3 FOOD- AND WATER-BORNE DISEASES

FOCUS FEATURE: Hepatitis E virus infection

Case report

A 29-year-old female was admitted to hospital on 21 February 2014 for investigation. She had recently returned from India where she had been living and working for five months. In early January 2014, she developed diarrhoea and consulted a doctor in India; she received treatment (presumed to be antibiotics) and the symptoms resolved. She returned to South Africa on 27 January 2014, travelling directly to the Kruger National Park for a few days before returning to Johannesburg; she did not take malaria chemoprophylaxis but did recall being bitten by mosquitoes. About two weeks later she experienced symptoms that included fever, malaise, faint transient rash, nausea, arthralgia and headaches. On examination, no rash or eschar was noted; no joint swelling was evident, the patient did not appear jaundiced, and no other abnormal findings were noted. Initial admission laboratory investigations included a full blood count (white cell count of 3.4 x 10^9/L and platelet count of 139 x 10^9/L, normal haemoglobin level); U&E (normal); elevated CRP (62.3 mg/L); negative malaria smear and antigen; and deranged liver function parameters (ALP = 179 IU/L, GGT = 129 IU/L, ALT = 647 IU/L, AST = 798 IU/L). Investigation of the clinically inapparent hepatitis included an abdominal ultrasound (which was unremarkable) and further laboratory tests. Repeat malaria smear and antigen tests were negative; tests for common infectious causes of hepatitis in the context of the patient's clinical presentation were negative (including hepatitis A IgM, all hepatitis B markers, hepatitis C Ab, Coxsackie virus serology, rubella IgM, measles IgM, rickettsia serology, *Coxiella burnetii* serology, CMV IgM, acute EBV infection markers, *Brucella* spp. serology, arbovirus HA screen – including chikungunya, Sindbis, West Nile and Rift Valley fever viruses). Auto-immune markers also tested negative. Blood, urine and stool cultures were all negative. In view of the travel history, hepatitis E serology was also requested; hepatitis E IgM and IgG were both positive. The patient's liver function parameters deteriorated over the following few days, with ALT and AST levels peaking at 2 904 IU/L and 2 816 IU/L respectively, and bilirubinemia peaking at 76.4 mmol/L (predominantly conjugated). She subsequently improved clinically, and by 17 March 2014 her liver function parameters were near normal (ALT = 37 IU/L, AST = 31 IU/L, ALP = 106 IU/L, GGT = 69 IU/L).

FOCUS ON HEPATITIS E VIRUS

Epidemiology and transmission

Hepatitis E virus (HEV) causes an acute hepatitis syndrome. It is spread by the faeco-oral route, typically through contaminated water, but increasingly also through contaminated food. Uncommon routes of transmission include blood-borne and vertical transmission. Unlike hepatitis A however, person-to-person transmission is uncommon. Although HEV infections have been reported worldwide, the highest incidence is in Asia, Africa, Middle East and Central America, where faecally contaminated waterborne transmission occurs. Waterborne outbreaks in developing countries have high attack rates and may result in massive, prolonged outbreaks; in a recent outbreak in Uganda (late 2013), 967 cases and 23 deaths (including 15 deaths in pregnant women) were reported. In the developed world, autochthonous cases are more typical, and outbreaks have been linked to consumption of insufficiently cooked HEV-contaminated meat products (mostly pork products, but also deer meat in one outbreak). Recent surveillance data have shown that HEV is abundant in pig populations and can be shed into the environment, and directly or indirectly be transmitted to humans.

Clinical features

The incubation period of HEV infection ranges from 15 – 60 days, with an average of 5 – 6 weeks. Asymptomatic infection does occur, notably in children in endemic areas. In developed countries, seroprevalence studies have shown relatively high HEV seropositivity rates, particularly in persons working in pig/pork-related occupations.

Symptoms of acute HEV infection include fever, fatigue, jaundice, nausea and vomiting, abdominal pain and hepatomegaly. Less common symptoms include diarrhoea, arthralgia, pruritus and urticarial rash. HEV infection is clinically indistinguishable from disease caused by hepatitis A virus. Usually the disease is self-limiting, but fulminant hepatitis

can occur, with a case fatality rate of <3%. Fulminant hepatitis and liver failure is more common in pregnancy (where up to 25% of cases in the third trimester are fatal), solid organ transplant recipients, and people with underlying chronic liver disease. Chronic disease is not a feature of HEV infection, but has been noted in some solid organ transplant recipients and immunocompromised persons (including one documented case in an HIV-infected individual).

Laboratory findings

Elevated hepatic transaminase levels and serum bilirubin levels are typical. Resolution of abnormal biochemical tests usually occurs 1-6 weeks after the onset of illness.

Diagnosis

The diagnosis of HEV infection can be made on the basis of positive serological tests, or where available, positive HEV PCR on serum or stool samples. Antibody tests are not ideal, given that both false-positive and false-negative results do occur; importantly, serological tests may be negative in a substantial proportion of patients with acute infection. PCR tests are the preferred method for diagnosis where available.

Management

There is no specific vaccine, antiviral or immunoglobulin therapy currently recommended for hepatitis E infection. Treatment is generally supportive. Case reports have suggested a benefit from ribavirin, particularly in solid organ transplant patients, but more data are needed to recommend this as standard treatment for HEV infection.

Hepatitis E virus infection in South Africa

The incidence of hepatitis E virus infection in South Africa is unknown, but seroprevalence of hepatitis E IgG antibodies ranging from 1%-15% has been reported in various high risk populations.

Laboratory testing for HEV infection in the public sector (serology for IgM) is available at the NHLS Immunology Laboratory in Braamfontein (Johannesburg), and serology is also offered by most private sector laboratories. At present, PCR testing is limited to academic research units and not widely available.

HEV infection should be borne in mind as a possible cause of acute infectious hepatitis. Viral hepatitis ('non-A non-B') is a notifiable condition in South Africa, and all cases of HEV infection must be reported to the Department of Health using the standard notification system (GW 17/5 forms) so that potential sources of infection can be investigated.

Source: Division of Public Health Surveillance and Response and Centre for Vaccines and Immunology, NICD/NHLS; NHLS Immunology Laboratory, Braamfontein; Pathlink, Pathcare, Lancet and Ampath Laboratories