

Acute Hepatitis C Infection without Anti-HCV Antibody in a Chronic Hemodialysis Patient

Yi-Jung Lee, MD; Chiz-Tzung Chang, MD; Mai-Szu Wu, MD

Liver disease caused by hepatitis C virus (HCV) may cause significant morbidity and mortality among patients with end stage renal disease under maintenance hemodialysis (HD). The anti-HCV antibody detection is the current method used to detect HCV infection. However, there are many seronegative HCV infections. Reverse transcriptase polymerase chain reaction for HCV RNA provides a better diagnostic tool to detect the infection. We present a chronic hemodialysis patient with HCV infection. HCV RNA was present in his blood, but not the anti-HCV antibody. Subtle clinical symptoms and slight elevation in hepatic enzyme was the only clue of the acute infection. The results of this case report indicated that small clinical signs and symptoms are helpful in the diagnosis of low viral load seronegative HCV infections in hemodialysis patients. (*Chang Gung Med J 2006;29(4 Suppl):35-8*)

Key words: Hepatitis C, hemodialysis.

Liver disease caused by hepatitis C virus (HCV) infection may lead to significant morbidity and mortality among patients with end stage renal disease under maintenance hemodialysis (HD).⁽¹⁾ HCV infection in dialysis patients has been associated with previous blood transfusion,⁽²⁾ mode of dialysis therapy⁽³⁾ and duration of hemodialysis.⁽¹⁾ Microbiological and molecular studies indicated that the spread of infection within the hemodialysis unit is the most probable cause.⁽⁴⁾ The possible routes of HCV infection within the hemodialysis unit include dialyzer reuse, sharing of HD machine and instruments, and environmental contamination.⁽⁵⁾ A reliable diagnostic tool is necessary to make accurate diagnosis and isolate the infected patients to be effective in preventing the spread of the infection.⁽⁶⁾

The early generation of enzyme linked immunosorbent assay (ELISA1), detecting anti-HCV antibodies among dialysis patients, was the method used to determine whether the patient had HCV

infection in the beginning. The advent of a second generation test (ELISA2) revealed an even higher prevalence of anti-HCV antibodies among hemodialysis patients.⁽⁷⁾ Pooled data from studies in which dialysis patients were tested using both ELISA1 and ELISA2 revealed that ELISA2 identified more than twice the number of patients with HCV antibodies than ELISA1 did.⁽⁷⁾ The third generation anti-HCV tests (ELISA3) are currently largely in use. Compared with the second generation tests, the ELISA3 tests have shown greater sensitivity and specificity in patients receiving renal replacement therapy.⁽⁸⁾

We present a case with acute onset of general malaise, elevated liver enzyme and HCV RNA, using the reverse transcriptase polymerase chain reaction (RT-PCR) test. During the entire clinical course, we did not detect the anti-HCV antibody. The presence of the antibody was thought to be the gold standard of the diagnosis of HCV infection.

From the Division of Nephrology, Chang Gung Memorial Hospital, Keelung.

Received: Apr. 12, 2004; Accepted: May 27, 2005

Correspondence to: Dr. Mai-Szu Wu, Division of Nephrology, Chang Gung Memorial Hospital, 222, Maijin Rd., Anle Chiu, Keelung, Taiwan 204, R.O.C. Tel.: 886-2-24313131 ext. 2501; Fax: 886-2-24335342; E-Mail: maxwu1@adm.cgmh.org.tw

This case report shows that the 3rd generation ELISA can be negative in some acute HCV infection in dialysis unit. The presence of the unnoticed acute hepatitis might be a possible source of infection within the dialysis unit.

CASE REPORT

A 39-year-old male started regular peritoneal dialysis as a result of advanced renal failure 5 years prior to this incident. He was shifted to hemodialysis therapy due to repeated peritonitis after 2 years of peritoneal dialysis. The peritoneal dialysis catheter was removed and arteriovenous fistula was created for the chronic hemodialysis. The peritonitis subsided after the removal of catheter. He was negative for hepatitis B surface antigen and negative for anti-HCV antibody when he entered the hemodialysis program. The laboratory test results indicated that he was free of chronic B and C hepatitis. He had no previous history or family history of hepatic disease.

