CASE REPORT

Overlap Syndrome: Autoimmune Sclerosing Cholangitis

ARPITA THAKKER AND SUNIL KARANDE

From Department of Pediatrics, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai 400 022, India.

Correspondence to:
Dr Arpita Thakker,
Developmental and Epilepsy Clinic,
Department of Pediatrics,
Lokmanya Tilak Municipal Medical College and General Hospital, Sion,
Mumbai 400 022, India.
arpitathakker@gmail.com
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A 9-year-old-girl presented with clinical features of autoimmune hepatitis and associated signs of cholestasis in the form of itching and elevated levels of serum alkaline phosphatase. There was histologic evidence of bile duct injury. Hence a clinical diagnosis of "overlap syndrome" of autoimmune hepatitis with primary sclerosing cholangitis was considered.

Key words: *Cholangitis, Cholestasis, Child.*

Overlap syndromes are autoimmune conditions with mixed immunological, clinical and histological features. They include combinations of autoimmune hepatitis (AIH) and primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), or chronic viral hepatitis(1). There are a few reports of AIH and PSC from India(2,3). We report a 9-year-old girl with autoimmune sclerosing cholangitis, an overlap syndrome of AIH and PSC.

CASE REPORT

A 9-year-old girl presented with history of fluctuating jaundice for 1 year. Each episode of jaundice lasted for a duration of 20 days. She also had itching, fever, fatigue and arthralgia. Clinical examination revealed a malnourished child (weight of 17.4 kg and height of 116 cm, both were below 5th percentile for her age) with hepatosplenomegaly. The liver was palpable 5 cm below the right costal margin and was firm, nodular with a span of 9.5 cm. The spleen was palpable 6 cm below the left costal margin and was firm. There was no clinical evidence of ascites. Abdominal veins were prominent but were not tortuous. There were no other stigmata of chronic liver disease. Ophthalmologic examination for KF rings with a slit lamp was normal.

The child's complete hemogram revealed pancytopenia with a Hb of 6 g/dL, WBC 2.2×10^3/µL and platelets 88×10^3/µL. Her serum alkaline phoshatase (970 U/L) was markedly elevated and serum bilirubin (2.1 mg/dL) and transaminases (SGOT 116 U/L, SGPT 73 U/L) were mildly elevated. There was hypergammaglobulinemia (gamma globulins of 65.6% of the total), decreased serum albumin (1.8 g/dL) and prolonged prothrombin time (31.6 s; control 14 s). The gamma glutamyl transpeptidase levels were minimally raised (66 U/L). HBsAg and anti-HCV antibody were negative. Antinuclear antibody was positive at a titer of >1:80.The serum ceruloplasmin level and urinary copper levels were normal.

Abdominal ultrasound examination showed coarse hepatic echotexture with nodularity, splenomegaly and ascites. Upper GI endoscopy revealed minimal erosive gastritis without any varices. Barium meal follow through showed no evidence of ulcerative colitis. A percutaneous liver biopsy yielded a small fragmented piece of tissue

which, histologically showed proliferation of bile ductules (***Fig.* 1**), interface hepatitis (***Fig.* 2**) and marked cholestasis. MRCP was normal and ruled out large duct PSC. A diagnosis of an overlap syndrome of small duct PSC with AIH (autoimmune sclerosing cholangitis) was made.

The child was given supportive treatment for decompensated liver disease. Corticosteroids could not be started due to neutropenia. Empirical treatment with ursodeoxycholic acid (15mg/kg/day) was started in view of marked cholestatic symptoms and continued for duration of three months. Regular follow up was advised to monitor the clinical response and improvement in liver function tests.

On follow up after 6 weeks, oral corticosteroids were started in the dose of 2mg/kg/day for duration of 4-6 weeks. Colonoscopy was done which showed no evidence of inflammatory bowel disease. To assess the severity of the disease, perinuclear Antineutrophil Cytoplasmic Antibody (pANCA) was done which was negative.

DISCUSSION

Autoimmune hepatitis (AIH), an unresolving inflammation of the liver of unknown cause(4,5), may present in atypical forms that lack established criteria, official nomenclature and standard treatment(1). Such patients have features associated with both AIH and another type of chronic liver disease 'overlap syndromes' or have findings that are incompatible with the diagnosis of AIH according to the criteria codified by the international panels 'outlier syndromes'. Overlap syndromes include combinations of AIH and PBC, or PSC, or chronic viral hepatitis(1). In our patient the diagnosis of an overlap syndrome of AIH with PSC, also called Autoimmune Sclerosing Cholangitis (ASC) was made(6). This syndrome has been reported only in 6 to 8% of children, adolescents, and young adults(7).

