jjogastroenterology.org

Japanese Journal of Gastroenterology

ISSN 2832-4870

DIRECTIVE PUBLICATIONS

Case Report

Overlap Syndrome Of Autoimmune Hepatitis And Primary Biliary Cholangitis: Nine Year Follow-Up.

Rahul Siwach, Parveen Malhotra, Bibin CF, Avani Sharma, Abhishek Yadav, Chitrakshi Bhardwaj, Himanshu, Shivanshu, Rajasvi, Taranjot Singh.

Department of Medical Gastroenterology, PGIMS, Rohtak, Haryana, India.

Abstract

Introduction: Autoimmune hepatitis–primary biliary cholangitis (AIH–PBC) M overlap syndrome affects 10–20% of patients with either disease, blending features of both and complicating therapy. Long-term outcomes include cirrhosis, portal hypertension, and variceal bleeding.
Case report: A thirty-three-year-old female, not a known case of any chronic illness presented nine years back with abdominal pain which was symptomatically treated and ultrasonogram abdomen done at that point of time revealed mild splenomegaly, for which no definitive treatment was started. One year later, she again developed pain abdomen, generalized fatigue and abdominal distension. She was seen by local private practitioner, on whose advice, routine evaluation revealed anemia, thrombocytopenia, mildly raised transaminitis with ratio reversal, low serum albumin level. The ultrasound abdomen showed small coarse liver, splenomegaly and ascites. After stabilization, liver biopsy was done which confirmed the diagnosis of Primary Biliary Cirrhosis with stage-2, and on serology workup overlap syndrome with autoimmune hepatitis was confirmed (ANA 166.42, weakly positive AMA 1:20, IgG 2118 mg/dL). She was started on ursodeoxycholic acid, immunosuppressive therapy, diuretics, beta-blockers in addition to symptomatic therapy. She had two endoscopic variceal band ligations for large oesophageal varices. She remained stable for next nine years but stopped immunosuppressive treatment on her own for few months and later on again presented with increased decompensation in form of excessive fatigue, menorrhagia, ascites, and pedal edema. She was restarted on immunosuppressive therapy, in addition to rest previously going treatment. She got stabilized, pedal edema & ascites subsided and fatigue decreased and was discharged under haemodynamically stable condition on above therapy. This case illustrates need of regular long-term treatment, including immunosuppressive treatment, even in cirrhotic stage for preventing recurrent decompensation.
Conclusion: AIH–PBC overlap syndrome requires lifelong, multimodal management. Despite initial control, recurrent varices and decompensation underscore the need for vigilant endoscopic surveillance, optimized beta-blockade, and consideration of adjunctive therapies (e.g., TIPS) in refractory portal hypertension.

Keywords: Autoimmune Hepatitis, Primary Biliary cholangitis, Overlap Syndrome, Oesophageal Varices, Ursodeoxycholic Acid, Immunosuppressive Therapy.

INTRODUCTION

Primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) are distinct diseases with their own characteristics. For most patients, distinguishing between the two entities is without issue. The presentations in clinical practice that raise the question of overlap are variable but may include, a biochemical overlap: patients with PBC manifesting a “hepatitic” laboratory profile (aspartate aminotransferase [AST] or alanine aminotransferase [ALT] values greater than 5x the upper limit of normal [ULN]); or patients with AIH who exhibit cholestatic liver biochemistry (alkaline phosphatase [ALP] greater than 3x ULN or gamma glutamyl transferase [GGT] greater than 5x ULN) or an immunologic overlap: patients who test positive for anti-mitochondrial anti- bodies (AMAs), alongside elevated immunoglobulin G (IgG) values and/or positive antinuclear antibodies (ANAs)/anti-smooth muscle antibodies (ASMAs); or patients with otherwise classical AIH albeit testing positive for AMA or a histologic overlap: florid bile duct lesions alongside a lymphoplasmacytic infiltrate with interface hepatitis. [1] Up to 25% of patients reported as having PBC/AIH overlap are ASMA positive; despite the fact that this antibody is found in over 40% of the general adult population. Similarly, ANAs can be found in 46% to 47% and 68% to 100% of PBC patients who are AMA-positive and AMA-negative PBC, respectively. However, these include antigen-specific ANA subtypes (anti-gp210 and anti-sp100), [2] which are diagnostic of PBC rather than AIH, and stratify a group of patients at greater risk of liver disease progression. [3] By contrast, approximately 10% of AIH patients are AMA positive. Autoimmune hepatitis–primary biliary cholangitis (AIH–PBC) overlap syndrome affects 10–20% of patients with either

