Hepatitis E in a Canadian traveller

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PS AKAI, K FONSECA, D HORNE, M HO. Hepatitis E in a Canadian traveller. Can J Infect Dis 1995;6(1):39-41. Hepatitis E is clinically indistinguishable from hepatitis A and is caused by an enterically transmitted RNA virus that is endemic in developing countries of Asia, Africa, the Middle East and North America. This report describes a Canadian traveller to Nepal, Thailand and India with one of the first confirmed cases of hepatitis E reported in Canada. Although this disease is usually self-limited with no known sequelae, it may produce fulminant hepatitis with a high case fatality rate in pregnancy. Diagnosis can be confirmed by serological tests. Apart from strict food and beverage hygiene, there are presently no prophylactic measures against this disease, and pregnant women in the third trimester should avoid travel to endemic areas.

Key Words: *Hepatitis E*

L'hépatite E chez un voyageur canadien

RÉSUMÉ : L'hépatite E ne se distingue pas sur le plan clinique de l'hépatite A et est causée par un virus à ARN transmis par voie entérique qui est endémique dans les pays en voie de développement de l'Asie, de l'Afrique, du Moyen-Orient et de l'Amérique du Nord. Ce rapport décrit le cas d'un voyageur canadien qui s'est rendu au Népal, en Thaïlande et en Inde et qui est l'un des premiers cas confirmé d'hépatite E au Canada. Bien que cette maladie rentre habituellement dans l'ordre spontanément sans séquelles connues, elle peut engendrer une hépatite fulminante et s'accompagne d'un taux de mortalité élevé dans la grossesse. Le diagnostic peut être confirmé par des épreuves sérologiques. À part une hygiène stricte sur le plan des aliments et des boissons, il n'y a pour l'instant aucune mesure prophylactique contre cette maladie. Les femmes enceintes en cours du troisième trimestre doivent éviter de se rendre dans des régions endémiques.

HEPATITIS E, PREVIOUSLY KNOWN AS ENTERICALLY TRANSMITted non-A, non-B hepatitis, is clinically indistinguishable from hepatitis A. It is etiologically associated with a recently identified single-stranded linear RNA virus structurally similar to a calicivirus (1).

Epidemic and sporadic disease have been recognized in tropical and subtropical developing countries of Asia, Africa, the Middle East and North America (Mexico), and infection is highly associated with contaminated water sources (1,2). Most cases identified in developed countries involve travellers returning from endemic areas (2). The average incubation period has been estimated to be six weeks, with a range from two to nine weeks (1).

The disease is usually self-limited with no chronic sequelae, except during the third trimester of pregnancy when fulminant hepatitis is more common, with a high case fatality rate of approximately 20% (1,2). In a large series of 583 cases from Turkmenistan during a 1985 outbreak (4), a prodrome of malaise and anorexia characteristically occurred a mean of 3.5 days before the onset of jaundice, along with right upper quadrant or epigastric pain (in 70.5% of patients), nausea (50%), vomiting (25%), fever greater than 37.7°C (15%) and fever greater than 38°C (3.1%). Jaundice, which was accompanied by pruritis in 10% of patients, lasted a mean of 14.2 days, and 3% of patients developed cholestasis with jaundice and pruritis lasting for almost a month. In four recently described cases among American travellers (2), total bilirubin levels between 43 and 129 μmol/L (normal 0 to 17 μmol/L), aspartate aminotransferase (AST) levels between 1262 and 2256 U/L, and alkaline phosphatase (ALP) levels between 172 and 516 U/L, were reported.

Until recently, no serological test was available to identify hepatitis E, and diagnosis depended on appropriate history of exposure, clinical presentation and exclusion of other causes of hepatitis (2,3). This report describes one of the first cases of hepatitis E reported in Canada, and was confirmed by Western blot and ELISA at the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia (4).

CASE PRESENTATION

A 27-year-old male presented to the International Travel and Immunization Clinic (ITIC) at the University of Calgary on September 3, 1993, three weeks following his return from a year-long trip to Nepal, Thailand and India. He gave a one-week history of dark urine, light-coloured stools and jaundice for less than 24 h. He dated his illness to a bout of nonbloody diarrhea (initially associated with fever and abdominal cramps), fatigue, anorexia and weight loss of 4.5 to 6.8 kg starting six weeks previously when he was in India.

The patient was previously healthy and had received tetanus, polio, measles, mumps, rubella, typhoid and meningococcal vaccines as well as immunoglobulin (Ig) before travel. During his travels he occasionally drank water that was not disinfected or boiled. He had had one unprotected heterosexual encounter with a European traveller more than seven months before presentation. To obtain a driver's license in India, he also had a finger prick six months before presentation, for a blood grouping test.

