Transpl Int (1994) 7 [Suppl 1]: S224–S226

J. Gugenheim
E. Baldini
D. Mazza
P. Fabiani
M.C. St. Paul
B. Goubaux
D. Ouzan
J. Mouiel

Recurrence of hepatitis C virus after liver transplantation

J. Gugenheim · E. Baldini · D. Mazza
P. Fabiani · M.C. St. Paul · B. Goubaux
D. Ouzan · J. Mouiel
Unité de Transplantation Hépatique,
Université de Nice,
5, Rue Pierre Devoluy, Hopital St. Roch,
F-06006 Nice, France

Abstract The hepatitis C virus is a common cause of chronic hepatitis after orthotopic liver transplantation (OLT). We evaluated 95 consecutive patients who underwent OLT at our institute between March 1988 and November 1992 and who had a follow-up period longer than 3 months. All patients had a second-generation test (ELISA + RIBA) for HCV antibodies (HCV Ab) before and monthly after OLT; all had a polymerase chain reaction (PCR) test for detection of viral RNA after the operation. Whenever biochemical abnormalities (hypertransaminasemia 2 times the normal range) were seen, a percutaneous liver biopsy was performed. Forty-two HCV Ab+ patients before OLT remained positive after OLT. In this group the PCR test was positive in 32 cases (78.5%). In 13/42 (30.9%) cases (all PCR+) with hypertransaminasemia histological examination showed signs of viral C hepatitis (score of Knodell minimum 3, maximum 12, median 5.5). Of 53 HCV Ab patients before OLT, only 1 became HCV Ab+ and PCR+ 15 months after OLT. In the remaining 52 patients 15 were PCR+. Twenty of 53 patients (37.7%) had a liver biopsy because of hypertransaminasemia: in no case did histology show any signs of hepatitis C. In conclusion, viral C recurs often after OLT for post-hepatitic C cirrhosis. The histological graft lesions are in most cases moderate. We did not observe any deaths related to viral C infection in grafted patients. According to our results post-hepatic C cirrhosis remains a good indication for OLT.

Key words Liver transplantation
Hepatitis C virus · Graft hepatitis
Polymerase chain reaction

Introduction

Infection with the hepatitis C virus (HCV) is an important etiology of liver disease in patients undergoing liver transplantation [2, 4, 5]. The characteristics of HCV recurrence after liver transplantation and its role in survival and in developing graft hepatitis are unknown. In this paper we analyzed a series of transplanted patients to study the evolution of HCV infection and its influence on prognosis.

Patients and methods

Between March 1988 and November 1992, 156 patients had orthotopic liver transplantation (OLT). Ninety-five patients were follow up for at least 3 months. Diagnosis before OLT was: 75

posthepatitic cirrhosis, 8 hepatocellular carcinomas, 8 alcoholic cirrhosis, 1 drug fulminant hepatitis, 1 B virus fulminant hepatitis, 1 sclerosing cholangitis, 1 alpha$_1$-antitrypsin deficiency. Seventy-eight were male, 17 female. Age at the time of OLT ranged from 24 to 67 years (44.2 ± 1.4). Only 3 patients received blood transfusions with no tested HCV antibodies (HCV Ab) products (two-thirds were HCV Ab positive before OLT).

At least once before OLT and monthly there after all had an HCV Ab detection test by the enzyme immunolinked assay (EIA – Abbott Laboratories). Serum samples of patients transplanted before April 1991 were stored at −70 °C and tested later. Every 6 months after OLT all patients had an HCV RNA detection test by the polymerase chain reaction (PCR) test. All had a flexible triple drug immunosuppressive regimen (cyclosporine, corticoids, azathioprine). A percutaneous liver biopsy was done where persistent increased serum aminotransferase levels were present or when clinically indicated. The diagnosis of viral chronic hepatitis was based on histological findings of lobular mononuclear cell infiltrate, portal inflammation and hepatocyte necrosis without bile duct lesions.

