CASE REPORT

Sporadic acute hepatitis E in the United Kingdom: an underdiagnosed phenomenon?

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Abstract

Background—Hepatitis E (HEV) is the primary cause of enterically transmitted non-A non-B hepatitis worldwide. Case reports of HEV in individuals in the United Kingdom relate to travel to endemic areas or contact with individuals who have visited these areas.

Case reports—Four individuals presented with acute hepatitis to a hepatology clinic in a teaching hospital. Serology confirmed acute hepatitis E in all four. Investigation by the Communicable Disease Control Department established no links between the cases, no travel to an endemic area, and no contacts.

Conclusion—Contrary to current belief, community acquired hepatitis E virus infection occurs sporadically in the United Kingdom and should be considered as a cause of seronegative hepatitis.

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We describe four patients with acute hepatitis E presenting to the Gastroenterology and Hepatology Unit of an NHS teaching hospital. All four cases had a history of acute viral-type hepatitis but no obvious risk factors for hepatitis E (specifically travel to endemic areas) and had negative results on routine hepatitis tests with which patients are normally screened. In each case hepatitis E was acquired in the United Kingdom.

Case reports

CASE HISTORY 1

A 44 year old female school teacher was admitted from the gastroenterology clinic. She described a 10 day history of malaise followed by vomiting and a seven day history of jaundice of gradual onset. Metoclopramide had been prescribed for nausea. She had no risk factors for liver disease and no foreign travel for two years. She had no known contacts with people who had travelled to an area endemic for hepatitis E and had not recently eaten seafood. She was deeply jaundiced, with 4+ bilirubin on urinalysis. Results of initial tests included the following: alanine transaminase 3947 IU/l, alkaline phosphatase 453 IU/l, bilirubin 295

µmol/l, INR 1.6. An abdominal ultrasound showed normal liver appearance and gall stones in a contracted gall bladder. Within 24 hours her condition began to improve, she required symptomatic support only and was discharged after five days. Ten days later her bilirubin was 60 µmol/l and alanine transaminase 79 IU/l. An initial viral hepatitis screen was negative for markers of hepatitis A, B, and C, CMV, EBV, and *Coxiella burnetii*. The specimen was referred for hepatitis E virus (HEV) antibody tests and was HEV IgM positive. The patient remained well on routine follow up, and antibody tests one year later showed her to be HEV IgM negative and HEV IgG positive, consistent with previous HEV infection. Her liver enzyme tests were normal and hepatitis A, B, and C markers were negative.

CASE HISTORY 2

A 51 year old woman presented to the hepatology clinic with a three week history of malaise and anorexia, followed by arthralgia and a macular rash associated with fever and rigors. She had been jaundiced with dark urine for 10 days. She was a domestic assistant working in a psychogeriatric hospital but had no contact with jaundiced individuals and no history of needlestick injuries. Neither she nor any of her close contacts had recently travelled abroad. Serology for HEV IgM was positive and HEV IgG negative. Blood tests taken at one month showed a rising HEV IgG antibody.

CASE HISTORY 3

A 70 year old man was admitted to hospital for investigation of jaundice, pale stools, and dark urine. He gave a 10 day history of general malaise and nausea associated with loss of appetite and aversion to alcohol. Serology for HEV IgM was positive and HEV IgG negative. Four weeks later liver function tests were normal and there was a rising HEV IgG antibody.

CASE HISTORY 4

A 71 year old woman presented with what was assumed to be a classical presentation of hepatitis A. She described a seven day history of general malaise, aches, fever, and headaches

Abbreviations used in this paper: HEV, hepatitis E; HAV, hepatitis A.

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before becoming jaundiced. The total duration of the illness was three weeks. There was a past history of a viral-type illness with jaundice at the age of 16. She was not receiving any regular medications. She was hepatitis A (HAV) IgM negative and HAV IgG positive consistent with HAV infection in the past. On referral for HEV antibody tests the specimen was HEV IgM positive and HEV IgG negative. Four weeks later tests were again negative for evidence of recent infection of hepatitis A, B, and C but the HEV IgG titre was positive and all liver function tests were normal.

Discussion

Causes of acute hepatitis include viral and bacterial infections, drug reactions, toxins, and immune attack such as autoimmune hepatitis. In 90% of cases the likely aetiology will become apparent from the history and results of blood tests, such as serology for hepatitis A, B, and C and autoantibodies. In cases of suspected acute viral hepatitis when patients test negative for the above agents it is important to exclude unsuspected idiosyncratic drug reactions and true seronegative hepatitis, as these diagnoses have important implications for prognosis and further management.

Hepatitis E virus (HEV), a single stranded RNA virus, is the primary cause of enterically transmitted non-A non-B hepatitis worldwide.¹ Signs, symptoms, and laboratory findings of HEV are similar to those of acute viral hepatitis A but HEV infection in pregnant women is more commonly associated with fulminant hepatitis.² Hepatitis E is considered to be endemic in parts of Asia, Africa, the Middle East, and Central America where large outbreaks are associated with inadequate sanitation and waterborne infection. In most countries where hepatitis E outbreaks have not been documented (non-endemic regions), hepatitis E accounts for less than 1% of reported cases of acute viral hepatitis. Most acute cases reported in these countries have been associated with travel to HEV endemic regions,³⁻⁴ as is the case in reports previously documented in the United Kingdom.⁵ Nevertheless, in several non-endemic countries, including Austria, Australia, Greece, New Zealand, and the USA, acute sporadic HEV cases have been reported among subjects with no history of travel to endemic countries.⁶⁻¹⁴ Thus a reservoir of HEV may exist in these countries. An alternative explanation may be consumption of imported contaminated foodstuffs. A standard screen in suspected acute viral hepatitis includes hepatitis A, B, and C. If these are negative we suggest that hepatitis E should be considered in acute infection even in the absence of clear risk factors. A provisional diagnosis should be based on a positive hepatitis E IgM. A rising HEV IgG measurement on a later specimen provides confirmation.

In conclusion, each of the four patients described above presented with a history consistent with acute viral hepatitis. All were

negative for the hepatitis viruses commonly seen in the United Kingdom and in each case a diagnosis of acute hepatitis E infection was established. No links were established between the cases, despite intensive investigation by the Communicable Disease Control department. None of the cases had any of the recognised risk factors for hepatitis E such as travel to or contact with persons from endemic areas. Moreover, in addition to the obvious risk factor assessment of travel and contacts, each patient was interviewed regarding dietary habits, including consumption of imported food: none had changed their diet around the time of infection or eaten food that could be identified as being imported other than fruit. The majority of fruit (limited to apples, oranges, pears, and grapes) was washed prior to consumption.

We believe this to be the first series of HEV infections noted in patients in the United Kingdom with no previous travel to an HEV endemic area, and no clear contact with any infectious individuals. It is likely that these cases represent true United Kingdom community acquired HEV infection. Acute hepatitis E should be considered in the investigation of seronegative hepatitis, even in the absence of specific risk factors.

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