Chronic Hepatitis E with Cirrhosis in a Kidney-Transplant Recipient

TO THE EDITOR: Hepatitis E virus (HEV) is an important cause of acute viral hepatitis worldwide.[1] Kamar et al. in this issue of the *Journal*[2] and others[3,4] have recently suggested that HEV infection might result in chronic hepatitis in immunocompromised patients. We report a rapidly progressing case of cirrhosis in a renal-transplant recipient with chronic HEV infection.

A 52-year-old man who had undergone kidney transplantation in March 2005 presented with increased aminotransferase levels in June 2006. Four months later, the alanine aminotransferase level reached 126 U per liter and thereafter plateaued at three times the upper limit of the normal range. Serologic testing for hepatitis C virus (HCV) and HCV RNA had been

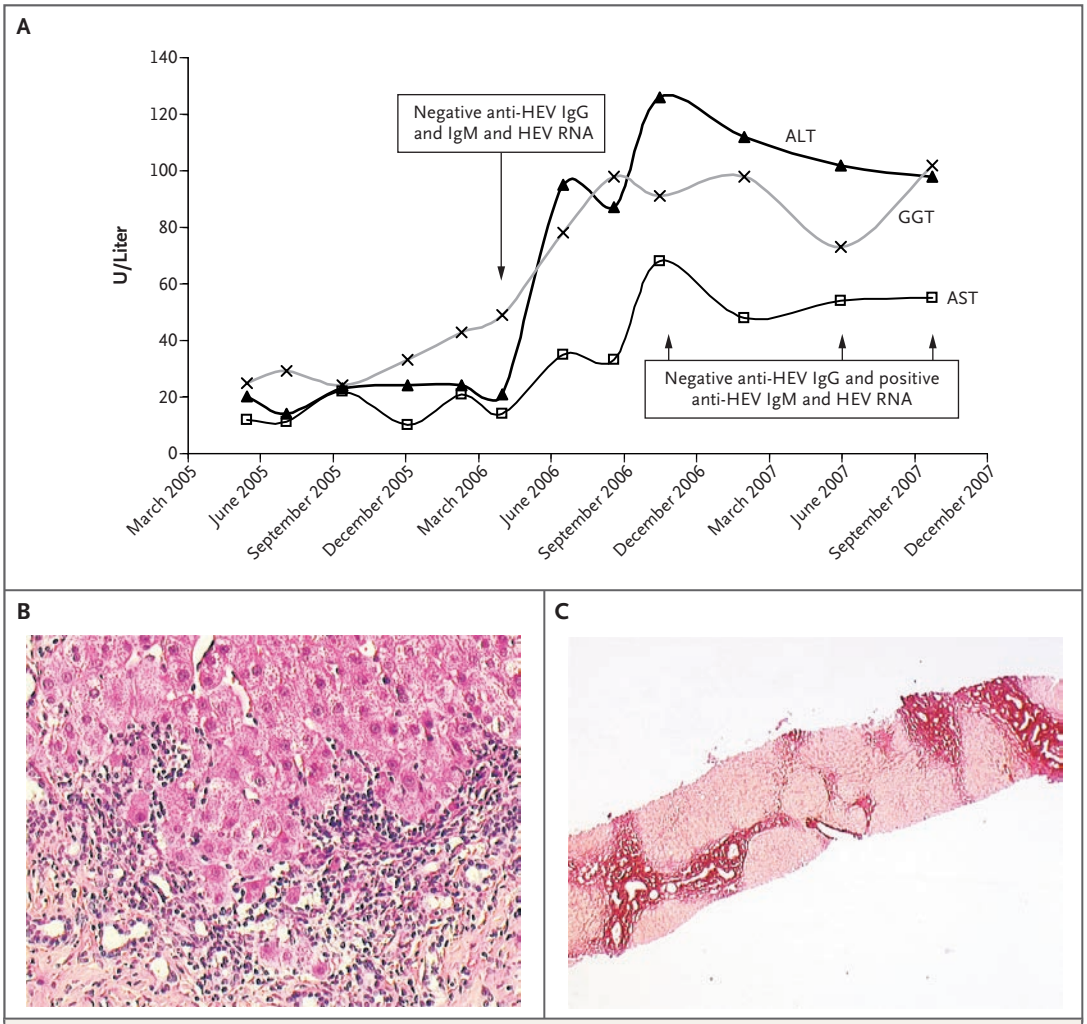

Figure 1. Results of Virologic Analysis and Liver Biopsy in a Patient with Chronic Hepatitis E Virus Infection.

