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CASE REPORT

Hepatitis E virus infection mimicking acute graft rejection in a liver transplant recipient

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KEYWORDS
Hepatitis E infection;
Acute graft dysfunction;
Liver transplantation

Summary
Introduction: In liver transplant (LT) patients, hepatitis E virus (HEV) can lead to acute liver failure, chronic hepatitis and graft cirrhosis. Few data on graft rejection associated with HEV are available and are subject to discussion.
Case report: Here we report the case of a 58-year-old male patient who underwent LT in July 2015 for cirrhosis due to NASH and chronic alcohol intake complicated by hepatocellular carcinoma. LT was performed with a deceased donor isogroup and a mismatch CMV (donor+ and recipient−). HEV serology was negative before LT. In February 2016, we noted abnormal liver function, with increased transaminases and cholestasis parameters, without functional complaints. The patient was immunosuppressed by tacrolimus (4 mg) and everolimus (2 mg). Abdominal ultrasound was normal and liver biopsy showed signs of acute rejection (Banff score 6/9). We dispensed 500 mg of methylprednisolone before obtaining positive serological results for HEV genotype 3 infection. Ribavirin (1,200 mg per day) for 3 months was started, leading to rapid improvement in liver tests. Viral load became negative one month later. To date, the patient is under LP 5 mg tacrolimus with normal liver tests.
Conclusion: We describe a case of HEV genotype 3 infection mimicking acute cellular rejection, with a favorable outcome due to ribavirin treatment. As intensive immunosuppressive therapy administered for graft rejection may promote viral replication and worsen liver damage, potential HEV infection must be considered in cases of pathological signs of acute cellular rejection, in order to avoid chronic graft hepatitis, cirrhosis and liver decompensation.

Abbreviations: HCV, hepatitis C virus; HEV, hepatitis E virus; LT, liver transplant.

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Introduction

Hepatitis E virus (HEV) is an emerging pathogen often resulting in self-limiting hepatitis. Fulminant hepatic failure has been described in pregnant women, chronic alcohol abusers and patients with chronic liver diseases. HEV has also been associated with chronic hepatitis, mainly related to genotype 3 infection, in solid organ transplant recipients, causing rapidly progressive cirrhosis, and in some cases, liver transplantation (LT) [1—4]. After organ transplantation, the incidence of HEV infection varies from 0.9 to 3.5%; around 60% of patients will develop chronic hepatitis [3]. Low platelet count and use of tacrolimus rather than cyclosporin A have been identified as independent predictive factors of chronic evolution [5]. Since HEV infection can mimic acute cellular rejection, data on graft rejection related to HEV remain unclear and may impact outcome [6]. Here, we describe HEV genotype 3 infection mimicking severe acute cellular graft rejection in a LT recipient with a favorable outcome due to ribavirin treatment.

Case report

We report the case of a 58-year-old male patient who received a LT in July 2015 for hepatocellular carcinoma developed on Child-Pugh A cirrhosis (NASH and chronic alcohol intake). His past history was composed of metabolic syndrome (type 2 diabetes, hypertension and dyslipidemia) and coronary heart disease. LT was performed via a deceased donor isogroup with mismatch CMV (donor+ and recipient−). HEV serology of the patient was negative before LT. Surgical follow-up was marked by scar collection and imbalance of diabetes.

In February 2016, we noted a typical pattern of acute hepatitis with elevated transaminases and cholestasis parameters (Fig. 1), with no functional complaints. Immunosuppressive treatment was satisfactory (tacrolimus 4 mg and everolimus 2 mg). Abdominal ultrasound was normal, without outflow obstruction or decreased blood perfusion. Ponderal dosage of immunoglobulin and autoimmune assessment showed no abnormalities. Viral load of cytomegalovirus, Epstein-Barr, herpes simplex virus 1 and 2, human herpes virus 6, hepatitis A, hepatitis B and hepatitis C virus (HCV) were negative. Liver biopsy showed lymphocytic portal inflammation with endothelial lesions and severe lymphocytic cholangitis. In liver lobules, acidophilic bodies and polymorphous lymphohistiocytic inflammation were found, leading to diagnosis of acute cellular rejection with a Banff score of 6/9 (Fig. 2).

On March 9, we initiated treatment with methylprednisolone (500 mg intravenously for 1 day) before obtaining positive HEV genotype 3 serology with high viral load (IgM+ IgG+ viral load: 2,300,000 IU/mL). We then began treatment with ribavirin 1200 mg per day for 3 months. Several days later, we observed rapid improvement in liver tests; viral load became negative on 14 April (Fig. 1). To date, the patient is under LP 5 mg tacrolimus with normal liver tests.

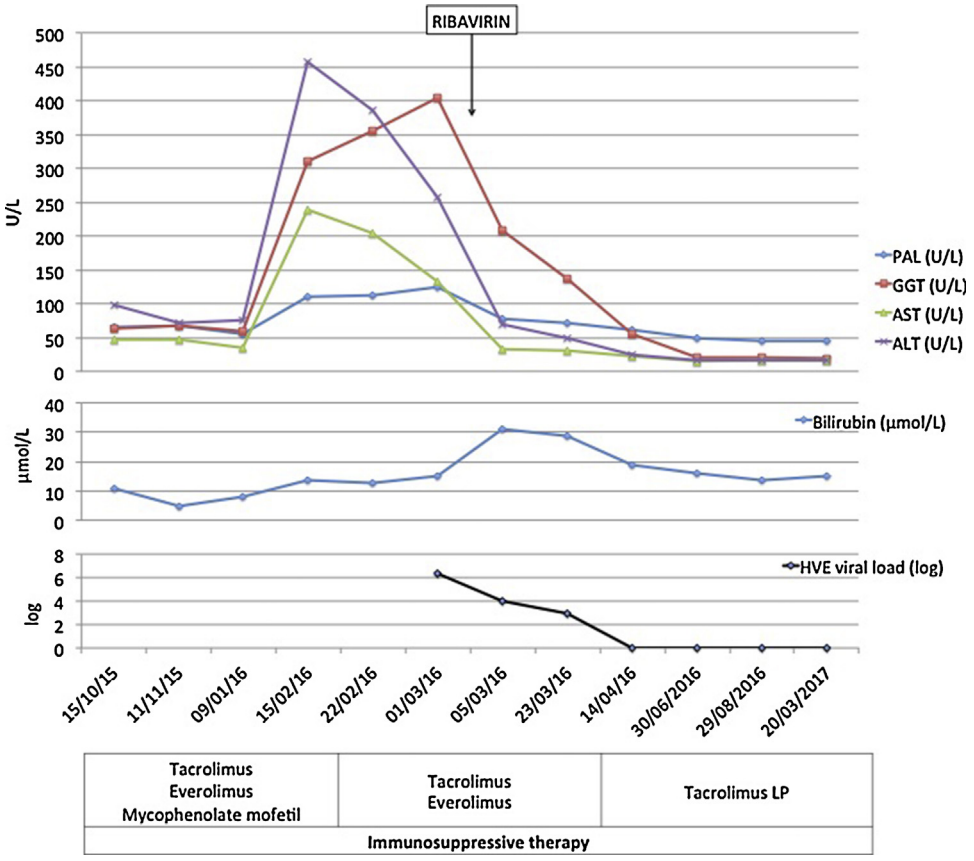

Figure 1 Biology and immunosuppressive therapy.

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