Case Report

Hepatitis E virus infection results in acute graft failure after liver transplantation: a case report

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Abstract

Hepatitis E virus (HEV) infection in most individuals is known as a self-limiting, acute, icteric hepatitis, but evidence shows HEV is responsible for choric hepatitis and rapid progressed liver cirrhosis in immuno-compromised patients. We present the case of a patient whose diagnosis of acute graft failure was due to a HEV infection 7 years after his first liver transplantation because of Wilson's disease. The process showed severe jaundice with fatigue, poor appetite and continually rising serum aminopherase. The blood serum was found positive for the anti-HEV IgG antibody but negative for anti-HEV IgM or other infections. Cholangiole cholestasis was detected in graft biopsy. Triple hepato-protective drugs (Transmetil, Polyene Phosphatidylcholine, and Compound Ammonium Glycyrrhetate S) alongside five times Artificial Liver Support System (ALSS) did not improve the patient's condition, but the total bilirubin level rose to more than 900umol/L. So re-transplantation was performed. Blood testing shows normal liver enzymes and bilirubin with persisting anti-HEV IgG antibody positive at the 3-month follow-up.

Key words: hepatitis E virus; graft failure; re-transplantation

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Introduction

Hepatitis E virus infection is known as one of the most common reported hepatitis viruses in developing countries, and was also described several times in solid organ transplant recipients both adults and children, and other immuno-compromised diseases [1,4]. It causes chronic hepatitis and cirrhosis, associated with chronic liver failure [5,6]. But no acute liver failure has been reported yet in liver transplant recipients. So we present this case of hepatitis E virus infection that rapidly led to liver failure in a liver transplant recipient, in which ordinary medicine therapy and Artificial Liver Support made no difference. So the patient had to receive a re-transplantation operation.

Case Report

In October 2012, a 23-year-old college student was referred to our department, First Affiliated Hospital of Zhejiang University, in Hangzhou, South China. He complained of fever, fatigue, bad appetite and dark-colored urine starting 3 days before admission. He firstly underwent liver transplantation because of Wilson's disease at age 16, and took tacrolimus 0.5mg q12h, making normal serum aminopherase and bilirubin in the previous 7 years.

Laboratory data showed elevated alanine aminotransferase (ALT) and aspartate aminotranferase (AST), as well as the total bilirubin level and Prothrombin Time (see Table 1). Magnetic Resonance Cholangiopancreatography (MRCP) showed no obvious bile ducts stricture or obstruction. Anti-HEV IgG antibody was observed as weakly-positive, twice, during the second week after the beginning of the clinical manifestations, while other hepatitis viruses, like HAV, HBV, HCV, as well as CMV, were negative. Therefore based on the symptoms below, the increasing of ALT and TBIL level, especially the absence of the anti-HEV IgG antibody, he was diagnosed with an acute hepatitis E virus infection. Thereby a liver biopsy was performed and cholangiole cholestasis was observed, which further confirmed the diagnosis (Figure 1).