On physical examination, he was afebrile but ill looking and had scleral icterus. He had mild right upper quadrant abdominal tenderness but no hepatosplenomegaly.

Two days before presentation, a family physician had ordered the investigations with the following results. Urinalysis showed occasional white blood cells and increased bilirubin. Complete blood count was normal with no evidence of anemia, and erythrocyte sedimentation rate was 0 mm/h. Serum electrolytes were normal but serum alanine aminotransferase (ALT) was 3110 U/L (normal range 7 to 56 U/L) and ALP 261 U/L (normal range 39 to 117 U/L). *Entamoeba histolytica* trophozoites and cysts, *Campylobacter jejuni* and *Salmonella ty-*

phimurium were identified in stool (along with *Endolimax nana*, *Escherichia coli* and *Entamoeba hartmani).* Serum antihepatitis A virus (HAV) IgM and hepatitis B surface antigen assays were negative. Additional investigations at the ITIC showed that chest x-ray was normal and serum antihepatitis B core antigen and antihepatitis C virus antibody assays were negative, as were serum anticytomegalovirus, anti-Epstein-Barr viral capsid antigen, antitoxoplasma IgM and antileptospira titres. Serum was also sent to the CDC for hepatitis E serology. For amoebiasis, the patient was prescribed oral metronidazole 750 mg three times daily for 10 days.

The patient was admitted to hospital September 7, 1993 because of increasing jaundice and weakness. At this time, serum ALT was 3230 U/L, ALP 325 U/L, gamma-glutamyltransferase 65 U/L (normal range 11 to 50 U/L), total bilirubin 390 μmol/L (normal range 3 to 20 μmol/L), conjugated bilirubin 337 μmol/L, albumin 34 g/L (normal range 3 to 20 g/L), prothrombin time 17.1 s (control 11.6 s), partial thromboplastin time 38.2 s (control 28.7 s) and glucose 4.7 μmol/L. Abdominal ultrasonography showed no evidence of biliary obstruction or hepatic mass or abscess. The patient improved symptomatically and was discharged September 10. To eradicate *E histolytica* cysts, he was subsequently given oral iodoquinol 650 mg three times daily for 20 days. Repeat anti-HAV IgM measurement on the day of discharge was negative. Electron microscopy on stool collected at discharge showed no viral particles, but serum collected on September 3 was positive for antihepatitis E virus (HEV) IgG and anti-HEV IgM by Western blot and ELISA.

The patient subsequently made an uneventful recovery and his liver enzymes and liver function tests returned to normal by September 30. At this time stool cultures were negative for enteric bacterial pathogens and parasites.

DISCUSSION

This patient most likely acquired hepatitis E through contaminated drinking water while in India. As this case illustrates, travellers to developing countries are at risk of acquiring hepatitis E, a disease that may be particularly severe and even fatal in pregnant women (1,2). In endemic areas subclinical infection may exist, and clinically overt disease occurs most often in the 15 to 40 year age group, including individuals who are already anti-HAV positive and presumably immune to HAV.

Apart from rigorous attempts to avoid contaminated drinking water and food, there are no prophylactic measures against this disease. Immunoglobulin obtained from nonendemic populations in developed countries is ineffective in prophylaxis (2). However, as with hepatitis A, protective immunity is thought to develop following infection but its duration is unknown (3).

Although viral antigen or genomic sequences in sera, stool, bile or liver biopsy tissue can be detected by a variety of techniques including immune electron microscopy, polymerase chain reaction and direct fluorescent antibody tests (1), such techniques are not generally used for diagnosis. HEV is a labile virus, and stool shedding decreases and
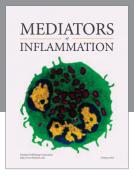
may be undetectable by the time patients present with symptoms (1,5). Hepatitis E is best diagnosed by detection of serum anti-HEV IgM, which indicates recent (less than four to five months) infection. Anti-HEV IgG remains persistently elevated following infection and is less useful in differentiating acute from previous infection. Anti-HEV antibody can be detected by fluorescent antibody-blocking assays using native HEV antigens, and by immunoblotting and enzyme immunoassay using recombinant HEV proteins (1,4). However, given that these tests are not yet widely available, and that hepatitis E clinically resembles hepatitis A, many cases of HEV infection in returning travellers may be missed. This diagnosis should be considered in any person returning from abroad with acute hepatitis and in whom other causes of viral hepatitis (including hepatitis A, which remains, by far, the more common enterically acquired hepatitis in travellers returning from developing countries [2]), systemic infections such as leptospirosis and Q fever, and noninfectious causes such as gallstone obstruction and drug-related hepatitis (eg, from sulpha drugs) have been ruled out.

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