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CASE REPORT | LIVER

Hepatitis E Infection With Acute Liver Failure

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ABSTRACT

A 21-year-old man from India presented with acute hepatitis associated with a 1-week history of abdominal pain, pruritus, and dark urine. Over a 7-day admission, the patient's acute hepatitis evolved into acute liver failure with low-grade encephalopathy, markedly elevated transaminases, bilirubin, and impaired hepatic synthetic function. He was eventually diagnosed with acute hepatitis E virus (HEV) and was transitioned to supportive management. Acute HEV is a rare cause of acute liver failure. Hence, this case highlights the importance of early consideration of HEV in all patients with acute hepatitis who have originated from endemic regions.

INTRODUCTION

Globally, hepatitis E virus (HEV) is responsible for 3 million cases of acute hepatitis and approximately 55,000 deaths.[1] HEV genotypes 1 and 2 predominate in developing regions such as Asia and are spread by the fecal-oral route via contaminated water. Conversely, most cases in developed countries such as North America are associated with genotypes 3 and 4, which are zoonotic infections from pigs or consuming undercooked pork products.[2]

The prevalence rates of HEV antibodies are greater in developing countries compared with developed countries (10%–70% and 1%–21%, respectively).[3] As such, HEV is often neglected as a cause of acute hepatitis and acute liver failure (ALF), given its low incidence in Western countries and the small proportion of cases that progress to fulminant hepatitis. ALF is defined as encephalopathy, increased aminotransferases, and impaired synthetic function (international normalized ratio [INR] $\geq$ 1.5) in patients without pre-existing liver disease.[4] Therefore, this case highlights the importance of early consideration of acute HEV in all patients with acute hepatitis returning from endemic regions. By recognizing HEV and instigating early testing, patients can avoid unnecessary diagnostic tests and treatments.

CASE REPORT

A 21-year-old man from India presented with a 1-week history of abdominal pain, pruritus, and dark urine. He had recently traveled from India to Australia 1 month before his presentation. Before his emigration to Australia, the patient was feeling unwell with a 1-week history of coryza and a viral exanthem extending over the chest and scalp, which self-resolved. The patient had no significant medical history and took no medications, including herbal preparations. There was no family history of liver disease. He did not drink alcohol, nor did he smoke. There was no significant sexual or intravenous drug use history.

At the time of admission, the patient was alert and oriented. He was afebrile and had a regular pulse rate at 100/minute with a blood pressure of 130/80 mm Hg. On inspection, he was frankly jaundiced with chest excoriations. He did not exhibit asterixis. Abdominal examination elicited tenderness in the right upper quadrant with no abdominal distension and no signs of chronic liver disease. Cardiorespiratory and neurological examinations were unremarkable.

Initial investigations revealed severe transaminitis on liver function tests (LFTs). His bilirubin was 256 μmol/L with alanine aminotransferase (ALT) of 2,625 U/L. There was minimal synthetic dysfunction with an INR of 1.2.

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The patient was admitted for 7 days. A liver ultrasound revealed no biliary tree dilatation and patent hepatic vasculature. A hepatitis screen was conducted, and negative tests included hepatitis A, B and C, human immunodeficiency virus, Epstein-Barr virus, and malaria thick and thin films. Iron studies, ceruloplasmin, and paracetamol levels were normal. Serological markers for autoimmune causes of hepatitis were negative. During the admission, HEV serology was pending because of interstate processing of the result.

Over time, the patient's clinical state deteriorated with increasing lethargy—suggestive of a low-grade encephalopathy. On day 5, the patient developed ALF with ALT 3,622 U/L, bilirubin 478 μmol/L, and INR 1.7 (Figure 1). Given his decline, an ultrasound-guided liver biopsy was conducted, which demonstrated nonspecific fulminant hepatitis (Figure 2). Subsequently, the patient was initiated on an N-acetylcysteine infusion over 72 hours and was administered a single dose of 100 mg intravenous methylprednisolone with minimal improvement. On day 7, he was transferred to the state's liver transplant unit for further management and transplant consideration.

After his transfer, the serological diagnosis of acute HEV was made on day 2. He was transitioned to supportive management, given his rapidly improving LFTs and a high likelihood of spontaneous viral clearance. The patient was discharged after 2 days of clinical improvement. At 2 weeks after discharge, blood tests with the general practitioner revealed significantly improved liver function with ALT 72 U/L, bilirubin 96 μmol/L, and INR 1.1.

DISCUSSION

Most individuals are asymptomatic or mount a flu-like illness in response to acute HEV infection. Classically, HEV presents as an "icteric hepatitis" in 5%–30% of patients.[5] There is an initial prodromal phase characterized by fatigue, fever, and nausea. Subsequently, the icteric phase involves jaundice and the production of dark urine, which resolves in days to weeks over the convalescence phase. Acute HEV usually spontaneously resolves in immunocompetent individuals. By contrast, chronic HEV mostly occurs via HEV genotype 3 or 4 infections of immunocompromised individuals such as organ transplant recipients or HIV coinfected patients. Chronic HEV is defined as the persistence of HEV replication for over 6 months and often results in minimal symptoms until progression to decompensated cirrhosis.[2] Extrahepatic manifestations are also becoming increasingly recognized, particularly neurological disorders such as neuralgic amyotrophy and Guillain-Barré syndrome.[6]