***Corresponding Author:** **Parveen Malhotra.** 128/19, Civil Hospital Road, Rohtak, Haryana, India (124001). **Email:** drparveenmalhotra@yahoo.com.
Received: 18-Mar-2026, Manuscript No. JJOGASTRO - 5510 **; Editor Assigned:** 20-Mar-2026 **; Reviewed:** 08-Apr-2026, QC No. JJOGASTRO - 5510 **;**
Published: 21-Apr-2026, **DOI:** 10.52338/jjogastro.2026.5510.
Citation: **Parveen Malhotra.** Overlap Syndrome Of Autoimmune Hepatitis And Primary Biliary Cholangitis: Nine Year Follow-Up.
Japanese Journal of Gastroenterology. 2026 April; 16(1).doi: 10.52338/jjogastro.2026.5510.

disease, blending features of both and complicating therapy. Long-term outcomes include cirrhosis, portal hypertension, and variceal bleeding. We present a nine-year course marked by initial response, recurrent varices requiring ligation, and decompensation—highlighting management challenges.

CASE REPORT

A thirty-three-year-old female, not a known case of any chronic illness presented nine years back with abdominal pain which was symptomatically treated and ultrasonogram abdomen done at that point of time revealed mild splenomegaly, for which no definitive treatment was started. One year later, she again developed pain abdomen, generalized fatigue and abdominal distension. She was seen by local private practitioner, on whose advice, routine evaluation revealed anemia (haemoglobin 8.8 g/dL), thrombocytopenia (platelet count 1 lakh/mm3), serum bilirubin (total bilirubin 1.26 mg/dl), mildly raised transaminitis with ratio reversal (AST 56 U/L, ALT 51 U/L), ALP 100 U/L with low serum albumin level (2.4 gm/dl). The ultrasound abdomen showed small coarse liver, splenomegaly and ascites. The viral screen was negative, renal function tests, blood sugar levels, thyroid profile, ECG and Chest- X-ray was normal. After stabilization, liver biopsy was done which confirmed the diagnosis of Primary Biliary Cirrhosis with stage-2, and on serology workup overlap syndrome with autoimmune hepatitis was confirmed (ANA 166.42, weakly positive AMA 1:20, IgG 2118 mg/dL). Liver biopsy was done, which revealed features suggestive of Primary biliary cirrhosis (PBC) with Autoimmune hepatitis (AIH) overlap. It showed chronic nonsuppurative destructive cholangitis along with interface hepatitis She was started on ursodeoxycholic acid, immunosuppressive therapy, diuretics, beta-blockers in addition to symptomatic therapy. She had two endoscopic variceal band ligations for large oesophageal varices. She remained stable for next nine years but stopped immunosuppressive treatment on her own for few months and later on again presented with increased decompensation in form of excessive fatigue, menorrhagia, ascites, and pedal edema. She was restarted on immunosuppressive therapy, in addition to rest previously going treatment. She got stabilized, pedal edema & ascites subsided and fatigue decreased and was discharged under haemodynamically stable condition on above therapy. This case illustrates need of regular long-term treatment, including immunosuppressive treatment, even in cirrhotic stage for preventing recurrent decompensation.

