Sarcoidosis Presenting as Recurrent Jaundice

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Sir,

A 22 year married Muslim female presented with recurrent yellowish discoloration of eyes and urine and intermittent episodes of fever for last one year. There were six to eight episodes of yellowish discoloration. Each episode lasted for approximately one month and during that period there was fluctuation of intensity of jaundice. There was associated anorexia, nausea, vomiting and generalised itching, which all increased with intensity of jaundice. In between each icteric episode, there were anicteric phases lasting approximately 15-20 days. Fever was low grade, intermittent, without any chills and rigor. Each episodes of fever lasted for approximately five to seven days with no diurnal variation.

No history of joint pain, photophobia and malar rash was present. No history of blood transfusion, unprotected sexual intercourse, prolonged drug intake and other major illness was present. She had one male child of ten months but she was nonlactating. There was no family history of similar illness.

Patient had icterus. Lymph nodes were palpable at the anterior and posterior triangles of the neck. They were soft, non-tender, not matted, not fixed to skin and underlying structures with no ulcer or discharging sinus. The largest one was 2 cm x 2 cm in posterior triangle. Bilateral central axillary nodes were also palpable. Largest one was 4 cm x 2 cm on the right side. No bony tenderness was detected. Few hyperpigmented maculopapular patches were present on the front of both legs.

Liver was palpable 3 cm below the right costal margin, non-tender with sharp margin, firm consistency, smooth surface, with a liver span of 14 cm. Spleen was also palpable 4 cm below left costal margin, with smooth surface, firm consistency. Fluid thrill and shifting dullness were absent, but puddle sign was present. Examination of other systems was unremarkable.

Her complete blood count showed hemoglobin -15.7 gm/dl; total leucocyte count-9900/ cu mm, with neutrophils 65%, lymphocytes 30%, monocytes 3%, eosinophils 2%, platelets-2.72 lakh/cu mm., ESR - 48 mm/hr. Blood biochemistry revealed random blood sugar- 96 mg/dl, urea-28 mg/dl, creatinine-0.8 mg/dl, Na+ 136 meq/l, and K+ 4.7 meq/l. Liver function test (LFT) revealed total bilirubin-5.6 mg/dl, direct-3.9 mg/dl, aspartate aminotransferase - 49 U/L, alanine aminotransferase - 24 U/L, alkaline phosphatase (ALP)-1118 U/L (normal level-33-96 U/L), total protein-7.8 mg/dl, albumin-2.9 mg/dl, globulin- 4.9 mg/dl. Prothrombin time was 18 seconds (control – 14 seconds) with INR-1.42. Serum cholesterol was elevated (280 mg/dl) but triglyceride was normal (146 mg/dl). HBsAg, Anti-HCV and HIV I and II were nonreactive. Antinuclear (by Hep2 method) and anti-mitochondrial antibodies were negative. Serum angiotensin converting enzyme (ACE) level was elevated (73 U/L, cut off 52 U/L) and lactic acid dehydrogenase was also elevated (415 U/L; normal value 115-221 U/L). Mantoux test was positive (22 mm in duration).

Chest x-ray and CT scan of thorax showed bilateral hilar lymphadenopathy. Ultrasonography of abdomen showed enlargement of liver with heterogeneous echotexture. Spleen was enlarged (17.7 cm). Mild ascites and few retroperitoneal nodes were detected. Upper gastrointestinal tract endoscopy was normal.

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Histology of right axillary lymph node biopsy showed multiple noncaseating epithelioid granulomas. Many of the granulomas showed intracytoplasmic inclusion bodies like Schaumann bodies and stellate Asteroid bodies which are common in sarcoidosis but are nonspecific (Figures 1-2). Liver biopsy showed features of granulomatous hepatitis.

The case was diagnosed as sarcoidosis presented as recurrent jaundice due to granulomatous hepatitis. She was treated with prednisolone 40 mg/day. With two months of therapy she improved clinically and her LFT gradually became normal.

Sarcoidosis is a multisystem inflammatory disease characterized by diffuse noncaseating granulomatous lesions. It preferentially involves the lungs, but can affect any organ. Liver involvement is common but it is usually asymptomatic. Sarcoidosis may occasionally be symptomatic with chronic cholestasis with features like pruritus and jaundice. Intrahepatic cholestasis may lead to portal hypertension. Most common liver function abnormality is elevation of ALP level. Elevated transaminase levels can also occur. Elevation of bilirubin level is seen in advanced liver disease.

Diagnosis of sarcoidosis is one of exclusion. It requires the presence of compatible clinical features and histologic demonstration of noncaseating epithelioid cell granulomas in affected organs, with all other causes of granulomas being ruled out. Biopsy of involved organ is indicated for all presumed to have sarcoidosis, except those with Lofgren’s syndrome. Histological features of sarcoidosis of liver usually consist of noncaseating epithelioid granulomas predominantly in the portal and perportal region, mononuclear cell infiltration, hepatocyte injury and foci of fibrosis or cirrhosis. There may be features of intra-hepatic cholestasis, periportal fibrosis and micronodular biliary cirrhosis. Severe intra-hepatic cholestasis and bile ductopenia may occur with advanced disease.

Cholestatic hepatitis with constitutional symptoms is treated with prednisone, 20–40 mg/day and ursodeoxycholic acid 15 mg/kg of body weight per day. Advanced cases may require liver transplantation.

Our patient had classical features of sarcoidosis like bilateral hilar lymphadenopathy and noncaseating epithelioid granuloma of lymphnode. Her liver biopsy revealed granulomatous hepatitis and blood biochemistry revealed features of cholestasis. Fluctuation of her disease activity led to recurrent jaundice. Her Mantoux test was positive but thorough work-up did not reveal any foci of tuberculosis (positive test among sarcoidosis patients is highly specific for coexisting tuberculosis - specificity of 97.6%). She responded to oral prednisolone without any antitubercular therapy.

Thorough clinical and laboratory examination should be done to diagnose recurrent jaundice. Without high level of suspicion diagnosis of sarcoidosis may be missed.

References