Liver disease in the traveller

Alicia D Yeap

Catherine A Cosgrove

Abstract

Liver disease in the returning traveller can present as an illness with jaundice or liver abscess. A full travel history with details of potential exposures is crucial to making the diagnosis. Clinicians should also take into account the patient's country of origin when assessing risks and interpreting results. It is important to identify underlying chronic liver disease and consider non-infectious causes of jaundice such as toxins. In recent years, there has been increasing recognition of hepatitis E as an important pathogen in travel-related (and locally acquired) hepatitis. Adventure tourism is gaining popularity and may put travellers at increased risk of leptospirosis. Health-related interventions undertaken abroad may increase the risk of hepatitis C acquisition. Liver abscesses may be amoebic or pyogenic and differentiation from cystic hydatid disease determines optimal management. Prognosis for infectious causes of liver disease is generally very good.

Keywords abscess; hepatitis; jaundice; liver; travel; tropical medicine

Introduction

Returning travellers occasionally present with jaundice or liver abscesses, although liver disease is not common in travellers. The 2007–2011 GeoSentinel survey of returning travellers reported 126 cases of hepatitis A and E and 83 cases of leptospirosis of a total of 9817 cases of febrile illness.[1] Jaundice caused by infections is often accompanied by other symptoms. Whereas acute illness is more common, it is important to establish if there is underlying chronic liver disease.

History and examination

The duration and onset of symptoms in relation to travel allow the incubation period to be estimated. A history of significant right hypochondral pain and tenderness with fever should prompt the clinician to consider liver abscess, in which jaundice is not usually a prominent feature. Abdominal pain and tenderness are seldom marked in acute viral hepatitis.

An exposure history should include sexual contacts, food and water consumption, activities, use of traditional medicines or recreational drugs, parenteral treatments received whilst abroad, blood transfusions and dialysis. Pre-departure vaccinations and malaria prophylaxis should be ascertained.

Jaundice may result from decompensation of chronic liver disease. Risk factors and features of chronic liver disease should be sought. People who have spent their early lives in developing world settings may have chronic liver disease from chronic hepatitis B infection or chronic schistosomiasis, the latter being more likely to present with portal hypertension with relatively preserved liver synthetic function.

Investigations

Initial tests that should be considered are listed in Table 1.

Unconjugated hyperbilirubinaemia indicates haemolysis, commonly caused by malaria. People with inherited haemolytic anaemias, such as sickle cell disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency, may have haemolytic attacks triggered by infections. The pattern of liver function test derangement, hepatocellular or obstructive, is helpful in differentiating the likely causes of jaundice (Table 2). A prolonged prothrombin time suggests failure of liver synthetic function and is a marker of poor prognosis.

Eosinophilia may indicate a parasitic infection such as fascioliasis or a toxic cause, whereas neutrophilia suggests a bacterial cause or amoebic liver abscess.

Abdominal ultrasonography may show biliary obstruction, signs of chronic liver disease or mass lesions (abscess or tumour). *Fasciola* infection may appear as mass lesions, and tracks through the liver parenchyma may be seen. Liver and biliary flukes can cause intrahepatic biliary duct dilatation and parasites can sometimes be seen. Other imaging modalities may be helpful to further characterize abnormalities.

Specific conditions

Malaria

Malaria must always be considered in travellers returning from malaria-endemic countries with jaundice. Jaundice results from haemolysis of infected erythrocytes in heavy infections, rather than hepatic or biliary dysfunction, and is associated with increased mortality.[2] Prompt treatment must be instituted as malaria can be rapidly fatal (see Malaria on pages 100–106 of this issue).

Hepatitis A and E

Hepatitis A and E viruses are found worldwide. They are transmitted faeco-orally, commonly by ingestion of contaminated water or food. There have been several outbreaks of hepatitis A in men who have sex with men.[3] Hepatitis E has been linked to the consumption of raw or undercooked deer[4] and wild boar meat[5] and an outbreak of hepatitis E on a cruise ship was attributed to contaminated shellfish. Both viruses can rarely be transmitted by blood transfusion. Hepatitis E is now more common that hepatitis A in the UK.[6] The incubation periods of hepatitis A and E are about 4 weeks and 6 weeks, respectively.

