



Case Report

# Overlap Syndrome of Autoimmune Hepatitis, Primary Biliary Cholangitis and Primary Sclerosing Cholangitis in a Patient with Systemic Lupus Erythematosus: A Case Report of Complex Autoimmune Liver Disease

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## Abstract

Overlap syndrome is a spectrum of clinical manifestations of autoimmune hepatitis (AIH), Primary Biliary Cholangitis (PBC) and Primary Sclerosing Cholangitis (PSC). It is extremely rare for PBC, PSC, and AIH to occur in the same patient. We present a 48-year-old Hispanic man with a history of SLE who presented with elevated liver enzyme. He was found to have liver cirrhosis and diagnosed with PBC, PSC, and probable AIH overlap syndrome. To our knowledge, this is only the second reported case of all these diseases overlapping in the same patient; and the first reported case in a patient with SLE.

## Keywords

AIH; PBC; PSC; Overlap syndrome

## Introduction

Overlap syndrome is a spectrum of clinical manifestations between autoimmune hepatitis (AIH), Primary Biliary Cholangitis (PBC), and Primary Sclerosing Cholangitis (PSC) [1]. Overlap syndromes between AIH-PBC and AIH-PSC are well recognized [2-4]. Overlap between PBC-PSC has only been reported in a few patients [5,6]. To our knowledge, it is extremely rare for PBC, PSC and probable AIH overlap syndrome to occur in a patient.

## Case Report

A 48-year old Hispanic male with history of SLE who presented to hospital with decompensated liver cirrhosis. Physical examination revealed an alert, oriented, moderate built Spanish-speaking gentleman with mild scleral icterus and presented of spider angiomas. Laboratory investigations significant for thrombocytopenia 30/cmm

(150-400), protime 14 sec (9-13), INR 1.4, alanine transaminase 65 U/l (7-35), aspartate transaminase 167 U/l (15-41), alkaline phosphatase 283 (32-91), total bilirubin 2.3 (0.3-1.2). HIV, Viral hepatitis serology, iron studies, celiac panel, ceruloplasmin and alpha-1 antitrypsin levels were unremarkable. Anti-nuclear antibody (ANA) was positive (1:320). Anti-dsDNA and P-ANCA were positive. Anti-smooth muscle antibody (ASMA) was positive 28 (0-19). Anti-Soluble liver antigen (anti-SLA) and anti-liver kidney microsomal 1 antigen (Anti-LKM1) were negative. Gamma globulin level was elevated at 2501 mg/dL (normal range 694-1617). Anti-mitochondrial antibody (AMA) was positive 71.9 (0-20), and AMA-M2 was elevated 56 (0-20). The patient met criteria for AIH-PBC overlap syndrome based on Paris Criteria [7]. He was started on oral Ursodeoxycholic acid. Endoscopic Retrograde Cholangiopancreatography (ERCP) revealed segmental irregularities of intrahepatic bile ducts with beaded appearance suggestive of sclerosing cholangitis, sphincterotomy was performed and multiple balloon sweeps without any stone was extracted (Figure 1). Based on patient's liver enzymes profile, autoimmune markers, and ERCP findings; he was diagnosed with AIH-PBC-PSC overlap syndrome. Unfortunately, the liver biopsy was not obtained since patient subsequently deceased from septic shock with multi-organ failure. Family members refused the autopsy request (Table 1).

## Discussion

Classical AIH, PBC and PSC possess its own clinical features. AIH, PBC and PSC share genetic factors that may predispose susceptible individuals to develop concurrent separate diseases [3]. The estimated overall frequency of an overlap syndrome in patients with classical AIH is 14%-18% [2]. AIH-PBC and AIH-PSC overlaps are well recognized; 7%-13% and 6%-11% respectively [4]. Only few cases of PBC-PSC have been reported thus far [5-7]. Kingham et al. reported a case of PBC, PSC and probable AIH overlap, however, the common bile duct stone with apparent ampulla stenosis was identified [6]. The International Autoimmune Hepatitis Group (IAIHG) has



**Figure 1:** Endoscopic Retrograde Cholangiopancreatography (Erpc) showed segmental irregularities of intrahepatic bile ducts with beaded appearance suggestive of Sclerosing Cholangitis.

