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# Overlap syndrome: an unusual combination of autoimmune hepatitis and primary sclerosing cholangitis

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**Abstract:** Autoimmune diseases of the liver include three major clinical entities, viz. autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). Overlap syndrome describes variant forms of these autoimmune diseases and presents with both hepatitic and cholestatic biochemical and histological features of AIH, PBC, and/or PSC. Overlap syndrome between AIH and PSC is rare and only a few cases have been reported worldwide. An unusual case of overlap syndrome between Type I AIH and PSC in a male who presented with cirrhosis and progressive hepatic failure is reported here.
**Keywords:** Autoimmune hepatitis (AIH), Primary sclerosing cholangitis (PSC), Overlap syndrome, Magnetic resonance cholangio pancreatography (MRCP).

## INTRODUCTION:

Autoimmune diseases of the liver are the chronic inflammatory diseases leading to an etiologically undefined immune-mediated attack aimed at the hepatocyte, small microscopic bile ducts and the entire biliary system, detectable by cholangiography. Three distinct major clinical entities have been described, viz. autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), and primary sclerosing cholangitis (PSC). Overlap syndrome describes variant forms of these three major hepatobiliary autoimmune diseases and presents with both hepatitic and cholestatic biochemical and histological features of AIH, PBC, and/or PSC, and usually shows a progressive course towards cirrhosis and liver failure without adequate treatment [1].

AIH can be easily diagnosed by the international autoimmune hepatitis group criteria [2, 3]. In India, AIH is seen less commonly and it usually presents as chronic hepatitis or cirrhosis [3]. PSC refers to an idiopathic disorder of intrahepatic and extrahepatic bile ducts characterized by chronic cholestasis, that can occur independently or in association with other diseases, most commonly inflammatory bowel disease. We report a rare case of overlap syndrome between AIH Type I and PSC that presented with advanced cirrhosis and liver failure. The patient died in spite of treatment, in a period of two weeks.

## CASE REPORT:

A 58-year old male presented with jaundice, abdominal pain, progressive abdominal distension, and generalized pruritus of one month duration and altered sensorium and sleep-rhythm of two weeks duration. He also had history of recurrent episodes of loose stools and bleeding per rectum in the past ten years. He was a nonsmoker and non-alcoholic. On examination, he was deeply jaundiced and disoriented. Multiple scratch-marks in the skin all over the body, ascites, firm hepatomegaly and asterexis also were noticed.

The liver function tests showed: total bilirubin 16 mg/dL (direct bilirubin 11 mg/dL) AST 123 Units/L, ALT 134 Units/L, Alkaline phosphatase 1234 Units/L, total protein 7.4 gram/dL, albumin 2.8 gram/dL and globulin 4.6 gram/L. The other hematological and biochemical investigations were within the reference range. The ultrasonography of the abdomen revealed ascites, hepatomegaly with a coarse and raised echo-texture of the liver, mild spleenomegaly and dilated portal vein suggestive of cirrhosis of the liver with portal hypertension. The pancreas and the biliary system appeared normal and there was no intraabdominal lymphadenitis.

An autoimmune screen was positive for ANA, Anti-smooth muscle antibody (SMA) and p-ANCA and negative for the other autoantibodies including anti-LKM and antimitochondrial antibody. A sigmoidoscopy showed normal appearance of the colonic mucosa but a sigmoid biopsy showed evidence of ulcerative colitis (Figure 1).

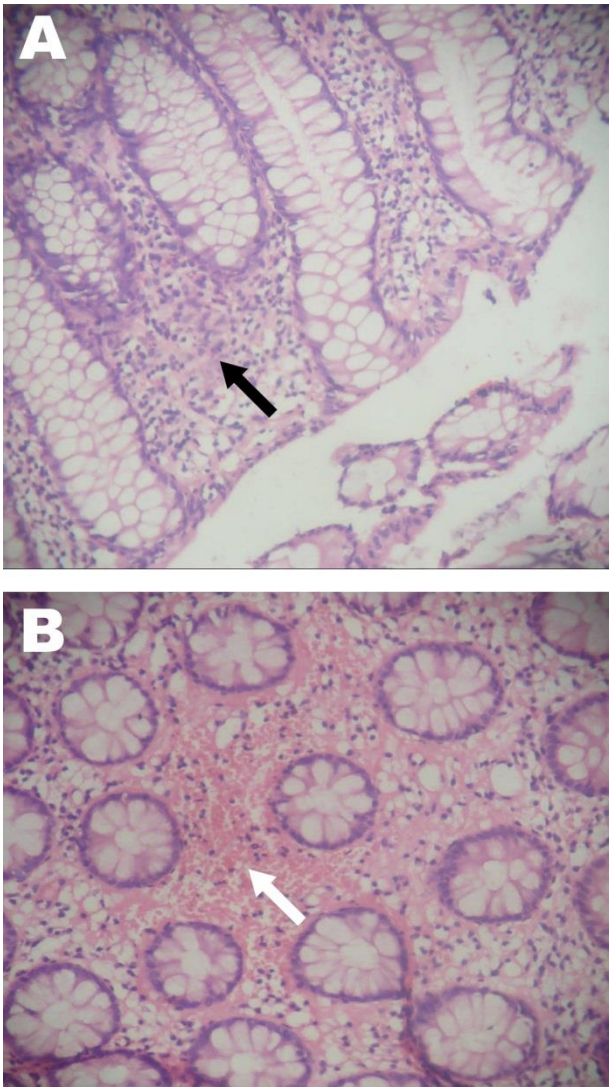


**Fig 1: Sigmoid biopsy showing evidence of ulcerative colitis A: infiltration of the submucosa with inflammatory cells (black arrow). B: Area of colitis (white arrow).**

Magnetic resonance cholangio-pancreatography (MRCP) showed diffuse pruning of the intrahepatic biliary radicles and sclerosis of the walls of common hepatic duct and common bile duct suggestive of early PSC. Liver biopsy showed sinusoidal dilatation, marked degree of extracellular bile stasis, peri ductal fibrosis and infiltration with round cells (Figure 2). A diagnosis of overlap syndrome between AIH Type I and PSC in a background of ulcerative colitis was made.

