A 43-year-old Asian female with a history of pulmonary sarcoidosis presented with elevated liver tests and weight loss of 20 lb over the preceding 6 months. Laboratory studies revealed: AST 36 IU/L, ALT 38 IU/L, Alkaline phosphatase 520 U/L, and Total bilirubin 0.4 mg/dL. Physical examination revealed hepatosplenomegaly. Computed tomography (CT) scan of the abdomen was performed and is shown in Figure 1. Liver biopsy findings are shown in Figures 2 and 3.

Questions
1. What is the diagnosis?
2. What are clinical manifestations of this disease?
3. What are the available treatment options?
DISCUSSION

The CT scan shows multiple low attenuation areas in the liver and spleen. Liver biopsy shows expansion of portal tracts by non-necrotizing granulomatous inflammation (Figure 2). The granulomas are partially confluent and trichrome stain shows the distorting nature of the granulomatous inflammation associated with dense fibrosis (Figure 3). Special stains for microorganisms including AFB and fungi were negative. Histologic evidence of noncaseating granulomas in Sarcoidosis is suggestive of hepatic involvement by the disease, when infection is ruled out.

The most common causes of hepatic granulomas in the United States are sarcoidosis, mycobacterial infection, primary biliary cirrhosis and drug reactions. Hepatic sarcoidosis is characterized histopathologically by epithelioid, noncaseating granulomas that tend to occur in the portal tracts or peri-portal areas (1,2). Although granulomas are found in as many as 50%–80% of liver biopsy specimens, clinically apparent liver disease is uncommon (1). Laboratory abnormalities include hypergammaglobulinemia and moderate increases in serum alkaline phosphatase. Aminotransferase levels are only mildly abnormal (2). Although the spleen is affected microscopically in about three-quarters of cases, the reported frequency of splenomegaly in sarcoidosis ranges from 1% to 40% (3).

Clinical manifestations of hepatic sarcoidosis include chronic intrahepatic cholestasis, portal hypertension and Budd-Chiari Syndrome. Causes of portal hypertension in Sarcoidosis include cirrhosis, nodular regenerative hyperplasia and granulomatous phlebitis of the portal and hepatic veins (1,4). Death from cirrhosis is rare. Other rare complications include obstructive jaundice secondary to hilar lymphadenopathy or biliary strictures with cholangiographic features of sclerosing cholangitis.

Prognosis of sarcoidosis is variable. Spontaneous remissions occur in nearly two thirds of patients, but chronic, progressive disease may result in severe sequelae. Asymptomatic patients with only mild liver function abnormalities do not require treatment. Corticosteroids are the mainstay of treatment and indicated in cases of symptomatic liver involvement or extensive liver fibrosis. Symptomatic and biochemical improvement have been reported with ursodeoxycholic acid and methotrexate. Chloroquine and azathioprine have also been used as steroid-sparing agents. End stage liver disease in Sarcoidosis has been treated successfully by liver transplantation (5). Management of splenomegaly due to sarcoidosis consists primarily of medical therapy with prednisone, methotrexate or chloroquine. Indications for splenectomy include massive splenomegaly, severe hypersplenism and to exclude lymphoma or malignancy (6).

References