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A Case Report About the Most Common Yet Most Forgotten Hepatitis E

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Patient: Male, 59
Final Diagnosis: Acute hepatitis E infection
Symptoms: Fever • jaundice • fatigue • loss of appetite
Medication: —
Clinical Procedure: Medical management
Specialty: Gastroenterology and Hepatology

Objective: Mistake in diagnosis

Background: Hepatitis E virus (HEV) is the most common cause of enterically acquired acute viral hepatitis worldwide with major prevalence in the developing countries. An increasing number of sporadic cases of acute HEV infection have also been found in developed countries, but there is still no role for HEV testing in cases of seronegative acute hepatitis in such nonendemic regions.

Case Report: A 59-year-old male residing in the United States for seven months with a history of malaria treated one year ago presented with fatigue and cholestatic jaundice with very high bilirubin levels. Hepatitis A, B, and C viral serology along with other atypical infections were ruled out. No history of any kind of drug intake was reported. Liver biopsy was obtained and was suggestive of acute hepatitis. Eventually hepatitis E immunoglobulin M was checked and was found positive. The patient was treated with supportive care and improved gradually with normalization of liver function test in a few weeks.

Conclusions: Autochthonous HEV infection must be suspected in cases of acute viral hepatitis in developed countries. Timely detection of HEV infection is necessary, especially in immunocompromised patients, in whom treatment is required to eradicate the infection.

MeSH Keywords: Developed Countries • Hepatitis E • Hepatitis, Viral, Human

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/899261

Background

Hepatitis E virus (HEV) was identified in 1983 when a researcher voluntarily ingested a pooled extract of feces from soviet soldiers suffering with acute hepatitis in Afghanistan. This resulted in acute hepatitis in the volunteer, and small virus-like particles were found in his stool with the help of electron microscopy [1]. Since then, HEV has been found to be the most common cause of acute viral hepatitis worldwide [2] and of large epidemics in developing countries [3,4]. Recent studies have now shown the occurrence of sporadic HEV cases in many developed countries [5,6]. Here we present one such case of acute hepatitis caused by HEV infection in a metropolitan city of a highly developed country.

Case Report

A 59-year-old male whose only medical history was of malaria in the past presented with yellowish discoloration of skin and dark urine for four days. The patient reported having subjective fever and chills for six days prior to presentation. These were associated with fatigue, body aches, and loss of appetite. He denied any other gastrointestinal or genitourinary symptoms, recent travel, or sick contacts. He emigrated from Guyana, a Caribbean country on the northern mainland of South America, 7 months ago. He was sexually inactive and denied any use of alcohol, tobacco, or illicit drugs. He denied taking any over-the-counter or prescribed medicines or herbal supplements. He denied any personal or family history of liver disease. Admission vitals revealed sinus tachycardia at 117 beats/min, but were otherwise normal.

Physical examination on presentation was significant for icteric sclera and distended abdomen with hypoactive bowel sounds. A nontender liver edge was palpable. Laboratory studies on admission were significant for white blood cell count (WBC) 16.8×10{9/L with 8% bands, platelet count 77×10{9/L, blood urea nitrogen (BUN) 31 mg/dL, creatinine 1.69 mg/dL, serum total bilirubin 9.27 mg/dL, and serum conjugated bilirubin 6.44 mg/dL. Aspartate aminotransferase (AST) was 50 IU/L and alanine aminotransferase (ALT) was 44 IU/L. Computed tomography scan of the abdomen without contrast showed hepatic enlargement with fatty infiltration, and cholelithiasis with no evidence of cholecystitis. Infectious disease and gastroenterology services were consulted. Peripheral smear for parasites including malaria was negative. Viral hepatitis serology (hepatitis A, B and C), Epstein-Barr virus (EBV), Venereal Disease Research Laboratory test-rapid plasma reagin (VDRL-RPR), Rocky Mountain spotted fever Ab, Ehrlichia, Anaplasma, HIV, Leptospira, and Brucella were all negative. Transferrin saturation was 11.68% with serum ferritin 535.9 ng/mL, ceruloplasmin 47.9 mg/dL (normal 25–63 mg/dL), and 24-urine Hg level <2 µg/L (normal <21 µg/L). Serum acetaminophen and salicylate levels were negative. Blood and urine cultures were negative.