He experienced mild malaise and anorexia suddenly for 1 to 2 weeks after 3 years of regular hemodialysis. The biochemistry test results revealed a slightly elevated alanine transaminase (ALT) up to 64 u/L. Repeated anti-HCV antibody tests (Ax SYM HCV III; Abbott Laboratories) using ELISA3 were negative (0.35/1.0/Abbott-3). Mildly elevated ALT (40 u/L) was still noted 3 weeks after the original testing, although the general malaise had improved. Therefore, we checked for HCV mRNA using RT-PCR, (Amplicor HCV test: Roche Diagnostic System Inc., Branchburg, NJ, USA) which showed a significant viral load (optical density 2.987/0.15, test value/cut-off value). In the mean time, the anti-HCV antibody using ELISA3 was still very low in titer (0.19/1.0/Abbott-3). He was then restricted to the hepatitis C area of our hemodialysis unit to prevent the spread of the infection.

The ALT level gradually went down to 11 u/L. The HCV RNA returned to normal 8 weeks after diagnosis (optical density 0.005/0.15, test value/cut-off value). The anti-HCV antibody remained below the cut-off point (0.21/1.0/Abbott-3). He felt subjectively well then and ALT levels had decreased to less than 10 u/L, which was his usual status.

He remained healthy after the episode. Monthly follow-up examinations did not reveal abnormal liver enzymes or elevated anti-HCV antibody titer.

Taken together, he had an episode of acute C hepatitis without appearance of elevated anti-HCV antibody titer during both the acute and recovery phase. The only evidence of his acute hepatitis were clinical malaise, slightly elevated ALT and transient elevation of the HCV RNA, detected using RT-PCR testing.

DISCUSSION

Patients with end-stage renal disease on hemodialysis are at increased risk for acquiring hepatitis C virus infection.⁽⁵⁾ The transmission of HCV has been reported to occur between patients receiving hemodialysis in the same unit. HCV infection is the most common cause of chronic liver disease among chronic dialysis patients.⁽¹⁾ Patients who were HCV RNA positive or those who are positive for anti-HCV antibody were at increased risk for death compared with patients who were negative.⁽⁷⁾ There is still no effective treatment or vaccine available for hepatitis C.⁽⁹⁾ The prevalence of HCV infection can be lowered by patient isolation.⁽⁶⁾ It is crucial to find the best measures for early diagnosis, by which we can track the potential transmission and prevent further spread of the virus.

There are two categories of diagnostic tests for hepatitis C. One is serologic assay that detects antibodies to hepatitis C virus (anti-HCV antibody). The other is molecular assay that detects RNA genomes within infected patients. The pathogenic pattern of HCV acquisition is invariable. There is an initial viremic phase when we can detect HCV RNA easily. The serum of patients in this phase is contagious. It is preferable if we can detect the infection and isolate the patients during this stage of infection. The phase is also associated with a concomitant increase in ALT activity and precedes anti-HCV seroconversion. The following recovery phase is characterized using HCV RNA clearance and normalization of ALT activity. Anti-HCV seroconversion occurs 1 and 2 months after the increase of ALT.⁽¹⁰⁾ Detection of HCV RNA in patients using RT-PCR provides evidence of active HCV infection. It is more rationale to detect HCV RNA instead of anti-HCV antibody in the diagnosis of acute HCV infection and viral load, which is more related with the viral spread in the hemodialysis unit. That is, to the point of view of public health, early detection of HCV infection pre-

vents further spread of HCV infection. Furthermore, HCV RNA testing can identify HCV infection before seroconversion in individuals with deranged liver function tests, which takes 1 to 2 months longer.

