCV-RNA (HCV 2.0 qualitative test [lower detection limit 50 IU/mL], Roche Molecular Systems, Branchburg, NJ). Approximately 1.5 months after sustaining the needle stick injury, he had noticed jaundice just for one day and he had experienced a very short period of fatigue, but due to workload he had ignored the symptoms. Another 1.5 months later on June the 5th of 2000, a next blood sample drawn from the physician (according to the needle stick injury protocol in our hospital) was positive for qualitative HCV-RNA, (genotype 1a) and antibodies to HCV. The HCV-RNA load in this sample was below the detection limit of the bDNA 3.0 assay (< 520 IU/mL) and the plasma ALAT level was normal. The following blood sample drawn on June the 19th contained an HCV-RNA viral load of \( 5.1 \times 10^4 \) IU/mL (by bDNA) and the plasma ALAT level was now 93 U/L. He was asymptomatic at that time. After deliberation the physician opted for therapy and treatment started on the 10th of July, 4.5 months after the needle stick. The treatment regimen was a one week induction course of IFN 3 MU sc. 3 times daily in combination with 1200 mg ribavirin daily, followed by IFN 3 MU 3 times per week in combination with 1200 mg ribavirin per day for subsequent 23 weeks. At the start of the induction period the ALAT level was normal. At the end of this period the ALAT level was just above the ULN.
Shortly hereafter the result of the analysis of a blood sample drawn at the start of the induction treatment became available and showed that HCV-RNA was undetectable by bDNA and qualitative PCR. When retested with TMA (VERSANT™ TMA assay [lower detection limit 50 IU/mL], Bayer Diagnostics, Berkeley, CA), HCV-RNA was also not detectable. Despite these findings the physician decided to complete the 24 week treatment schedule to maximize the chance of inducing a sustained virological response and hence, preventing a chronic HCV infection. The plasma ALAT level normalized during the second week of treatment and remained normal throughout the remainder of the treatment period and during the entire follow-up period of 6 months. HCV-RNA remained undetectable during treatment, at the end of the treatment and at the end of follow-up. Antibodies to HCV decreased by EIA 3.0 during this period. Results of the recombinant immuno blot confirmatory test (SIA, RIBA 3.0, Chiron Corp., Emeryville, CA) were positive for NS3 and NS4 throughout this period, decreased for NS5, but remained negative for antibody responses to Core. During the induction treatment the patient experienced muscle pain and a short period of fever. At the end of the induction week the physician had general malaise and experienced difficulties in doing his routine work in hospital wards. After the reduction of the IFN schedule to three times a week, treatment was well tolerated, only a slight fall in haemoglobin level was noticed and he lost no time from work. The physician was, however, aware of an increasingly depressive mood during treatment.

**Discussion**

Approximately four and a half months after a needle stick injury a physician started treatment for an acute hepatitis C infection. The decision for treatment was based on a rising HCV-RNA viral load, from <520 to $5.1 \times 10^4$ IU/mL (genotype 1a) and a rising ALAT level to 93 U/L within a period of 2 weeks. While on treatment, he was confronted with the situation that the HCV-RNA was undetectable by TMA (5 IU/mL), the day the treatment started. So what to do? Stop the treatment because apparently the infection was already spontaneously resolving and avoid the potentially adverse effects and spare the costs of the combination therapy. Or continue the medication as scheduled.

In favor of continuing therapy was the fact that in the first months of infection HCV-RNA levels may fluctuate considerably and HCV-RNA may be even undetectable at some time point (8;9). Thus, one negative HCV-RNA test does not exclude an ongoing infection. However, the patients in the above mentioned studies were all tested with quantitative assays with a cut-off much above the 5 IU/mL of the TMA test. As the physician wanted to have the maximum chances in preventing the development of a genotype 1 chronic hepatitis C infection, he decided to continue the medication. Till now he is HCV-RNA negative by TMA test.

We have changed our policy since this case report. As HCV-RNA can become detectable 7 to 21 days after exposure (10), we decided that 2 weekly blood samples must be obtained following a known HCV contaminated needle stick injury, and tested with a TMA test for HCV-RNA at least during the first 3 months after the injury. We advice to start antiviral therapy for 24 weeks immediately after HCV-RNA is detected. In view of the results obtained by Jaeckel et al. with IFN monotherapy (6), the choice is PEG-Interferon monotherapy. Every healthcare worker must have the maximal chance to clear the hepatitis C virus as soon as possible, with a wait and see policy for a couple of months, they will become a victim of calculation of probabilities.
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References