Panel A shows changes in liver biologic markers alanine aminotransferase (ALT), aspartate aminotransferase (AST), and γ-glutamyltransferase (GGT) and virologic measures of HEV RNA and IgG and IgM anti-HEV antibodies in serum. HEV RNA titers remained stable from November 2006 to September 2007, and tests for IgG anti-HEV antibodies remained negative during the entire follow-up period. Panel B shows a liver-biopsy specimen, obtained in September 2007, with an inflamed portal tract and mononuclear cells extending beyond the limiting plate and surrounding individual or small clusters of hepatocytes (hematoxylin and eosin). Panel C shows Sirius red staining of collagen, indicating cirrhosis, with an advanced fibrosing phenomenon isolating parenchymal nodules.

negative at the time of transplantation and during follow-up. The results of serologic testing for hepatitis B virus (HBV) were consistent with past immunization, and HBV DNA was undetectable. The patient's alcohol consumption was lower than 10 g per day. Other causes of chronic hepatitis were ruled out.

Hepatitis E was diagnosed in June 2007 on the basis of positive results on IgM anti-HEV antibody testing (EIAGen kit, Adaltis) and HEV RNA detection (genotype 3f; GenBank accession number, EU116340).[5] The patient did not report any recent travel, and no potential route of HEV transmission other than consumption of pork was identified. Retrospective analysis showed that HEV RNA was undetectable in the patient's serum in April 2006, whereas it was repeatedly detected in available serum samples from November 2006 to September 2007 (Fig. 1A), when the diagnosis of active chronic hepatitis and cirrhosis was confirmed on liver biopsy (Fig. 1B and 1C).

HEV-related cirrhosis appears to be a novel observation. Other unusual features in this patient were a low peak alanine aminotransferase level (no higher than 126 U per liter) and the absence of IgG anti-HEV antibody seroconversion. The unusual course might be explained to a great extent by the patient's immunosuppressed state. A few cases of protracted HEV infection and even HEV-related chronic active hepatitis have recently been described in patients who received solid-organ transplants.[2-4] Our observation further suggests that chronic HEV infection may induce rapid and severe liver disease.

Persistently negative results of IgG anti-HEV antibody testing have previously been observed in the context of immunosuppression, despite evidence of HEV infection, as assessed by HEV RNA detection in blood.[6] The present case highlights the need to diagnose HEV infection on the basis of molecular testing rather than only serologic assays in such settings.

In conclusion, this case indicates that HEV infection may result in active chronic hepatitis and rapid progression to cirrhosis in organ-transplant recipients. Further studies are needed to assess the actual incidence, prevalence, and clinical effect of autochthonous HEV infection in these patients.

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1. Shrestha MP, Scott RM, Joshi DM, et al. Safety and efficacy of a recombinant hepatitis E vaccine. N Engl J Med 2007;356:895-903.
2. Kamar N, Selves J, Mansuy J-M, et al. Hepatitis E virus and chronic hepatitis in organ-transplant recipients. N Engl J Med 2008;358:811-9.
3. Banas B, Tausch U, Hofstadter F, et al. Infection with hepatitis E virus: first report of a chronic case and molecular characterization of the virus. J Clin Virol 2006;36:Suppl 2:S162. abstract.
4. Kamar N, Peron JM, Ouezzani L, et al. Hepatitis E virus infection can evolve to chronic hepatitis in organ-transplant patients. J Hepatol 2007;46:Suppl 1:S70-S71. abstract.
5. Colson P, Borentain P, Motte A, et al. First human cases of hepatitis E infection with genotype 3c strains. J Clin Virol 2007;40:318-20.
6. Tamura A, Shimizu YK, Tanaka T, et al. Persistent infection of hepatitis E virus transmitted by blood transfusion in a patient with T-cell lymphoma. Hepatol Res 2007;37:113-20.