Schistosomiasis is the most common of the trematode infections, affecting more than 200 million people worldwide.\textsuperscript{1,2} Hepatosplenic schistosomiasis occurs primarily with infection due to \textit{Schistosoma mansoni} and less often with \textit{Schistosoma japonicum}.\textsuperscript{1,3} If left untreated patients may ultimately develop massive hepatosplenomegaly, portal hypertension, and variceal hemorrhage.\textsuperscript{1–3} The diagnosis of hepatosplenic schistosomiasis and the severity of periportal fibrosis can be made on liver biopsy, although liver ultrasonography may provide useful diagnostic clues.\textsuperscript{4,5} Early treatment with praziquantel may result in reversal of periportal fibrosis.\textsuperscript{5–7} In the patient presented, the diagnosis of hepatosplenic schistosomiasis was masked by tuberculous involvement of the liver and alcoholic hepatitis. Hepatosplenic schistosomiasis should be considered in the investigation of chronic liver disease in patients from endemic areas of the world.

**Case Report**

A 30-year-old man was referred for investigation of chronically abnormal liver function tests. The patient was born in Mindanao in the Philippines before migrating to Australia in 1992, aged 27 years. He had a history of alcohol abuse, had received bacille Calmette-Guérin (BCG) vaccine at the age of 7 years and a chest x-ray performed on immigration to Australia was normal. The patient first presented with left supraclavicular lymphadenopathy and hepatosplenomegaly. He had not experienced any respiratory symptoms, fevers, night sweats, or weight loss. There were no other stigmata of chronic liver disease. Investigations revealed that the alanine aminotransferase (ALT) was 100 U/L, aspartate aminotransferase (AST) 52 U/L, alkaline phosphatase (ALP) 405 U/L, gamma glutamyltransferase (GGT) 556 U/L, and serum bilirubin 21 mmol/L, with a normal full blood analysis. Chest x-ray revealed left hilar lymphadenopathy.

A provisional diagnosis of primary pulmonary TB with associated tuberculous lymphadenitis and granulomatous hepatitis secondary to tuberculosis, and possibly underlying alcoholic liver disease, was made. Smears of sputum, an aspirate of the left supraclavicular lymph node, and bronchoscopy specimens were negative for acid fast bacilli. Empiric antituberculous therapy was commenced with isoniazid 600 mg/d, rifampicin 300 mg/d, ethambutol 900 mg/d, and pyrazinamide 750 mg/d. After 6 weeks, cultures of sputum, lymph node aspirate, and bronchial washings were all growing \textit{Mycobacterium tuberculosis} that was resistant to isoniazid. After week 8 of therapy, pyrazinamide was ceased. The remaining three antituberculous medications were continued a further 6 months followed by rifampicin and ethambutol to complete a total treatment duration of 9 months. While on treatment, the right hilar lymphadenopathy and the left supraclavicular lymphadenopathy resolved; however, liver function tests remained abnormal, despite a reduction in alcohol intake and the cessation of isoniazid (Table). Following cessation of all antituberculous medications, the liver function tests remained abnormal (see Table). An abdominal ultrasound performed prior to antituberculous treatment demonstrated an enlarged liver with distended portal and splenic veins, a diffuse increased echogenicity with a lobular appearance and splenomegaly, consistent with cirrhosis and portal hypertension. A computed tomography scan of the abdomen showed a lobular liver with increased attenuation and mild splenomegaly. Collateral vessels at the splenic hilum consistent with varices were present, and diffuse dystrophic calcification was noted in the right lobe of the liver, raising the possibility of a parasitic infection, such as schistosomiasis. Fecal microscopy did not reveal parasitic ova; however, schistosoma serology was positive with a titer...
of 1:2048. A liver biopsy revealed mild to moderate fibrosis of the portal tracts without bridging fibrosis or cirrhosis. Epithelioid noncaseating eosinophilic granulomas were noted in portal tracts. Hepatic lobules were of normal architecture. Numerous ovoid calcified masses, representing ova of *Schistosoma japonicum*, were noted in the portal tracts (Fig. 1). The patient was treated with praziquantel 20 mg/kg/day for 3 days. On review 1 month later the schistosoma antibody titer had fallen to 1:1024, and 4 months later the titer had fallen further to 1:256. Liver function tests, however, had not yet returned to normal (see Table). The persisting abnormalities of liver function tests were considered to be the consequence of continuing alcohol abuse. The patient refused a repeat liver biopsy and was subsequently lost to follow-up.

