Dear Editor,

Hepatitis E virus (HEV) infection is a cause of acute epidemic hepatitis in developing countries and of acute sporadic acute hepatitis in developed countries. From 2008 there have been published cases of persistent infection with development of chronic hepatitis in immunosuppressed patients (1). We present two cases of renal transplanted patients and HEV chronic infection successfully treated with ribavirin (RBV).

Case reports

The first patient is a 51-years-old male sent to outpatient consult of hepatology in June 2010 from nephrology where he was followed after a renal transplant in 1999 and on immunosuppressive treatment with prednisone and sirolimus. The last 4 months, there was evidence of a rise in liver enzymes that were previously normal. Laboratory findings: GOT: 107 UI/L (superior normal level 34 UI/L), GPT 265 UI/L (snl 55 UI/L), alkaline phosphatase 203 U/L (snl 150 UI/L) and total bilirubin (TB) 0.3 mg/dl (snl 1.20 mg/dl). Serology of HBV and HCV including RNA HCV and DNA-HBV were negative, normal immunoglobulin levels, and negative autoantibodies.

Abdominal ultrasound was normal. Serology for HEV was requested and resulted positive for IgG and IgM antibodies against HEV confirmed with RNA-PCR (polymerase chain reaction). Percutaneous liver biopsy showed signs of mild necro-inflammatory activity and fibrosis grade I/IV (Fig. 1). Once the diagnosis of HEV was made, treatment started with ribavirin (RBV) 800 mg/day. After two weeks of treatment, LFT (liver function tests) normalized. The patient showed anemia of 8.3 d/dl that motivated the reduction of the dose to 400 mg/d and the administration of erythropoietin at 30,000 UI/week. The RNA HEV after 12 weeks turned negative and the treatment was stopped. In subsequent analysis at 12, 24 and 48 weeks after treatment suspension, transaminases remained normal and RNA HEV negative.

The second case is a 44-year-old woman, history of renal transplant in 2005 and under treatment with tacrolimus and mycophenolate. He was sent to hepatology consult in February 2011 due to an increased level of GPT 62-149 UI/L since October 2009, from previously normal levels. Alkaline phosphatase and total bilirubin remained in normal limits. Serology for HBV, HCV including RNA HCV and autoantibodies were negative. Abdominal ultrasound was normal. The serology for HEV was positive for anti-HEV IgM and RNA-HEV. Liver biopsy showed peri-portal chronic hepatitis with activity of 5/8 and fibrosis of III/IV. RBV treatment started at 600 mg/day, reaching normal levels of transaminase after 2 weeks but also a progressive decline in hemoglobin that did not respond to lowering doses of RBV neither to administration of erythropoietin, in consequence treatment had to be stopped at week 7 (RNA-HEV turned negative). RNA-HEV continued undetectable at 12 and 24 weeks after treatment suspension and transaminases within normal limits.

Discussion

Since Kamar described for the first time the persistent infection of HEV after renal or hepatic transplantation in 2008, there have been many publications of series of patients under immunosuppressive treatment diagnosed with HEV chronic hepatitis (2,3). This has also been found in patients under chemotherapy for hematological disease (4).

In our environment, the transmission is caused mainly due to raw or undercooked meat ingestion or due to direct contact with...
infected animal (5). It is a recent observation the fact that HEV infection in immunosuppressed patients can evolve to severe chronic hepatitis and cirrhosis in more than 50% of the patients; this evolution takes place rapidly, mean time 58 months, there are some cases in which this took place in little more than a year (3). This is the reason to start treatment early as soon as chronicity is evidenced. In transplanted patients, the first step after diagnosing acute infection is to lower the immunosuppressant dose if this does not carry a risk of transplant rejection, and, in case the virus could not been eliminated from bloodstream, start pharmacologic treatment (6). Our patients did not reduce their immunosuppressant doses due to the risk of rejection.

Although pegylated interferon has been used with good response (7), inasmuch as in renal or cardiac transplanted patients this drug can cause the rejection of the organ, the current recommendation is to treat these patients with RBV due to its satisfactory outcomes (4,8-10). The main side effect is the anemia that forces to lower its doses in the majority of patients and can lead to no response or reactivation.

We contribute with 2 cases, to the literature supporting the use of RBV in the management of chronic infection of HEV.

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References