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A Case of Acute Hepatitis E after a Trip to Nepal and India

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Summary. **A 20-year-old male student was referred to our university hospital with complaints of anorexia, fever and diarrhea on May 10, 1992, having previously made a trip to India and Nepal from February 26 to April 8, 1992. On admission, physical examination revealed a temperature of 37°C, jaundice and hepatosplenomegaly. Blood chemical tests showed the increased levels of aspartate aminotransferase (1,261 IU/L), alanine aminotransferase (2,586 IU/L) and total bilirubin (12.0 mg/dl). He had no history of blood transfusion or habitual intake of alcohol more than 75 g/day or drugs. There were no family members with liver diseases. Positive reactions of antibody to hepatitis E virus were obtained from the sera in the acute and convalescent stages by enzyme linked immunoassay with recombinant synthetic peptide antigen and western blotting with the structural protein of HT3-B. Negative reactions were obtained for HBsAg, anti-HA-IgM and anti-HCV, indicating the absence of hepatitis A, B and C virus infections. The PCR technique also failed to detect HCV-RNA from the patient serum in the acute stage. Other viral markers, such as anti-EB VCA IgM, anti-cytomegalovirus antibody and anti-herpes zoster antibody did not turn out to be positive. Serum levels of aminotransferase and bilirubin decreased, and returned within normal ranges 30 days after the onset of symptoms. These serologic results with clinical symptoms indicated that this patient suffered from acute hepatitis E contracted during the trip to Nepal and India. Thus, the measurement of anti-HEV antibody is recommended in acute hepatitis cases with negative serological results for hepatitis A, B and C in Japan, especially in those with a history of traveling to endemic areas of hepatitis E.**

Key words—HEV, acute viral hepatitis, epidemic area.

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CASE REPORT

A 20-year-old patient, a Japanese male college student, first visited a general practitioner on May 8, 1992, complaining of unpleasant feelings in the right upper quadrant together with nausea and diarrhea. Jaundice gradually became visible and increased levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were indicated. He was then referred to our university hospital on May 10, 1992. Physical examination revealed a temperature of 37°C, jaundice and hepatosplenomegaly on admission. Serum AST and ALT levels were 1,261 and 2,586 IU/L, respectively, and total bilirubin was 12.0 mg/dl (Table 1). Peripheral blood analyses showed no abnormal findings. Negative reactions were obtained for HBsAg, anti-HA-IgM and anti-HCV, indicating the absence of hepatitis A, B and C virus infections, although these tests were carried out repeatedly in the acute and convalescent stages. The PCR technique also failed to detect HCV-RNA from the patient serum in the acute stage. Other serological tests for cytomegalovirus, Epstein Barr virus and herpes virus types 1 and 2 did not turn out to be positive. Accordingly, we suspected this patient of having hepatitis E virus infection due to his history of traveling to Nepal and India, and an antibody to hepatitis E was determined. Positive reactions of the antibody to hepatitis E virus were obtained through enzyme linked immunoassay with recombinant synthetic peptide antigen and by western blotting with the structural protein of HT3-1B from the sera of the acute and convalescent stages, as shown in Figs. 1 and 2a. Serum levels of aminotransferase and bilirubin decreased, and returned to within normal ranges 20 days after the onset of symptoms in accompaniment with the reduction of his several subjective

Table 1. Laboratory data on admission

Peripheral blood		Blood chemistry		Coagulation test	
RBC	494×10^4/mm^3	TP	6.7 g/dl	PT	13.4 sec (73.5%)
Ht	46.2%	Alb	3.6 g/dl	APTT	31.0 sec
Hb	15.6 g/dl	γ-gl	1.8 g/dl	HPT	65.0%
WBC	5400/mm^3	T-Bil	12.0 mg/dl	TT	45.0%
Neutro	59.6%	D-Bil	10.1 mg/dl		
Ly	33.8%	TTT	15.2 Mc.U	Serological test	
Mo	4.2%	ZTT	20.5 K.U	CRP	(−)
Eo	1.3%	GOT	1261 IU/I	anti-HAIgM	(−)
Ba	1.1%	GPT	2586 IU/I	anti-HAIgG	(−)
Plt	29.1×10^4/mm^3	LDH	843 IU/I	HBsAg	(−)
		ALP	412 IU/I	anti-HBs	(−)
Urinalysis		γ-GTP	46 IU/I	anti-HBclgM	(−)
Protein (−)	Bilirubin (3+)	ChE	3744 IU/ml	anti-HBc	(−)
Suger (−)	Urobilinogen (−)	T-Chol	140 mg/dl	anti-HCV	(−)
		BUN	9 mg/dl	HCV-RNA	(−)
Stool		Cr	1.0 mg/dl	anti-EBVIgM	(−)
O (±) G (−) Hb (−)				anti-CMVIgM	(−)

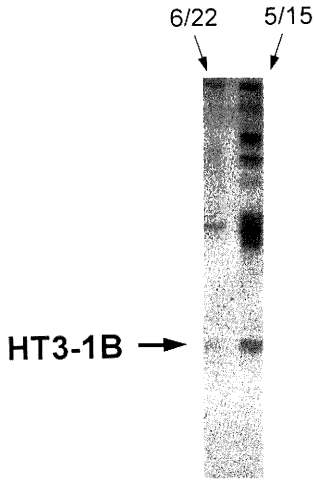

Fig. 1. The detection of the antibody to hepatitis E virus by western blot with the structural protein of HT3-1B from the sera of the acute and convalescent stages.

complaints. No specific therapy or treatment was needed for this spontaneous recovery. Longitudinal series of ALT and total bilirubin in the present case are depicted in Fig. 2b.

