Accelerated liver failure in an HCV positive renal allograft recipient: beware of cytomegalovirus.

Hepatitis C is a common problem in renal allograft recipients. In most cases, it is a slowly progressive disease with median survival of 10 years or more usual even in renal allograft recipients. Two recent reports in the journal[2,3] prompted us to report of a renal allograft recipient with an unusually rapid progression of liver disease.

A 56-year-old man with autosomal dominant polycystic kidney disease was diagnosed to have end-stage renal disease in 2004. At baseline, HBsAg, HCV and HIV were negative. After one year on hemodialysis he underwent renal transplantation from a live-related donor. Prior to transplantation he was negative for HCV, HBsAg and cytomegalovirus. He had an episode of acute rejection on day 4 of transplant which was controlled with methyl prednisolone after which he was maintained on mycophenolate, cyclosporine and prednisolone. Five months later he developed jaundice and was found to be anti-HCV as well as HCV-RNA positive. His liver function gradually worsened during hospital stay. Investigations showed INR 2.1, bilirubin to 20.2 mg/dL, ALT 70 IU/L, and alkaline phosphatase 76.5 IU. As he was not willing for interferon treatment he was given supportive and symptomatic care. He gradually improved with near normalization of liver biochemistry.

After 5 months, he developed jaundice, coagulopathy and ascites. He improved again with supportive and symptomatic care. After 6 months, liver function deteriorated again with severe coagulopathy and ascites. Ascitic fluid analysis showed a high SAAG with high cell count, and culture grew E. coli. Markers for hepatitis A, B and E were negative, and iron profile and renal function were normal. As the clinical course was not typical of HCV infection, PCR for CMV DNA and HCV were done, and were found to be positive (CMV 21,13,750 copies/mL, HCV 43,289,800 copies/mL). He was started on oral valgancyclovir. However he deteriorated steadily and died 18 months after the transplant.

Two recent publications[2,3] in the journal described accelerated liver failure in renal allograft recipients with HCV infection. Seth et al[2] reported six renal allograft recipients with accelerated liver failure with no evidence of FCH clinically or on biopsy. The patients succumbed to liver disease within 53 months of transplant and no explanation could be found for the rapid worsening. CMV serology was found to be negative, however PCR for CMV was not done. Hooda et al[3] reported a case of hepatitis C with fibrosing cholestatic hepatitis and rapidly progressive liver failure; however, cytomegalovirus coinfection which is not infrequently associated with fibrosing cholestasis was not looked for.

In our patient, high titer of CMV-DNA was found confirming active infection; pretransplant CMV serology was negative. Though biopsy was required to confirm the liver pathology, it was precluded by severe coagulopathy.

Due to immunosuppression, renal allograft recipients may not mount antibody response and CMV serology alone may not be a good test to exclude CMV infection. In renal as well as liver transplant, CMV coinfection has been reported to accelerate liver damage in chronic hepatitis C and cause greater liver injury as compared to those without CMV infection.[3,4,5] Infection with one virus may cause immune suppression or otherwise stimulate replication of other viruses (e.g., CMV and hepatitis C) in a form of viral “cross-talk”. Specific immunosuppressive agents have been suggested as increasing risk for specific viral infections, including tacrolimus in BK nephropathy, anti-thymocyte globulin in CMV, mycophenolate mofetil in late CMV. This patient had received methyl prednisolone for acute rejection and was maintained on mycophenolate, both of which could have triggered reactivation of cytomegalovirus infection which in turn aggravated the hepatitis C infection.

Being a treatable condition, CMV infection needs to be actively looked for with PCR in HCV positive Renal allograft recipient with accelerated liver failure.

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References


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References


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