Case Report

First report of acute autochthonous hepatitis E in Portugal

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Abstract

Hepatitis E infection is usually a self-limiting disease. In industrialized countries, sporadic cases of acute hepatitis E virus (HEV) infections have been described; their number seems to be increasing in European countries. We report the first human case of autochthonous acute hepatitis E confirmed in Portugal. Patients with acute non-A-C hepatitis should be tested for HEV in Portugal and hepatitis E infection should be considered in the differential diagnosis of unexplained hepatitis cases.

Key words: sporadic; acute hepatitis E; Portugal

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Introduction

Autochthonous, sporadic cases of hepatitis E have been reported in various countries from Europe and North America, including the United Kingdom, France, Italy, Spain, the Netherlands, Greece, Hungary, Germany, Austria, Poland, and in various regions from the USA. Most of these human cases are due to HEV genotype 3 which is common in swine livestock and is considered a zoonosis of porcine origin.

Transmission to humans may occur through the consumption of raw or poorly cooked meat. The majority of patients present during early winter and summer [1].

Case report

In November 2010, a 65-year-old male patient was referred to our hospital and admitted to the infectious disease service on 16 November 2010, with a provisional diagnosis of acute hepatitis. Six days prior to the admission, the patient presented a progressive onset of a fever, fatigue, loss of appetite, upper abdominal discomfort and dark-coloured urine noticed in the day of referral.

Laboratory results revealed elevated serum liver enzymes with a total bilirubin level of 6 mg/dL. Direct bilirubin level was 3.9 mg/dL, serum aspartate aminotransferase (AST) concentration was 1458 U/L, alanine aminotransferase (ALT) was 2232 U/L, alkaline phosphatase (AP) was 196 U/L and GGT was 524 U/L. Thrombocytopenia (112,000/mm3) was observed. The peak of liver enzymes was observed on the tenth day after the start of the clinical manifestations and returned to normal values on day 25. The platelet count dropped to 90,000/mm3 and returned to normal values on day 17 after the start of the clinical manifestations.

C-reactive protein values were slightly elevated and reached 2.07 mg/dL and rapidly normalized.

Hepatitis types A to C were excluded by serological and molecular tests. Acute infection with herpesviruses, parvovirus B19, syphilis, Q-fever, brucella, HIV-1/2 and *Leptospira interrogans* were also excluded.

Anti-hepatitis E virus IgM and IgG were positive in ELISA (HEV IgM ELISA 3.0 and HEV ELISA, MP Biomedicals, Singapore) in a blood sample taken 10 days after the start of the clinical manifestations. Four additional blood samples were collected from the patient, and all were positive for IgM and IgG antibodies against hepatitis E. No liver biopsy or molecular studies were performed for hepatitis E virus.

Electrocardiogram showed an atrial flutter. Echocardiography showed a good left and right ventricular pump function without any evidence for liver congestion due to chronic right-sided heart failure.

Abdominal ultrasound showed a slight hepatomegaly without splenomegaly.

The patient's medical history included insulin controlled type 2 diabetes mellitus and cardiac arrhythmia.

The patient's medication included long-acting insulin and anticoagulation with warfarin. No history of alcohol consumption or drug-induced hepatotoxicity was observed.

He resided in an urban area. There was no travelling history in the last six months; contact with animals, as well consumption of raw meat and contact with water or sewage were denied. The patient had no past history of drug addiction or sexually transmitted diseases. However, he recalled to have eaten traditional homemade pork sausages made of raw meat about two weeks prior to the development of the clinical manifestations of acute hepatitis. The patient was admitted to the infectious diseases ward on 16 November and was discharged on 3 December 2010. He started feeling better over the first week of hospitalization and was discharged asymptomatic. He was observed once at the outpatient's clinic on the 23 March 2011, and was sent home to be followed by his local family physician.

Discussion

The clinical features of autochthonous hepatitis E range from asymptomatic infection to mild hepatitis or subacute liver failure. Hepatitis E infection in most individuals manifests as a self-limiting, acute, icteric hepatitis. The presentation seems to be similar to that from endemic regions; however, the mortality rate is higher, ranging from 8% to 11% associated with fulminant hepatitis and liver failure [2].Icterus was described as occurring in 75% of the affected individuals [3].

The incubation period of autochthonous hepatitis E varies from two to nine weeks. The concentration of serum liver enzymes, with a predominant transaminitis, peaks at about six weeks post exposure before falling to normal levels by week 10. The rise in serum transaminases and bilirubin usually peaks at presentation except in the few individuals who go on to develop liver failure.

The outcome can be poor in individuals with underlying chronic liver disease, with mortality close to 70% [4,5].

A chronic hepatitis E infection has been documented in patients receiving immunossupressive therapy following organ transplantation [6].

HEV RNA is cleared from the blood a few days to weeks after the onset of clinical symptoms; however, the virus continues to be shed in stools for another two weeks [7].

In the developed world most autochthonous hepatitis E infections are reported in middle-aged and elderly man [2].

HEV is comprised of at least five genotypes: genotypes 1 and 2 are strictly human; genotypes 3 and 4 are probably of swine origin but infect humans; genotype 5 is of avian origin and probably does not infect humans [7]. HEV genotypes 3 and 4, which infect both humans and swine, have been recovered from pigs in regions that roughly parallel the distribution of these viruses in human infections. It is likely that HEV infections are acquired from an animal reservoir, such as swine. There is support for a zoonotic source of HEV infection in industrialized countries either through occupational exposure to pigs, as happens in veterinarians and pig industry workers, or through the consumption of uncooked or poorly cooked pig, wild boar and deer meat [8]. Widespread infection has been demonstrated in pigs, with more than 90% of farms infected in Spain at least since 1980 [9].

In areas of southwest France where the incidence of hepatitis E is stable, 97% of the cases are autochthonous and occur predominantly in males. Genotype 3 is most commonly found in humans and is closely related to the swine strains isolated in Spain and France [10,11]. However, in these countries, the main routes of transmission have yet to be established.

The routine laboratory diagnosis of hepatitis E depends on serology and nucleic acid amplification techniques. Antibody response to hepatitis E infection follows a conventional course with specific IgM antibodies usually detectable at the onset of the symptoms persisting for an average of three months and IgG reaches a peak shortly after and can be detected for at least 12 years after acute infection.

Real-time RT-PCR assays have been used to detect HEV RNA in clinical specimens and seem to be more sensitive than serology; however, the window of detectable viraemia is narrow (range 17-48 days).

In our case the first blood sample was collected on 19 November (three days after hospital admission and nine days after clinical manifestations started). Four additional blood samples were collected from the patient (3 and 15 December 2010, and 11 January and 23 March 2011), and all were positive for IgM and IgG antibodies against hepatitis E. No molecular studies were performed for hepatitis E virus because

they are not currently performed at the Portuguese National Institute of Health.

The diagnosis of acute hepatitis E infection rests on the demonstrations of specific IgM, rising levels of IgG, or detection of HEV RNA [2].

Hepatitis E is still regarded by many health care professionals as a travel-associated disease. Thus a considerable amount of autochthonous infections associated with acute hepatitis may remain undiagnosed. There is no data available on incidence of hepatitis E in Portugal. However, published data showed a seroprevalence of 2.5% for Hepatitis E in Portuguese blood donors [12].

In conclusion, patients with acute non-A-C hepatitis should be tested for HEV in Portugal and hepatitis E infection should be considered in the differential diagnosis of unexplained hepatitis cases.

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