In a prospective study conducted by Schroter et al.,⁽¹¹⁾ they found that there was a small percentage (5%) of seronegative HCV infections in hemodialysis patients. The small percentage of patients can be contagious and become the source of hemodialysis unit infection. However, it is difficult to perform the RT-PCR tests on a daily basis to detect this small percentage of occult HCV infections in a hemodialysis unit. Some associated symptoms and signs might be helpful to alert the dialysis physicians of HCV infection in seronegative hemodialysis patients. Our patient presented with mild malaise and slight elevation in hepatic enzymes, which are usually low in hemodialysis patients. The clinical pictures could indicate an acute low viral load HCV infection in a hemodialysis patient, who might be also infectious in the hemodialysis unit.

In summary, we presented a hemodialysis patient with mild malaise and mildly elevated hepatic enzyme. The HCV RNA analysis was positive, although the serologic tests remained negative during the recovery phase. This case indicates that small clinical manifestations and timely HCV RNA tests are important in the diagnosis of low viral load seronegative HCV infections in hemodialysis patients.

REFERENCES

1. Pol S, Vallet-Pichard A, Fontaine H, Lebray P. HCV infection and hemodialysis. *Semin Nephrol*, 2002;22:331-9.
2. Taal MW, van Zyl-Smit R. Hepatitis C virus infection in chronic haemodialysis patients--relationship to blood transfusions and dialyser re-use. *S Afr Med J*, 2000;90:621-5.
3. Akpolat T. CAPD: a control strategy to prevent spread of HCV infection in end-stage renal disease. *Perit Dial Int*, 2001;21:77-9.
4. Taskapan H, Oymak O, Dogukan A, Utas C. Patient to patient transmission of hepatitis C virus in hemodialysis units. *Clin Nephrol*, 2001;55:477-81.
5. Fabrizi F, Poordad FF, Martin P. Hepatitis C infection and the patient with end-stage renal disease. *Hepatology*, 2002;36:3-10.
6. Yang CS, Chang HH, Chou CC, Peng SJ. Isolation effectively prevents the transmission of hepatitis C virus in the hemodialysis unit. *J Formos Med Assoc*, 2003;102:79-85.
7. Pereira BJ, Levey AS. Hepatitis C virus infection in dialysis and renal transplantation. *Kidney Int*, 1997;51:981-99.
8. Fabrizi F, Lunghi G, Pagliari B, Mangano S, Faranna P, Pagano A, Locatelli F. Molecular epidemiology of hepatitis C virus infection in dialysis patients. *Nephron*, 1997;77:190-6.
9. Curtis JJ. Hepatitis C and management of end-stage renal disease. *Nephrol Dial Transplant*, 2000;15:49-51.
10. Okuda K, Hayashi H, Yokozeki K, Kobayashi S, Kashima T, Irie Y. Acute hepatitis C among renal failure patients on chronic haemodialysis. *J Gastroenterol Hepatol*, 1998;13:62-7.
11. Schroter M, Feucht HH, Schafer P, Zollner B, Laufs R. High percentage of seronegative HCV infections in hemodialysis patients: the need for PCR. *Intervirology*, 1997;40:277-8.

透析病人合併 C 型肝炎抗體陰性之急性 C 型肝炎感染

李怡蓉 張志宗 吳麥斯

C 型肝炎是慢性透析病人常見的併發症，檢測血中 C 型肝炎抗體是目前診斷 C 型肝炎感染的方法。我們報告一個血液透析患者合併急性 C 型肝炎感染及輕度肝功能生化檢驗異常病人，C 型肝炎抗體呈陰性反應，但 C 型肝炎 RNA 呈陽性。本報告顯示輕度肝功能異常之抗體陰性 C 型肝炎可用 HCV RNA 來輔助診斷。(長庚醫誌 2006;29(4 Suppl):35-8)

關鍵字：C 型肝炎、血液透析。

長庚紀念醫院 台北及基隆院區 腎臟科

受文日期：民國93年4月12日；接受刊載：民國94年5月27日

索取抽印本處：吳麥斯醫師，長庚紀念醫院 基隆院區 腎臟科。基隆市204安樂區麥金路222號。Tel.: (02)24313131 ext. 2501; Fax: (02)24335342; E-mail: maxwu1@adm.cgmh.org.tw