DISCUSSION

The overlap syndromes occur in 3% -7% of patients with autoimmune liver disease.[4] Patients with overlap syndromes usually present with nonspecific symptoms, including fatigue, arthralgias and myalgias. A biochemical profile of hepatitis typically coexists with cholestatic laboratory changes. [5] It remains unclear whether these overlap syndromes form distinct disease entities or are only variants of the major immune hepatopathies. [6,7] PBC, also known as chronic nonsuppurative destructive cholangitis, is a disease mainly involving intrahepatic bile ducts. Its diagnosis is established on basis of cholestatic serum enzyme pattern, serum AMA and PBC-specific AMA- M2 and a compatible histology including bile duct lesions. Treatment of the patient with ursodeoxycholic acid (UDCA) can slow down the course of the disease, but till today, no drug is available which can stop the progression of PBC. [8] AIH is a chronic inflammatory disorder characterised by periportal inflammation, hypergammaglobulinemia, circulating autoantibodies and necrosis of the liver. It can affect any age group. In hypergammaglobulinemia, mainly IgG levels are raised. On histological examination, interface hepatitis is hallmark of the disease. These cases have a favourable response to steroid therapy. Patients with features of AIH and PBC who have a serum alkaline phosphatase level less than two-fold ULN respond well to corticosteroid therapy as patients with classical autoimmune hepatitis. [9] In contrast, patients with the AIH- PBC overlap syndrome patients having serum alkaline phosphatase levels ≥ 2-fold ULN are commonly treated with corticosteroids in combination with low-dose ursodeoxycholic acid. This treatment improves serum ALP, GGT and ALT levels and limits hepatic fibrosis. [10] In end-stage disease, liver transplantation is the treatment. This nine-year trajectory reflects the heterogeneous natural history of AIH–PBC overlap. Early biochemical stability on UDCA and immunosuppression was overshadowed by persistent portal hypertension, necessitating two EVLs. Recurrent large varices (despite ligation and beta-blocker therapy—suggests progressive fibrosis or inadequate portal pressure control. Carvedilol, chosen for its superior splanchnic vasodilation, did not prevent decompensation, possibly due to steroid withdrawal, menorrhagia-related anemia, or cirrhosis progression. This aligns with literature showing higher re-bleeding risk in overlap syndrome compared with isolated PBC or AIH. Early TIPS placement or non-selective beta-blocker titration might have altered the course, though evidence remains anecdotal. Long-term immunosuppression withdrawal remains controversial—some centers advocate low-dose continuation to suppress hepatocellular damage, while others prioritize liver fibrosis progression.

CONCLUSION

Patients with overlap syndromes mainly present with nonspecific symptoms, including fatigue, arthralgias and myalgias, thus meriting strict vigilance by treating team. Timely diagnosis has a significant impact on the treatment of

patients leading to decrease in the need of liver transplantation and improved survival. AIH–PBC overlap syndrome requires lifelong, multimodal management. Despite initial control, recurrent varices and decompensation underscore the need for vigilant endoscopic surveillance, optimized beta-blockade, and consideration of adjunctive therapies (e.g., TIPS) in refractory portal hypertension. This case supports close follow-up beyond biochemical remission.

REFERENCES

1. Hussain and Trivedi. The Inconvenient Truth of Primary Biliary Cholangitis/ Autoimmune Hepatitis Overlap Syndrome. Clin Liver Dis 26 (2022) 657–680 https://doi.org/10.1016/j.cld.2022.06.007

2. Bogdanos DP, Komorowski L. Disease-specific autoantibodies in primary biliary cirrhosis. Clin Chim Acta 2011;412(7–8):502–12.

3. Haldar D, Janmohamed A, Plant T, et al. Antibodies to gp210 and understanding risk in patients with primary biliary cholangitis. Liver Int 2021;41(3):535–44.

4. Czaja AJ. The overlap syndromes of autoimmune hepatitis. Dig Dis Sci 2013; 58 (2): 326-43.

5. Beuers U. Hepatic overlap syndromes. J Hepatol 2005; 42 (Suppl): S93-S99

6. Czaja AJ. The variant forms of autoimmune hepatitis. Ann Intern Med 1996; 125: 588-98.

7. Poupon R. Autoimmune overlapping syndromes. Clin Liver Dis 2003; 7: 865-78.

8. Fauci AS, Braunwald E, Kasper DL. Harrison's Principles of Internal Medicine. 17th ed. Ch. 300, 302. New York, NY: McGraw Hill; 2008.

9. Czaja AJ. Frequency and nature of the variant syndromes of autoimmune liver disease. Hepatology 1998; 28: 360-5.

10. Heurgue A, Vitry F, Diebold MD et al. Overlap syndrome of primary biliary cirrhosis and autoimmune hepatitis: A retrospective study of 115 cases of autoimmune liver disease. Gastroenterol Clin Biol 2007; 31: 17-25