In patients with AIH, the most common findings that suggest an overlap variant are features associated with cholestasis and histologic findings of bile duct injury(8). Our patient had cholestatic changes i.e. itching and atypical elevation of serum alkaline phosphatase. Also there was bile duct proliferation with cholestasis on histology suggestive of bile duct injury.

In such patients, further assessment with cholangiography should be considered to confirm the diagnosis of PSC(1). Cholangiographic changes associated with PSC, however, are absent in 14% of patients with typical histologic disease(9). This discordance suggest that overlap syndrome can involve only the intrahepatic bile ducts (small-duct PSC) as in our case(9,10).

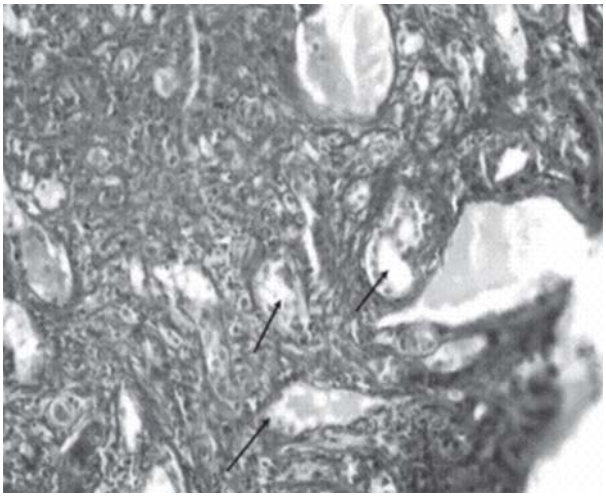

FIG. 1 *Liver biopsy specimen (hematoxylin and eosin x200) revealing bile ductular proliferation (com-patible with primary sclerosing cholangitis).*

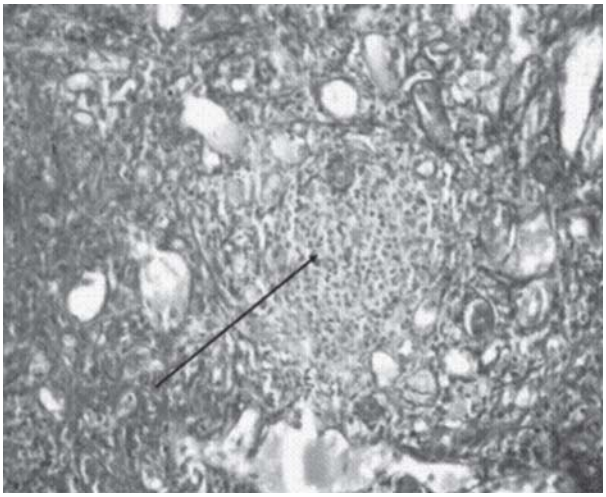

FIG. 2 *Liver biopsy specimen (hematoxylin and eosin x 200) revealing plasma cells infiltrate (compatible with autoimmune hepatitis).*

Treatment strategies are empirical in all instances, but they must be logical and carefully monitored(1). In an overlap of AIH-PSC, corticosteroids should be started (prednisone 2mg/kg/day) if autoimmune symptoms are predominant. Patients who do not respond to corticosteroids are candidates for investigational protocols, treatment of symptoms, or empirical therapy with ursodeoxycholic acid (13-15mg/kg/day), if cholestatic symptoms are marked(1). Alterations in treatment are dictated by the changes in the predominant character of the disease and by the adequacy of the patient's response. Liver transplantation is required for children who progress to biliary cirrhosis and hepatic decompensation.

In conclusion, a child presenting with features of autoimmune hepatitis such as hypergammaglobulinemia or autoantibodies in the serum and associated signs of cholestasis i.e. itching or elevated levels of serum alkaline phosphatase and histologic evidence of bile duct injury, should be considered to have a clinical diagnosis of "overlap syndrome" of autoimmune hepatitis with primary sclerosing cholangitis and appropriate investigations should be initiated to confirm the diagnosis.

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