The patient was managed with ursodeoxycholic acid, injection methylprednisolone, salazopyrin, folic acid & antibiotics but he died because of progressive hepatocellular failure after 2 weeks of admission.

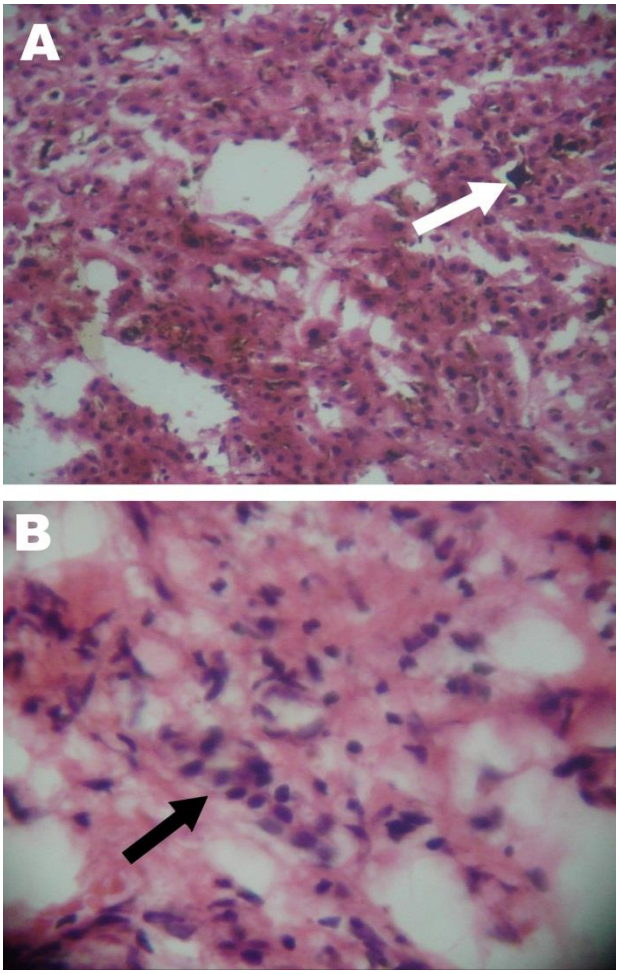


**Fig 2: Liver biopsy showing features of primary sclerosing cholangitis (PSC). A: white arrow shows a bile lake. B: black arrow shows infiltration with round cells.**

## DISCUSSION

In India, autoimmune diseases of the liver accounts for about 1.7% of all liver diseases and 5.7% of chronic liver diseases[3,4]. These disorders show a distinct female preponderance. AIH was the commonest among the three major autoimmune diseases of the liver (AIH, PBC and PSC) in a large series reported from western India [4].

AIH is a classical autoimmune disease with a female predisposition, circulating autoantibodies, elevated immunoglobulins, and the association of other extrahepatic autoimmune diseases, and a dramatic response to treatment with immunosuppressive agents. Many patients with AIH can have other coexistent autoimmune diseases [3].

Depending on the presence/ absence of autoimmune markers, AIH is categorized into type I and type II [2]. The major variety seen in India is AIH type I [3, 5]. Clinical presentation of AIH can be as acute hepatitis, chronic hepatitis and/ or cirrhosis. The majority of AIH cases in India are diagnosed late and

they present with chronic hepatitis/ cirrhosis at the time of diagnosis [3, 5]. PSC is a progressive disease associated with significant morbidity and mortality for which efficient medical treatment is not available. Many cases may be asymptomatic when diagnosed. Nevertheless, even asymptomatic cases can progress to end-stage liver disease, albeit at a highly variable rate. The patients with PSC are predisposed to several malignancies, especially cholangiocarcinoma, which contributes to their decreased survival. Liver transplantation is the only treatment modality that can offer significant survival benefit in patients with PSC. The prevalence of PSC in India was found to be only 4.9% of the autoimmune liver diseases [4]. Overlap or cross over syndrome between autoimmune liver diseases is a well-described clinical entity and about 18% of cases present with this syndrome, the pathogenesis of which is poorly understood, and few data are available regarding the clinical characteristics and outcome of this disease [6].

Overlap syndrome is characterized the coexistence of serological parameters of PBC and AIH, of cholestasis and hepatitis, or the consecutive manifestation of PBC and AIH, or AIH and PSC. An overlap syndrome between PSC and AIH can be diagnosed in the presence of a mixed cholestatic/ hepatocellular liver chemistries, the presence of auto antibodies including ANCA, a cholangiogram consistent with PSC, and peri ductal fibrosis and necroinflammatory activity of the portal tracts consistent with autoimmune hepatits [6].

Empiric medical treatment of AIH-PSC overlap syndrome includes anticholestatic therapy with ursodeoxycholic acid and immunosuppressive therapy with corticosteroids and azathioprine, but in the end-stage disease, liver transplantation is the treatment of choice [1].

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