DISCUSSION

The endemic area of hepatitis E occurs in the developing countries, including India,[1] Myanmmar,[2] Nepal,[3] Mexico[4] and African countries.[5] The incubation period ranges from 15 to 60 days, with the average of 35 days after infection to the liver. It is reported to complicate influenzalike symptoms and gastrointestinal symptoms similar to those of hepatitis A. Hepatitis E is usually mild, particularly in children where it is passed off as gastroenteritis. Prognosis of this hepatitis is excellent with full clinical recovery. Mortality rates in large epidemics are about 10 per 1000.[6] Chronicity does not develop. However, the disease is more serious and prolonged in pregnant women, especially in those in the third trimester. The incidence of fulminant hepatitis in this group is significantly higher as compared with non-pregnant women.[2,7,8]

A diagnosis of type A hepatitis was initially suggested for this patient because of his young age and clinical symptoms. However, IgM class anti-hepatitis A antibody was not detected in the acute stage, together with the absence of HBsAg and anti-HCV antibody. The PCR technique also failed to detect the HCV-RNA from the patient serum in the acute stage. These was no history of drug ingestion or habitual alcohol intake by this patient. Antibodies to non-hepatotropic viruses and antoantibody did not show positive. Thus, we suspected this patient of having hepatitis E infection, and the positive reactions of antibody to HEV were ultimately obtained.

There have been two incidences of hepatitis E infection in Japan up to now.[9] In both cases, the

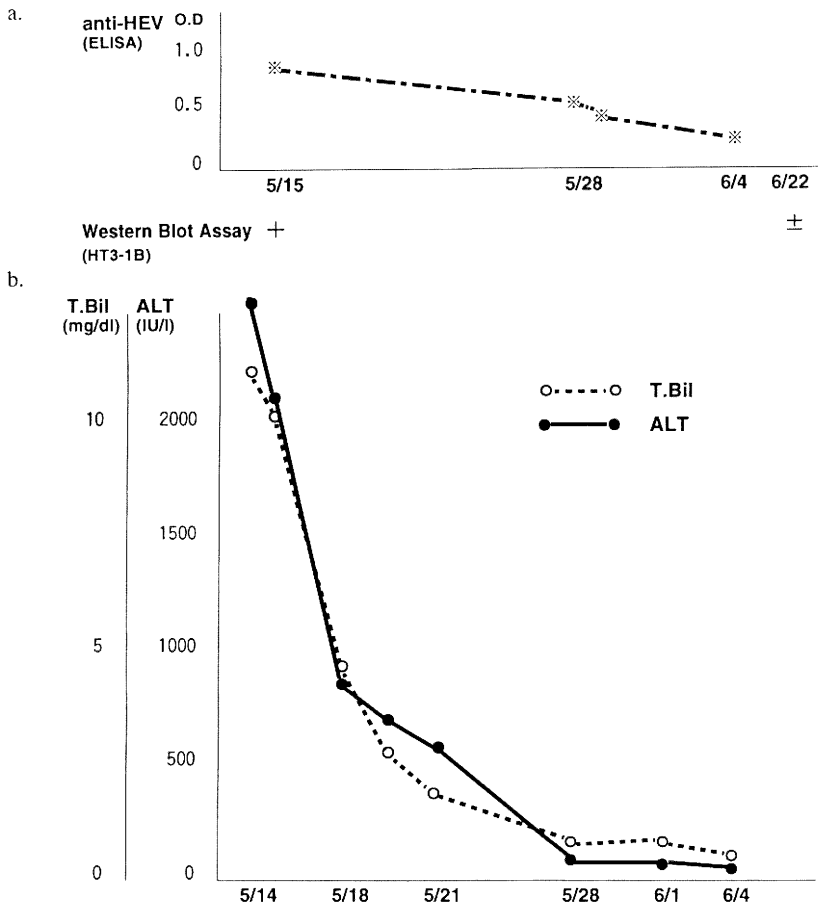

Fig. 2. Longitudinal series of alanine aminotransferase (ALT) and total bilirubin, and results of the detection of the antibody to hepatitis E.

patients had histories of traveling to India and Pakistan. It is presumed that the prevalence of hepatitis E will increase in parallel with the growing numbers of oversea trips to the developing countries. Accordingly, the measurement of the anti-HEV antibody is recommended for acute hepatitis with negative serological markers for hepatitis A, B and C in Japan, especially when there is a history of traveling to endemic areas of hepatitis E.

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