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**Table 1:** Laboratory results.

Laboratory	Result	Normal value
IgG	2501	(694-1618)
ANA	1:320	Homogenous pattern
ASMA	28	(0-19)
Smith Ab	>8	(<1)
Anti-DsDNA	>8	(<4 Negative, intermediate 5-9, >10 Positive)
C-ANCA	Negative	Negative
P-ANCA	Positive	Negative
atypical P-ANCA	Negative	Negative
Anti-SLA	2.5	(0-24.9)
Anti-LKM1	3.7	(0-24.9)
AMA	87.7	(0-20)
AMA-M2	56	(0-20)
C3	67	(90-180)
C4	9	(16-47)
CH50	43	(31-60)
Hepatitis serology	Non-reactive	Non-reactive
Iron saturation	34%	(24-50)
Transferrin	196%	(180-329)
Ferritin	104	(24-336)
Ceruloplasmin	31	(15-30)
A1AT	224	(90-200)
Gliadin peptide IgA	Negative	Negative
TTG IgA	Negative	Negative
Cryoglobulins	Negative	Negative
CA19-9	97.4	(6-35)
AFP	1.7	(0-8)

published diagnostic criteria and scoring system, which are instituted in research studies and clinical practice to increase discrimination of AIH from potential differential diagnoses [1].

This case presented with elevated liver enzymes, ANA, ASMA and gamma globulin, the diagnosis of probable AIH was made based on revised original scoring system of the IAIHG [8]. Serological hallmarks of PBC AMA and AMA-M2 were positive. The diagnosis of AIH-PBC overlap syndrome was then made based on the Paris criteria [9]. The concomitant positivity for anti-dsDNA and AMA is highly specific for of AIH-PBC [10]. The diagnosis of PSC in this patient relies on the cholangiographic findings without identifiable causes of secondary sclerosing cholangitis.

The frequency of AIH during the course of SLE appears to range from 2.1 %-3.7%, with higher incidence in juvenile-onset SLE. Gamma globulin elevation and positive ANA are characteristic for both AIH and SLE. Anti-dsDNA is very specific for SLE (specificity 95.9%) but also common in patients with type 1 AIH [10]. Despite specific autoantibodies for AIH include SLA and anti-LKM antibody were negative, it does not rule out the diagnosis of AIH. It is well recognized that PBC is an overlapping condition between the autoimmune liver disease and rheumatologic conditions. The incidence of coexisting PBC in patients with SLE is  $\leq$  2%. PSC is best known for its hepatobiliary manifestations accompanied by ulcerative colitis. 4 cases of concomitant PSC with SLE have been reported [11].

We are presenting a case with complex clinic spectrum of autoimmune liver diseases; AIH, PBC, and PSC. The transitional stages of hepatic manifestations may represent sequential presentations of classical disorders, or concomitant presence of two distinct disorders with immature presentation. In this case, he predominantly was diagnosed with AIH with incidental PBC and PSC overlap

syndrome. SLE is considered as a distinct disorder from classical autoimmune liver diseases. The etiology of this complex remains unknown. Whether these diseases coexisted by chance or they were sharing similar immunologic pathogenesis remains unclear. To our knowledge, this is the first case report of AIH, PBC and PSC overlap syndrome in a patient who also fulfills the diagnostic criteria for SLE.

## Conclusion

We are presenting a case with complex clinical spectrum of autoimmune liver diseases, which include AIH, PBC, and PSC. To our knowledge, this is only the second reported case of all these diseases overlapping in the same patient; and the first reported case in a patient with SLE.

## Author Contribution

A Likhitsup authored all sections of the manuscript. M Abu Ghanimeh provided the radiology image. T Tamimi reviewed the manuscript and is the article guarantor.

## Financial Disclosure

All authors have no financial to disclose.

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