Figure 1. Pathology shows cholangiole cholestasis in the liver

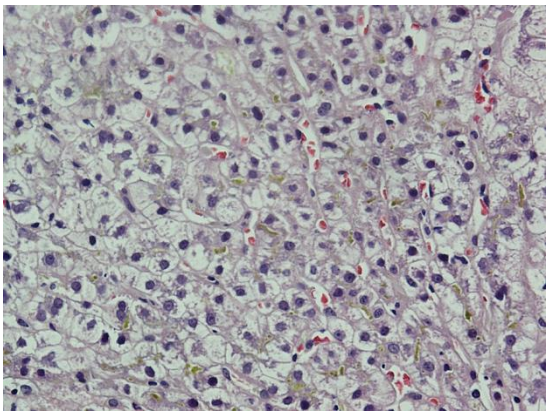

Figure 2. The total bilirubin level changes during the course of the disease

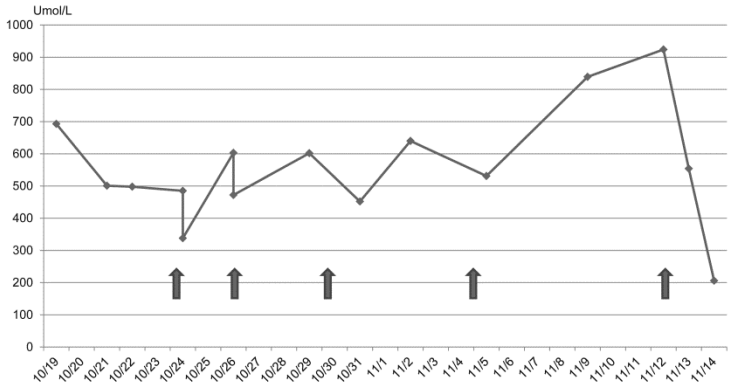

Table 1. Serial liver tests for this patient

Date	**19/10**	**24/10**	**26/10**	**26/10**	**29/10**	**31/10**
Event	2nd day admitted	After 1st ALS		After 2nd ALS		After 3rd ALS
Alanine transaminase (normal:5-40 IU/L)	934	192	193	93	119	75
Aspartate transaminase (normal:8-40 IU/L)	1035	109	201	54	87	68
Bilirubin (Normal:0-21umol/L)	693	338	603	472	602	452
Albumin Protein (Normal:35-55g/L)	34.4	31.1	29.8	32	31.3	33.1
Prothrombin Time (normal:10-13.5s)	23.4	19.9	22.4	17	20	16.7

Date	**2/11**	**5/11**	**9/11**	**12/11**	**13/11**	**14/11**
Event		After 4th ALS			After 5th ALS	1st day post LT
Alanine transaminase (normal:5-40 IU/L)	96	71	143	208	89	101
Aspartate transaminase (normal:8-40 IU/L)	103	64	130	165	75	133
Bilirubin (Normal:0-21umol/L)	640	531	839	924	554	206
Albumin Protein (Normal:35-55g/L)	32	33.6	35.1	36.4	29.8	23.2
Prothrombin Time (normal:10-13.5s)	20.6	15.9	21.2	18.8	20.4	17.7

After some ordinary medicine treatment, which showed no improvement, he was transferred to the infectious disease department, where the first Artificial Liver Support was performed. After that, the total bilirubin level showed some decline, but increased again on the following test. The second ALS also played a minor role, and the total bilirubin level increased as high as 900 umol/L (Figure 2) and over. So the re-transplantation was considered. And after five times of ALS to buy some time, he was lucky to undergo the operation on the fifth week of the disease.

After undergoing another 3-week post-transplant treatment, the patient recovered and was discharged with normal liver function and a very positive anti-HEV IgG marker in his serum, which was still detected at the 3-month follow-up.

Discussion

Acute hepatitis E virus (HEV) infection is known as a self-limiting symptomatic or asymptomatic disease in people and usually does not need any treatment. It was also observed in immuno-compromised individuals, like solid organ transplant recipients and patients with severe hematologic disorders [1,4]. In these patients, about 50%-60% of the cases of acute hepatitis E infection were reported to have developed into chronic hepatitis with rapid progression to liver cirrhosis [7,8].

HEV is a single-strand, positive-sense RNA, non-enveloped virus with five different genotypes, genotype 1 and 2 infections are restricted to humans, while genotypes 3 and 4 appear to be zoonotic, especially in pigs, and genotype 5 is of avian origin and probably does not infect humans [9]. In China, genotype 1, 3 and 4 were mostly observed, especially genotype 4, which seemed to become the dominant genotype instead of genotype 1, since 2004 [10].

The diagnosis of HEV infection is based on detection of HEV IgG and/or IgM antibodies in blood serum along with typical clinical symptoms also needs to exclude other types of hepatitis infection. In this case: fatigue, bad appetite and jaundice were the first symptoms, then elevated liver enzymes with significantly increased total bilirubin, both direct and indirect, were observed in the next testing. Finally, anti-HEV IgG antibody was detected as weakly-positive on the second week of the disease, with anti-IgM antibody negative, as well as other hepatitis viruses, so the diagnosis was confirmed.

Artificial Liver Support System (ALSS) has been used as a promising liver assistance system for years and has efficiently decreases the mortality of patients with severe hepatitis in the early and middle stages [11-12], as well as liver cirrhosis and liver failure [13-14]. For patients who developed massive necrosis of hepatocytes and lost ability of liver regeneration, several times of ALSS and sequential timely LT were needed [15].

In China, the hepatitis B virus (HBV) infection was very common, and most liver transplantation recipients are HBV related cirrhosis or hepatocellular carcinoma individuals. Thus, in the routine post transplantation check-up, HBV was given careful attention, but hepatitis E virus, as well as hepatitis A virus, which can be infected by oral transmission, are not usually on the list. So we suggest that in some unknown graft, fibrous and abnormal liver function of patients who received liver transplantation, HEV deserves to be considered.

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