High Incidence of Hepatitis C Virus Antibodies in Hemodialysis Patients

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Dear Sir,

Most cases of non-A, non-B hepatitis are associated with blood transfusion and blood products, but the frequent occurrence of non-A, non-B hepatitis in the absence of any obvious parenteral exposure has been well documented [1, 2]. Recently, it has been clarified that hepatitis C virus (HCV) is a major cause of non-A, non-B hepatitis [3]. Hemodialysis patients have a high risk of HCV infection because of their exposure to blood transfusion, repeated extracorporeal hemocirculation, and a state of immunodeficiency due to uremia [4, 5]. We have assessed the seroprevalence of HCV antibody in hemodialysis patients and tried to clarify the relationship between HCV infection and chronic renal failure.

The patient population consisted of 1,435 patients undergoing maintenance hemodialysis at 18 hospitals in Kumamoto Prefecture. Most of the patients were born and all were living in Kumamoto Prefecture. 853 were male (mean age: 54.3 years) and 582 were female (mean age: 55.4 years). 967 of the patients had a known history of blood transfusion, and the duration of hemodialysis was known in 1,384 of the patients. Normal serum samples were obtained from 58,103 blood donations (33,590 male and 24,503 female) in Kumamoto prefecture. All serum samples were tested using a recombinant enzyme-linked immunosorbent assay (ELISA) (Ortho Diagnostic Systems) for HCV antibodies [3] and by reversed passive hemagglutination (Fujirebio, Japan) for hepatitis B virus surface (HBs) antigen.

In Kumamoto Prefecture, 1.3% (male; 1.4%, female; 1.1%) blood donations have been found to be reactive. On the other hand, of the 1,386 hemodialysis patients, 312 (22.5%) were positive for antibodies against HCV. This ratio was significantly higher ($p < 0.001$) than that in the blood donors. The prevalence of HCV infection increased with the duration of the period of hemodialysis (0-1 years: 8.9%, 1-3: 12.9%, 3-5: 14.2%, 5-10: 24.5%, > 10: 43.5%).

Sixty (23.5%) of the 255 who had received many blood transfusions (> 5 units), and 71 (20.0%) of the 355 who had received a few blood transfusions (5 < units), had antibodies against HCV, as compared to 64 (18.1%) of the 348 who had not received a blood transfusion. The difference in antibody seroprevalence was not significant among the groups with few blood transfusion, many transfusions and the untransfused group.

Many cases of HCV hepatitis are associated with blood transfusion, and hemodialysis patients have more blood transfusions than healthy individuals. Therefore, blood transfusion may be one of the major routes of HCV infection in hemodialysis patients. It is important that blood donors are effectively screened in order to decrease HCV infection following blood transfusion. The Japan Red Cross Blood Center started screening for HCV antibodies in November 1989 because of this consideration.

On the other hand, the seroprevalence of HCV antibodies in hemodialysis patients in this study was not influenced by the history of

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blood transfusion. Our data indicate that we should investigate causes other than blood transfusion for the high seroprevalence of HCV antibodies in hemodialysis patients. Because hemodialysis patient have repeated ex-tracorporeal hemocirculation, they have a high risk of parenteral infection other than from blood transfusion. However, all hemodialysis procedures were done using disposable kits, syringes, and needles, therefore, care should be taken with many blood products, dialysis fluid, air entry into extracorporeal hemocirculation, non-sterilized replacement of needles in the angioaccess, and surgery. Moreover, other causes may include the fecal-oral route of infection and a previous contact with an infected person. The immunodeficiency state due to uremia may facilitate viral infection in all the cases described above. Our data indicating that the seroprevalence of HCV antibodies in hemodialysis patients increased with the duration of the period of hemodialysis might suggest the possibility of these routes of HCV infection.

Similar results have been reported. Este-ban et al. [4] reported that the 20% seropositivity among hemodialysis patients seems to be almost exclusively related to blood transfusion. Schlupkoter et al. [5] reported a 10.1% seropositivity in hemodialysis patients, and found no correlation between HCV antibody positivity and the use of blood transfusions or blood products. They mentioned that there were other modes of transmission.

The incidence of HCV was significantly higher in hemodialysis patients (49.6%) who had a history of increased serum alanine aminotransferase (sALT) than in those (15.8%) who had no history of increased sALT ($p < 0.001$). Hepatitis B virus surface antigen (HBsAg) positivity rate was only 2.5% (34 of 1,423) and did not correlate with the duration of hemodialysis. Seroprevalence of HBsAg in blood donors in Kumamoto Prefecture was 1.2% (2,048 of 172,519). We have seen many hemodialysis patients with a history of elevation of

sALT. The extremely high rate of seroprevalence of HCV antibodies in those patients indicates that the main cause of the elevation of sALT may be HCV, and not HBV. Therefore, HCV infection seems to play an important role in the prognosis of hemodialysis patients, because HCV hepatitis may lead to hepatic cirrhosis and hepatocellular carcinoma.

We were able to determine the cause of chronic renal failure from the patient's record. The seroprevalence rate of HCV antibodies in the patients due to chronic glomerulonephritis (228/967, 23.6%) was not significantly different from those due to diabetes mellitus (41/192, 21.3%) and others (30/178, 16.9%). Several studies have demonstrated the existence of HBs antigen or HBe antigen circulating immune complex and implicated them in the pathogenesis of glomerulonephritis [6, 7]. Expression and replication of HBV genome in the liver and kidneys of transgenic mice was reported [8], and this may suggest the HBV infection is toxic to the liver and kidney. There was no clear relationship between HCV antibody seroprevalence and the etiology of chronic renal failure in our study, however, there remains the possibility that HCV infection is implicated in the pathogenesis of glomerulonephritis and progression to chronic renal failure.

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