Results

Forty-two patients were HCV Ab positive before OLT. All remained positive permanently after OLT (average follow-up 19.3 months; minimum 7, maximum 55). At the time of the last check-up, the PCR was positive in 32 (78.5%) cases.

Fifty-three patients were HCV Ab negative before OLT. All were negative during the first follow-up year average follow-up 23.6 months; minimum 4, maximum 58). Only 1 patient showed a positive PCR 15 months after OLT and 2 months later HCV Ab conversion without clinical and biological pathological findings; this patient did not receive transfusions after OLT. In 16/53 (30.1%) cases PCR was positive.

The actual survival rates of HCV Ab positive and HCV Ab negative patients were 97.9% and 97.4% at 1 year and 88.7% and 89.4% at 2 years, respectively. No deaths were observed that clearly correlated with a HCV infection. Among 43 patients with positive HCV Ab after OLT (group 1), 26 (60.4%) had normal serum aminotransferase levels and 17 (39.6%) elevated levels (> 2 N). Among 52 patients with negative HCV Ab after OLT (group 2), 43 (82.6%) had normal aminotransferase levels and 9 (17.4%) elevated. The serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were 66 ± 27 U/l, 81 ± 35 U/l, respectively, in group 1 and 46 ± 19 U/l, 58 ± 21 U/l in group 2. No significant difference was found between the aminotransferase levels of PCR positive and PCR negative patients.

Thirteen patients in group 1 had percutaneous liver biopsies after OLT (mean interval 9.4 months, range 4–26); in all cases there was evidence of chronic active hepatitis with a median Knodell score of 5.5 (range 3–12). All cases had positive PCR. No histological evidence of cirrhosis was found. Twenty patients in group 2 had percutaneous liver biopsies: 3 cases of chronic active hepatitis lesions and 1 case of posthepatitis cirrhosis lesions were found. These 4 patients showed a recurrence of B virus infection.

Discussion

Our results showed that HCV recurrence in pre-OLT HCV Ab positive patients is frequent. The infection is usually associated with moderate cytolysis. Even when biological abnormalities became important, histologically minimal or moderate hepatitis lesions were found. These data and the absence of HCV-related cirrhotic evolution in our series agreed with the typically slow progression of HCV infection in non-transplanted patients. The role of immunosuppressive treatment in this evolution remains to be determined (faster development of cirrhosis by HCV infection was demonstrated in patients infected by human immunodeficiency virus). Positive PCR in HCV Ab negative patients without clinical and biological pathological findings could be explained by a HCV infection without the conversion of antibodies [3]. Evidence that HCV Ab positive patients remained positive after OLT seems to demonstrate that immunosuppressive treatment does not change HCV Ab expression in our series although its influence on viral RNA expression must still be elucidated. Moreover, the PCR has been reported to have limited reliability [1]. No patients with postoperative serological HCV Ab conversion were found because of HCV Ab controlled hemoderivated product use in 92/95 cases. It was concluded that HCV-related end-stage liver disease is a good indication for OLT.

References

1. Zaaijer HL, Cuypers HTM, Reesink HW, et al (1993) Reliability of polymerase chain reaction for detection of hepatitis C virus. Lancet 341:722–724
2. Read AE, Donegan E, Lake J et al (1991) Hepatitis C in liver transplant recipients. Transplant Proc 23:1504–1505
3. Poterucha JJ, Rakela J, Lumeng L et al (1992) Diagnosis of chronic hepatitis C after liver transplantation by the detection of viral sequences with polymerase chain reaction. Hepatology 15:42–45
4. Read AE, Donegan E, Lake J, et al (1991) Hepatitis C in patients undergoing liver transplantation. Ann Intern Med 114:282–284
5. Moreno Gonzales E, Loinaz C, Garcia I et al (1993) Liver transplantation in chronic viral B and C hepatitis. J Hepatol 17 [Suppl 3]:S116–S122