A small percentage (0.5%–4%) of HEV cases develop ALF, resulting in overall mortality of 0.5%–3%.[7] Furthermore, the ALF rate increases to 15%–25% in pregnant women.[2,7] Patients with established acute HEV should be monitored for ALF development.[2] ALF requires timely recognition with the involvement of centers capable of liver transplantation. ALT and bilirubin should be monitored daily. Based on patient clinical status, more frequent arterial pH, coagulation profile, and electrolyte testing are paramount to ascertain the need for hepatic transplantation.[5]

HEV-infected patients who progress to ALF may warrant active therapy to avoid hepatic decompensation and transplantation. Few case studies are available on ribavirin treatment for acute HEV hepatitis resulting in ALF.[8] Ribavirin administration was associated with rapid normalization of LFTs and an undetectable HEV RNA viral load. Furthermore, case reports have shown improved LFTs after corticosteroid administration in patients with ALF from HEV infection.[9] Our patient was trialed on corticosteroid therapy instead of ribavirin because a diagnosis of HEV was not yet established. In addition, there is some evidence to suggest that steroid therapy improves prognosis in patients with ALF.[10] However, the steroid trial was ineffective in improving our patient's liver function and clinical status. N-acetyl cysteine was also administered because it may improve transplant-free survival in patients with ALF with low-grade encephalopathy.[11] After the patient's formal HEV diagnosis, ribavirin therapy was not administered considering the patient's rapid clinical improvement and ribavirin's unfavorable side effect profile.[12] Currently, high-level evidence for the effectiveness of ribavirin or corticosteroid therapy in HEV infection is poor. Active treatment of acute HEV remains to be an area for further investigation.

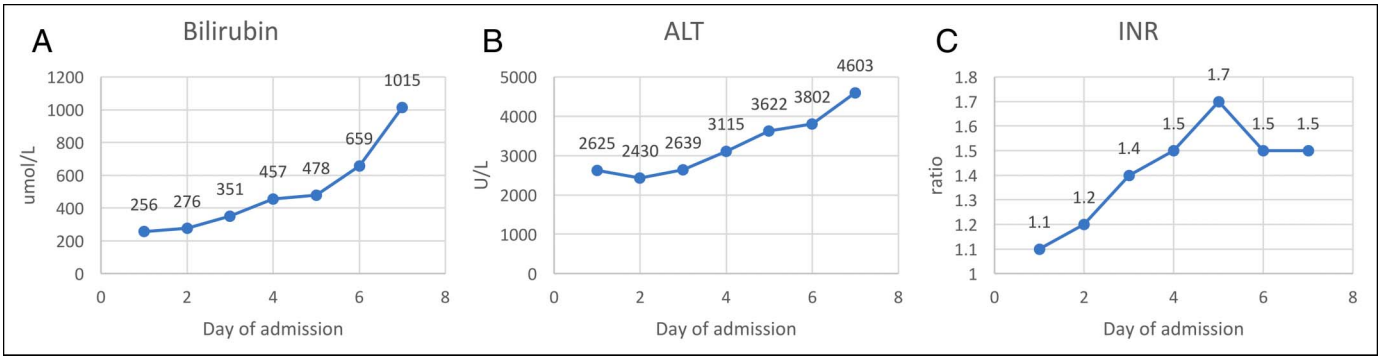

Figure 1. Graphical representation of biochemical trends over 7-day admission showing (A) bilirubin, (B) ALT, and (C) INR. Ten milligram intravenous vitamin K was given on day 4 before liver biopsy. ALT, alanine aminotransferase; INR, international normalized ratio.

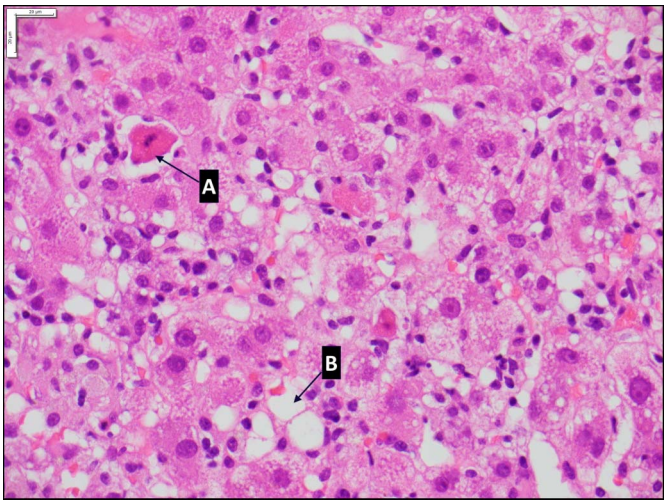

Figure 2. Histologic examination of liver lobule showing nonspecific fulminant hepatitis with extensive single-cell necrosis and (A) councilman-like bodies, and (B) empty vacuolated spaces indicating confluent lobular necrosis (hematoxylin and eosin ×20).

DISCLOSURES

Author contributions: T. Phan wrote the manuscript, approved the final version, and is the article guarantor. C. Desmond edited the manuscript and approved the final version.

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