Hepatosplenic schistosomiasis remains a significant problem in developing countries. This case illustrates the difficulty faced in making a diagnosis in an immigrant from an endemic area of the world, in the setting of coexisting co-morbidities, which may mask abnormalities caused by hepatosplenic schistosomiasis. Establishing the diagnosis is essential in these patients to avoid the subsequent development of late complications.

Liver damage results from the deposition of ova within portal veins and the immune response to dead adult flukes, resulting in perportal granulomas and fibrosis. Piecemeal necrosis without fibrosis may also occur early in the course of infection. The prevalence of hepatosplenic schistosomiasis within endemic areas is low, occurring in less than 1% of patients infected with *Schistoma mansoni* or *japonicum*. However, the annual incidence of variceal hemorrhage following the development of portal hypertension is as high as 10 to 15%. The diagnosis of hepatosplenic schistosomiasis is made histologically and from the degree of perportal fibrosis, but not from the presence of varices. Both can be assessed by liver ultrasound. An increase in portal and splenic vein diameters correlates with the degree of perportal fibrosis and the frequency of bleeding from endoscopically proven esophageal varices. Unfortunately, ultrasound failed to detect perportal fibrosis in our patient, although, the portal and splenic veins were dilated, consistent with the presence of portal hypertension.

Praziquantel is the drug of choice in the treatment of schistosomiasis, achieving a 75-100% cure rate. Liver ultrasound assessment of patients treated early in the course of hepatosplenic schistosomiasis may demonstrate a reversal of perportal fibrosis, and a reduction in portal venous blood pressure in those with no prior episodes of hemorrhage or ascites, especially in children. Patients with advanced hepatosplenic schistosomiasis and established portal hypertension are less likely to benefit. Our patient had a slow response, with persisting abnormal liver function tests several months after therapy, despite a fall in the anti-schistosoma antibody titer. This may have reflected more advanced disease in this patient, although the continuing alcohol intake was another likely contributing factor.

Once advanced hepatosplenic schistosomiasis with portal hypertension develops, other treatment modalities may be necessary.
ities such as beta blockers and variceal sclerotherapy may be of benefit.\textsuperscript{3,10} Sclerotherapy results in variceal eradication in 70\% of patients with portal hypertension due to hepatosplenic schistosomiasis. It is effective in controlling rebleeding in 97\% of patients who had undergone previous portosystemic shunting, and in 73\% of those who had not.\textsuperscript{10} Mortality at 5 years is also reduced from 28 to 3\%, in those treated with sclerotherapy.\textsuperscript{10} Of the surgical approaches available, esophagogastric devascularization with splenectomy has the lowest mortality, although recurrent bleeding occurs in 12 to 24\%.\textsuperscript{11} Our patient did not require sclerotherapy, nor surgical intervention, and responded to medical management alone. The aim of managing patients with hepatosplenic schistosomiasis includes both early diagnosis and treatment, in order to avoid the development of more severe complications which require complex treatment modalities.

In conclusion, our patient illustrates the need to consider a diagnosis of hepatosplenic schistosomiasis in an immigrant with chronically abnormal liver function tests, due to another cause of granulomatous liver disease such as tuberculosis. The diagnosis may well have been missed if the patients ethnic origin had not been considered, particularly after failing to improve with antituberculous treatment. Alcohol abuse and the potential hepatotoxic effects of the antituberculous medications may have contributed to the abnormalities observed in the liver function tests. In addition, the persistence of abnormal liver function tests following treatment with praziquantel, and despite a fall in the schistosoma antibody titer, reflects the multifactorial nature of this patient’s liver disease. Screening for schistosomiasis should be considered early in the diagnostic workup of patients with chronically abnormal liver function tests and a potential exposure to \textit{S. japonicum} or \textit{S. mansoni}.

References