Case report

Clinical complexity unveiled: A case of primary biliary cholangitis autoimmune hepatitis overlap syndrome

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Abstract

Overlap syndrome with primary biliary cholangitis and autoimmune hepatitis (PBC-AIH) remain uncommon liver autoimmune-related disorders. Diagnosis is based on clinical, biochemical, serological, and histological findings. Early diagnosis of the disease will give the best outcome even though evidence-proven treatment is still unavailable to tackle this disease entity. Here, we present a case of a Sri Lankan woman diagnosed with PBC-AIH overlap syndrome. She presented with symptoms of jaundice and pruritus. Extensive investigations, including liver biopsy were instrumental in confirming the diagnosis.

Keywords: primary biliary cholangitis, autoimmune hepatitis, primary biliary cholangitis autoimmune hepatitis overlap syndrome

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Introduction

Overlap syndrome with primary biliary cholangitis (PBC) and autoimmune hepatitis remain uncommon (AIH) combinations of liver-related autoimmune disorders. The prevalence of PBC-AIH overlap is around 2% among those initially diagnosed as AIH and about 10% among PBC [1]. Liver-related autoimmune conditions are common among females, with a 1:10 ratio with males, and the worldwide incidence rate is estimated at around 0.33 to 0.58 per 100,000 population, which is common in the fourth and fifth decade of life [2]. Pathogenesis is related to the inflammation triggered by autoantibodies, leading to inflammation around the intrahepatic bile ducts, causing PBC and liver parenchyma, causing AIH [3, 4]. Diagnosis is based on Paris criteria using biochemical, serological markers, and histological findings [5]. Here, we describe a case of PBC-AIH overlap syndrome in a Sri Lankan woman in her fifth decade of life.

Case report

A 57-year-old female patient from Kandy presented to the gastrointestinal department with jaundice for six months. Before the onset of jaundice, she had developed generalized pruritus, which was more prominent at night. Apart from these symptoms, she had dry eyes and a dry mouth. However, she did not have dark urine or pale stools. She had not consumed alcohol throughout her life.

On examination, she was a thin-built person and had jaundice, alopecia, oral ulcers, and darkly pigmented rash over the sun exposure areas; however, her abdomen was soft and non-tender, and other system examination was unremarkable.

With the above clinical findings, she was investigated for liver pathology and found to have high bilirubin levels, a total bilirubin level of 32 µmol/L (normal range: 5.1-17), direct bilirubin level of 25.5 µmol/L (normal range: 1.7-5.1) and indirect 6.5 µmol/L (normal range: 3.4-12). With high alkaline phosphate level of 471 IU/L (normal range: 44-147), alanine aminotransferase (ALT) 186 IU/L (normal range:4-36), aspartate aminotransferase (AST) 108 IU/L (normal range:8-33), and international normalization ratio of 0.79. Her erythrocyte sedimentation rate was 100 with 29 mg/dl Albumin (normal range: 34-54) and 32 mg/dl Globulin (normal range: 20-35).

After those investigation findings, the autoimmune profile was evaluated. Her antinuclear Antibody (ANA) was positive in 1:80 dilution with cytoplasmic pattern in indirect immunofluorescence method, and Anti mitochondrial antibody (AMA) was also positive. However, her serological markers for hepatotropic viral aetiologies were negative.

With the above findings, she underwent ultrasonography of the abdomen; it revealed a mildly echogenic liver without intrahepatic or extrahepatic bile duct dilatation.

Primary biliary cholangitis was suspected due to clinical, biochemical, and serological markers. Hence, a guided liver biopsy showed interface damage, prominent lobular inflammation, and prominent plasma cells within the portal tracts, which favour acute on chronic autoimmune hepatitis (Figure 1A). There were degenerative changes in bile duct epithelium and lymphoid collection in the portal tracts, consistent with primary biliary cholangitis (Figure 1B).

Her ultimate diagnosis was overlap syndrome of primary biliary cholangitis (PBC) and acute on chronic AIH, which was made according to Paris criteria [5] based on clinical, biochemical, serological, and histological findings (Table 1).

Table 1: Diagnostic criteria according to Paris's suggestions. (At least 2 of the 3 components each should be required to diagnose overlap syndrome)

Disease	Requirement	Our patient's results
Autoimmune Hepatitis (AIH)	1. ALT >5 ULN	186 (4-36)
	2.serum IgG levels > 2ULN or positive ASMA	Not done
	3 positive liver biopsy for AIH	interface damage, prominent lobular inflammation
Primary biliary Cholangitis (PBC)	1. ALP >2 ULN	471 (44-147)
	2. positive AMA	AMA positive
	3. positive liver biopsy for PBC	Degenerative changes in bile duct epithelium and lymphoid collection in the portal tracts with some Bile ductular proliferation.