During the patient's hospital stay, liver function tests (LFTs) were consistently deranged with the highest AST 108, ALT 182, lactate dehydrogenase (LDH) 313, serum total bilirubin 21.4, and serum conjugated bilirubin 17.6 (day 4 of hospitalization). Mildly positive values for anti-smooth muscle antibody at 1: 20 and immunoglobulin G4 (IgG4) at 128 mg/dL (2.4–121 mg/dL) were noted. Antinuclear antibody (ANA) and anti-mitochondrial antibody tests were negative. A liver biopsy showed mild portal inflammation, predominantly lymphocytic, with mild intra-hepatocellular cholestasis, focal ductile proliferation, and minimal fibrosis suggestive of acute hepatitis. The patient was initially empirically treated with doxycycline for 5 days for suspected leptospirosis, which was then discontinued because of a negative workup. HEV IgM antibody was later checked and was found to be positive. LFT continued to improve gradually with symptomatic treatment and patient was discharged home on as-needed oral hydroxyzine for pruritus after an in-hospital stay of about 2 weeks. At 90 days post-discharge, the patient was symptom free with normal LFT, kidney function, and platelet count.

Discussion

HEV is a small, spherical, nonenveloped virus with a single-stranded, positive-sense RNA. It is 7.2 kb in length and has short 5' and 3' noncoding regions and three open reading frames [7]. HEV has four major genotypes: Genotypes 1 and 2 are found mostly in developing countries, genotype 3 is found mostly in North America, South America, and Europe, and genotype 4 is found mostly in Asia [8]. HEV is suspected in patients with recent travel to endemic countries, where it is mainly transmitted via the fecal-oral route; but many cases of HEV are autochthonous, possibly related to zoonotic transmission via consumption of raw or undercooked pigs, wild boar, and deer [8–10].

HEV has an incubation period of 3 to 8 weeks, followed by a short prodromal phase and then symptoms of jaundice lasting days to several weeks [7]. HEV infection is highly unrecognized in developed countries and can be mistaken for drug-induced liver injury [6] in patients with otherwise negative viral serology. It is also known to cause extra-hepatic disorder like pancreatitis and aplastic anemia, and neurological disorders like Guillain-Barre syndrome, polyradiculopathy, cranial nerve palsies, and seizure.

Acute HEV can be diagnosed with the detection of anti-HEV IgM, which is present on day 4 after the onset of jaundice and can persist for 3–5 months. Detection of anti-HEV IgG signifies previous exposure to HEV. The gold standard for the diagnosis

of active HEV infection is by detection of HEV RNA in biologic specimens. It can be detected in stool and serum for about 6 and 4 weeks, respectively, since the onset of illness. HEV RNA detection depends on early suspicion of HEV infection on patient presentation and timely specimen collection; thus, undetectable HEV RNA does not rule out recent infection. HEV RNA detection has a significant role in the detection of active HEV infection in immunocompromised and transplant recipient patients, in whom HEV serology can be false-negative because of immunosuppression [8].

HEV infection is generally self-limiting in immunocompetent patients, but is known to cause chronic hepatitis in immunocompromised patients and needs to be treated. Treatment mainly consists of reducing the dosage of immunosuppressive therapy to help in the clearance of HEV. Ribavirin has also been shown to be effective in solid organ transplant recipients and in patients with persistent chronic infections [8].

Our patient did not have any associated risk factors for HEV infection, and the only meat he reported to have consumed in the six months prior to this hospitalization was cooked chicken, last eaten about a month before the illness. He was found to have only mild elevation in hepatic transaminases, with a very high bilirubin level. This is similar to the case series of HEV outbreak on a cruise ship returning from a world tour in the UK, where only five of the ten symptomatic patients had ALT >2 times the upper normal limit and only two out of three had AST >2 times the upper normal limit [11]. Similarly, among the cases reported by Dalton et al. [12] in New Zealand, one of the case patients had only a modest elevation in ALT (552 IU/L). Also, the wife of another symptomatic patient was found to be positive for HEV (IgM, IgG, and polymerase chain reaction [PCR]), but had normal LFT. In the case under discussion, specimens of HEV RNA and genotype were not collected early in the disease course due to late suspicion of HEV infection, and then due to the nonavailability of the test in local laboratories. Until now, the U.S. Food and Drug Administration has not approved the use of any serological tests to diagnose HEV infection in the United States [10]. Despite its increasing incidence in developed countries, there is no place yet for HEV testing in the diagnostic algorithm for acute hepatitis in developed countries.

Conclusions

Autochthonous HEV infection must be suspected in cases of acute viral hepatitis in developed countries.

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