Clinical picture: infection with either virus can be asymptomatic. Clinical illness presents as jaundice with non-specific symptoms such as anorexia and lethargy (see Case 1). Serum transaminase is often very high (>1000 U/l). Although the illness is self-limiting in most, fulminant liver failure and death can

Alicia D Yeap *MRCP FRCPath is a Specialty Registrar in Infectious Diseases and Medical Microbiology at St George's Hospital, London, UK. Competing interests: none declared.*

Catherine A Cosgrove *MRCP PhD DipHIV is a Consultant and Honorary Senior Lecturer in Infectious Diseases and Medicine at St George's Hospital, London, UK. Competing interests: none declared.*

Initial investigations for jaundice or suspected liver abscess

- Full blood count, clotting
- Electrolytes and renal function
- Liver function tests
- C-reactive protein, erythrocyte sedimentation rate
- Blood films for malaria
- Blood cultures
- Hepatitis A, B, C, E serology
- EBV, Epstein–Barr virus; CMV, cytomegalovirus serology
- HIV test
- Abdominal ultrasound scan

Table 1

occur. Older age, underlying chronic liver disease, and immunosuppression have been identified as risk factors for severe disease for both hepatitis A and E. Mortality in pregnant women with hepatitis E infection has been reported to be as high as 20%,[7] though the reasons for this are unclear. Chronic infection with hepatitis E occurs extremely rarely and only in solid organ transplant patients[8] or patients with HIV.

Prevention: immunity after infection with hepatitis A and hepatitis E is lifelong. Vaccination with hepatitis A has a protective efficacy of 95%. Several hepatitis E vaccines are in development but none has yet been licensed for use. Susceptible contacts of hepatitis A who are at risk of severe disease should be considered for prophylaxis with vaccination or immunoglobulin.

Causes of jaundice by pattern of liver function test derangement

Hepatocellular

Common
- Acute viral hepatitis A, B, C, E
- EBV, CMV
- Bacterial sepsis
- Chronic viral hepatitis B, D, C
- Ethanol, methanol
- Non-alcoholic steatohepatitis (NASH)

Uncommon/rare
- Leptospirosis
- Enteric fever (typhoid/paratyphoid)
- Syphilis, brucellosis
- Tuberculosis, malaria
- Rickettsial infections
- HIV, measles, dengue
- Yellow fever, viral haemorrhagic fevers
- Toxins: aflatoxin, bush teas, traditional herbal remedies

Obstructive

Common
- Bacterial cholangitis
- Pyogenic liver abscess
- Amoebic liver abscess
- Hydatid liver disease
- Hepatocellular carcinoma

Uncommon/rare
- Tuberculosis
- Liver flukes
- Hepatobiliary ascariasis
- Chronic schistosomiasis

EBV, Epstein—Barr virus; CMV, cytomegalovirus.

Table 2

Case 1. Hepatitis E

A 44-year-old woman was admitted to hospital with a week's history of jaundice, dark urine, nausea, vague abdominal pain, anorexia, malaise and generalized arthralgia. She had returned from a 3-week holiday to India 3 weeks before becoming unwell. She had eaten local food and drunk bottled water whilst there. She took ramipril for hypertension. She had also taken paracetamol 4 g during the day before admission. She was a smoker and drank an average of 14 units of alcohol every week. There was no history of recreational drug use, including injection drug use. She had no tattoos or history of previous blood transfusions and had not taken any non-prescription medications, traditional medicines, herbal remedies or unusual food. Examination revealed jaundice only with no signs of chronic liver disease.

Blood tests showed a leucopenia with a slight neutropenia. Liver function tests were deranged: alanine transaminase (ALT) 2368 U/l, bilirubin 59 micro mol/l, alkaline phosphatase 359 U/l, albumin 32 g/l, international normalized ratio 1.2. C-reactive protein was 46 mg/l. Malaria blood films were negative. Hepatitis A, B, C and cytomegalovirus serology was negative. Epstein—Barr virus serology showed evidence of past infection. HIV test was negative. An abdominal ultrasound scan revealed no abnormalities.

ALT peaked on day 3 at 2888 U/l. She started to feel better soon after admission and was discharged home on day 5. Hepatitis E serology revealed a positive immunoglobulin M (IgM) and IgG. She was seen in clinic the following week, by which time most symptoms had resolved and liver function tests were settling.

Hepatitis B and C

Hepatitis B and C viruses are acquired through contact with infected blood or sexual contact. Hepatitis B infection in adults commonly causes an acute jaundice illness, which can progress to fulminant liver failure; 5—10% of patients become asymptomatic carriers or develop chronic infection. Hepatitis B vaccine offers good protection. Acute hepatitis C infection is often asymptomatic but can present acutely with jaundice. Hepatitis C acquisition from dialysis and other medical procedures performed abroad is well described.[9] Treatment given during acute hepatitis C infection is effective at preventing chronic infection.[10] Antibodies may take 3 months or longer to develop and hepatitis C virus RNA polymerase chain reaction should be performed if acute hepatitis C infection is suspected.

Leptospirosis

Epidemiology: there were 52 cases of laboratory-confirmed leptospirosis in the UK in 2011[11] and the incidence has been stable in recent years. The reservoir is rodents and livestock. Infection occurs through contact of contaminated water with mucous membranes and broken skin, and through aerosol inhalation.

Presentation: the majority of infections are subclinical or a self-limiting flu-like illness. The incubation period is usually 10—12 days. Classic leptospirosis is a biphasic illness. In the septicaemic phase, there is fever, myalgia, headache, vomiting and conjunctival suffusion, which improve after 5—7 days, often