Abbreviations - ALT- alanine transaminase, ALP- alkaline phosphatase, ULN- upper limit of normal

Then, to find out associations of the disease, the patient underwent a thyroid function test and was found to have a TSH level of 65 µIU/mL (0.3-4.5) with anti-TPO 1000 IU/mL (0-30), which indicates autoimmune thyroiditis.

Following the above diagnosis of disease, the patient was treated with Ursodeoxycholic acid (UDCA) 300mg BD dose with prednisone 1mg/kg/day tailing off dose with azathioprine 50mg mane dose and levothyroxine 100µg for her hypothyroidism. Currently, she is followed up in a liver clinic, where she has biochemically stable liver functions.

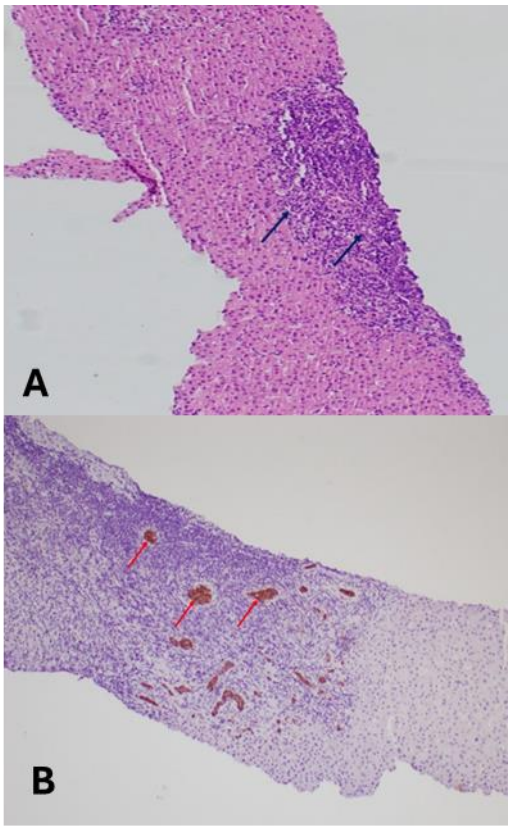

Fig 1: Histopathology (Haematoxylin and eosin, X200 magnification)**. A**. Hepatocytes showing interface activity with prominent lobular inflammation (blue arrows), **B.** Hepatocytes with immunohistochemistry cytokeratin 7 showing proliferating bile ductules (red arrows).

Discussion

Primary biliary cholangitis autoimmune hepatitis overlap syndrome is a relatively uncommon clinical entity. In our clinical scenario, the patient initially manifested with clinical features suggestive of PBC but, upon further investigations, was diagnosed through liver biopsy as having an overlap syndrome involving both PBC and AIH. This case serves as a reminder of the complexity and diversity of autoimmune liver disease, emphasizing the importance of comprehensive diagnostic evaluation for accurate disease classification and appropriate management.

Our patient's initial diagnosis was PBC according to the clinical and biochemical parameters; however, after the liver biopsy, her diagnosis was modified to PBC AIH overlap syndrome according to the Paris criteria. Here, a liver biopsy plays a significant role in diagnosing the disease because, without a liver biopsy, the patient could have diagnosed only the part of the disease. Hence, liver biopsy remains a significant asset even in the era of serological markers.

According to the current concepts, there are two subgroups of the disease, and treatment is suggested according to the subgroups: 1. AMA positive without histological evidence of PBC 2. ANA and SMA positive with histological changes suggesting PBC. The first category mainstay of treatment is corticosteroids, and the second group treatment is corticosteroids with ursodeoxycholic acid. Our patient had features of both AIH and PBC in her liver histology; apart from that, her AMA and ANA were positive. However, we could not do SMA due to the test not being available in our labs. Considering these facts, we have started a second treatment regime after a modified diagnosis with prednisolone and UDCA. Later, azathioprine was also added and continued. It is shown that higher transplant-free survival in patients with AIH PBC overlap syndrome can be achieved with the above treatment regimes. [6]. However, UDCA has promising benefits for slowing down the disease progression even though it did not improve the prognosis of the disease. [7,8]. Still, this disease entity has no trial-proven medications [8].

When we consider the other associations, our patients tested positive for an autoimmune thyroid disorder, evidenced by elevated TSH levels and positivity of TPO antibodies. According to the medical literature, it is estimated that around 10 % to 20 % of patients with autoimmune hepatic disorder patients are associated with thyroid disorders, and the hypothesis to explain this relationship is based on the cross-reactivity of autoantibodies [9].

Conclusion

Our case demonstrates the challenges of diagnosing the PBC-AHI overlap syndrome and the importance of liver biopsy in achieving an accurate diagnosis. Furthermore, an associated autoimmune disorder in our patient highlights the interconnected nature of autoimmune conditions and the importance of a multidisciplinary approach in managing complex autoimmune liver diseases to provide adequate care.

Informed consent

The patient has given verbal and written consent to publish her history and images as a case report

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