Epidemiology of HCV infection: disease and renal transplantation


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Abstract. We studied the prevalence of HCV infection in a cohort of 346 patients who received renal transplantation between January 1989 and April 1994. Assessments were made at the time of surgery, one year later and at the last follow-up visit. The hepatic consequences of HCV infection were also studied. The prevalence of HCV infection at the time of surgery was 21.4% (74/346). The risk factors associated with the presence of anti-HCV antibodies were: duration of haemodialysis, the number of transfusions and the number of previous renal transplantsations. The incidence of HCV infection was 3% (8/272) and was accompanied by either transient (n=4) or chronic (n=3) hepatic cytolysis; five patients underwent liver biopsy which revealed persistent chronic hepatitis (n=2) or active chronic hepatitis (n=3). Seroconversion always occurred within one year following transplantation. In the long-term, 91% of HCV+ patients remained viremic. The HCV genotype was predominantly lb. Fifty-six per cent (56%) of HCV+ patients had normal ALAT at the time of transplantation, which remained normal on follow-up in two-thirds of cases. After transplantation, 39 HCV+ patients underwent liver biopsy. ALAT were normal in 13 of those; liver biopsy elicited either normal liver (n=1) or chronic persistent hepatitis (CPH) (n=8) or chronic active hepatitis (CAH) (n=4). ALAT were chronically elevated in 26 patients; liver histology revealed: 7 CPH, 19 CAH including 12 cases with bridging fibrosis. No deleterious effect of azathioprine on liver histology was found. Lastly, four patients were co-infected with HBV: all had elevated ALAT; liver biopsy always revealed severe chronic active hepatitis. Post-transplantation hepatitis C is a worrying problem. Liver enzymes are not correlated with the severity of histological disorders, which are frequent. Interferon-α therapy should be proposed to HCV+ patients before renal transplantation.

Introduction

Following renal transplantation, the major cause of chronic liver disease is chronic hepatitis C. The prevalence of hepatitis C virus (HCV) infection in renal transplantation ranges between 10 and 30% [1,2]. The evolution of chronic hepatitis C can then be insidious with a definite cirrhogenic potential [3]. It is not known, however, if it has an impact on long-term survival of grafts and recipients whereas in renal transplantation patients, chronic hepatitis B is known to reduce patient survival by 10 years because of complications often related to liver cirrhosis [4]. This study analyses the prevalence and incidence of HCV infection in 346 renal transplanted patients.

Materials and methods

Between the January 1, 1989 and April 30, 1994, 346 patients received renal grafts in the Toulouse transplantation unit. In that cohort we analysed the prevalence of HCV infection on the day of transplantation (DO) then at the outset (1 year) and at the last follow-up visit; we also assessed the hepatic consequences of HCV infection by monitoring transaminases (ALT) and by performing liver biopsy (Knodell’s score). All patients initially received quadruple sequential immunosuppression associating anti-thymocyte antibodies (ATG), azathioprine, corticoids and cyclosporin in 336 cases; ATG was replaced by either monoclonal anti-LFA1 (n=8) or anti-CD3 (n=2) antibody. The HCV status was serologically determined: anti-HCV antibody screening by second or third generation EIA confirmed by RIBA 2 or RIBA 3 tests. HCV seropositive patients were subjected to viraemia detection using the Amplicor® test (Roche).

Results

On DO, 74 patients had anti-HCV antibodies (group I), corresponding to a 21.4% prevalence and 272 patients were HCV negative (group II). Group I included 44 men and 30 women (sex ratio = 1.46) aged 41 ± 11 years, haemodialysed for 101 ± 69 months and having received 17 ± 2 packed cell units (PCU) on average before renal transplantation; 38 of those (51%) had been re-transplanted; Group II included 179 men and 93 women (sex ratio 1.92) aged 42 ± 13 years who had been haemodialysed for 43 ± 48 months and having received 7.7 ± 0.5 PCU on average; it was not the first renal transplantation for 38 (14%). The risk factors
associated with the presence of anti-HCV antibodies on D0 were the duration of haemodialysis, the number of PCU received before transplantation, and the number of previous renal grafts (P < 0.001). All group I patients remained HCV seropositive throughout follow-up. Eight patients from group II (all transplanted before January 1992) exhibited HCV seroconversion within the year following renal transplantation, accompanied by transient liver cytolysis in four cases and chronic liver cytolysis in three cases; five underwent liver biopsy puncture (LBP): when there was chronic cytolysis it revealed chronic active hepatitis (CAH) in two cases and chronic persistent hepatitis (CPH) in the other; when there was no cytolysis, there was CPH in one case and CAH in the other.

In Group I, 64 patients were followed-up for more than 6 months following transplantation: 56 underwent repeated HCV-RNA screening, which proved positive in 51 patients (91%); five patients had no detectable long-term viraemia and could thus be considered as cured. On D0, 36 out of 64 patients (56%) had normal ALT concentration; among those, 12 (33%) exhibited chronic increase in ALT later on in renal transplantation; the other 24 presented with constantly normal (n = 19) or in contrast exhibited a single transaminase peak followed by persistently normal values (n = 5). Twenty-eight patients exhibited chronic increase in ALT on D0; these remained chronically high in 22 of those patients (78.5%) and remained constantly normal in the others. LBP was performed in 39 of the 64 patients (61%). Among the patients with normal ALT after transplantation (n = 13), one patient had normal liver, eight had CPH (Knodell’s mean score = 3.75) and four had CAH (Knodell’s mean score = 7.5); bridging fibrosis was observed in two patients only (14%). Conversely, in patients with high ALT after transplantation (n = 26), CPH was noted in seven patients (27%) with a mean Knodell score of 3.7 and CAH was present in the other 19 patients (73%) with a mean Knodell score of 7.8; bridging fibrosis was observed in 12 cases (46% of patients).

Four patients had HBV/HCV co-infection; all presented with chronic liver cirrhosis; three underwent LBP that revealed severe CAH each time.

In the long term, all patients received cyclosporin with or without corticoids and/or azathioprine. In HCV-positive patients, long-term azathioprine therapy had no deleterious effect on liver histology. So, in patients with chronic persistent hepatitis, the mean Knodell score was 3.66 for those taking azathioprine as well as for those who did not; when there was chronic active hepatitis, the mean Knodell score was 7.25 for those who did not take azathioprine, versus 8.5 for those who did; that difference however was not significant.

Throughout the follow-up period, no patient with HCV infection alone exhibited any clinical, biological or histological sign evocative of liver cirrhosis.

Discussion

Our study revealed a 21.4% prevalence of HCV infection in renal transplanted patients on D0; that prevalence is fully comparable to that noted in series of chronic haemodialysed patients [5,6]. The incidence of HCV seroconversion following transplantation is 3%; however, it has to be noted that no seroconversion has occurred since January 1992. In the long term, 91% of HCV-positive patients are viraemic. The biochemical consequences of HCV infection are reflected by elevated liver enzymes in 53% of patients. Among those, 73% have histological lesions related to chronic active hepatitis. Those whose transaminases remain normal in the long term often have chronic persistent hepatitis lesions (61.5%). The most worrying factor is surely the existence of bridging fibrosis in 38% of patients because those lesions carry a strong evolutive potential. Lastly, in our experience, azathioprine does not seem to have any long-term deleterious effect on liver function.

The existence of chronic active hepatitis lesions in 59% of long-term immunodepressed patients should raise the issue of IFNα recombinant therapy before renal transplantation, to eradicate HCV.

References