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A Cluster of Hepatitis E Virus Infection in Hokkaido, Japan

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On November 16, 2004, the Kitami Health Center (KHC) of Hokkaido, Japan, was notified of a case of hepatitis E in a 69-year-old man who had shown symptoms of diarrhea and fever in the middle of September. He deteriorated rapidly and died of fulminant hepatitis on October 14. A retrospective survey revealed that the patient and his family members had visited a barbecue restaurant on August 14. The survey further revealed that total of 388 individuals visited the restaurant on the same day and might have eaten barbecued meat such as beef, pork, chicken as well as various organs of these animals. Because the case described here was also reported in the news media, an unrelated customer who visited the same restaurant on the same day and subsequently developed hepatitis-like symptoms consulted the staff of the KHC about a potential hepatitis E virus (HEV) infection.

In total, the initial patient and 13 of his family members (termed Group A), the unrelated customer and 7 of his family members (Group B), and 5 employees of the restaurant (Group C), were examined to see whether they had HEV infections.

Virological studies using nested reverse transcriptase-polymerase chain reaction (RT-PCR) showed that only one serum sample (obtained from one of the family members) of the 26 sera and 12 stool specimens taken from Group A was positive for HEV G4 RNA (Table 1). PCR was carried out using HEV-F1/HEV-R2 and HE044/HE040 as first PCR primers and HEV-F2/HEV-R1 and HE044/HE041 as second PCR primers (1). However, the serum of the index patient, which was available only in a sample which had been taken after approximately 3 weeks of illness, did not show any trace of HEV RNA. HEV RNA was also negative in the 8 sera and 8 stool specimens from Group B, and the 5 sera and 2 stool specimens from Group C. The nucleotide sequence of the PCR product from the only positive sample was most closely related to that of JSM-Sap 95 (AB1617171.1) (2).

Since meats and organs were not stored at the restaurant, 30 different samples of pork liver were collected from the regional wholesaler and were tested for the presence of HEV RNA by nested RT-PCR. Real-time PCR was also performed using a HECOM-S/HECOM-AS primer set and a TP-HECOM probe. All samples tested were negative for HEV RNA.

Three different sera from Group A including that of the index patient and a serum from a family member of the unrelated customer of Group B were found to be positive for anti-HEV IgM antibody by enzyme-linked immunosorbent assay (ELISA) (3), however, these antibodies were not detected in the serum of the Group A patient whose serum was positive for HEV RNA. A serum sample from the unrelated customer was negative for anti-HEV IgM antibodies even though he was symptomatic. All patients whose sera were positive for anti-HEV IgM antibodies were also positive for anti-HEV IgG antibodies. Additionally, 5 individuals from Group A, 3 from Group B and 1 from Group C were positive for only anti-HEV IgG antibodies, suggesting that they had previously had HEV infections.

Table 1. Detection of hepatitis E virus RNA and the presence of antibodies in individuals tested

Group	No. of people examined	Detection of HEV RNA	Detection of antibody	
			positive for anti-HEV IgM	positive for anti-HEV IgG
A[1)]	14	1	3	8
B[2)]	8	0	1	4
C[3)]	5	0	0	1
Total	27	1	4	13

[1)]: Patient and his family members.
[2)]: Unrelated customer who consulted with and his family members.
[3)]: Employees of the restaurant.

Initially, food items were suspected as the source of infection in these cases because of the occurrence of primary infection in two different tested groups. However, we were unable to confirm this possibility without further information about the stored materials. No other food that all subjects had eaten was identified.

In summary, 4 individuals in Group A, including the initial patient, and 1 in Group B were considered to be infected with HEV due to the detection of HEV RNA and/or the presence of anti-HEV IgM antibodies. HEV infection is generally subclinical during approximately 6 weeks following primary infection even in individuals who develop the illness (4). Most HEV-infected cases recover spontaneously without developing obvious hepatitis or even any symptoms. The period in which it is possible to detect the viral gene from clinical specimens is limited to the acute phase. Therefore, it is generally difficult to identify the source of infection or trace the route of infection.

It is important to obtain detailed epidemiological data in order to be able to distinguish cluster cases from sporadic ones. It is essential to develop more sensitive and specific methods of confirming HEV infection in suspected cases.

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