CASE REPORT

JIACM 2019; 20(2): 137-38

An Unusual Case of Altered Sensorium: Primary Biliary Cirrhosis-Autoimmune Hepatitis Overlap Syndrome

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Abstract

The overlap syndromes are clinical descriptions rather than distinct pathological entities. They are relatively common and the major clinical relevance of these syndromes is their failure to respond in a consistent fashion to conventional corticosteroid therapy. They have uncertain clinical outcomes. The common clinical feature of these atypical phenotypes is the presence of a cholestatic component. We hereby report a case of a middle-aged woman who presented in altered sensorium with no history suggestive of autoimmune or cholestatic liver disease and on investigation was found to have Autoimmune Hepatitis – Primary Biliary Cirrhosis overlap syndrome.

Key words: Primary biliary cirrhosis, autoimmune hepatitis, overlap syndromes.

Introduction

The main autoimmune disorders of the liver are Autoimmune Hepatitis (AIH), Primary Biliary Cirrhosis (PBC) and Primary Sclerosing Cholangitis (PSC); variants are called overlap syndromes. The overlap syndromes occur in 3% - 7% of patients with autoimmune liver disease[1]. 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[2]. The major clinical relevance of these syndromes is their failure to respond, in a consistent fashion, to conventional corticosteroid therapy[1].

Case report

A 45-year-old woman, a housewife, resident of Delhi presented in the emergency with the chief complaint of altered sensorium for one day. At onset of symptoms, patient became drowsy but was responding to commands. Then the patient gradually lost consciousness within a span of 1 - 2 hours. There was history of constipation present in the preceding two days. There was no history of jaundice, fever, seizure, abdominal distension, pruritus, malaena or bleeding from any site.

There was history of fatigue since 2 - 3 months. There was no significant medical or surgical history. No history suggestive of alcohol dependence or smoking. There was no history of drug abuse or promiscuous behaviour. On examination, the patient was stuporous with a Glasgow Coma Scale (GCS) of E2M4V2. The patient had pandigital clubbing (grade 2). Patient's plantar reflex was mute bilaterally. On per abdomen examination, there was no organomegaly or shifting dullness. Patient had a reduced liver span of 8 cm on percussion. Rest of the general physical and systemic examination did not reveal any abnormality.

Non Contrast Computed Tomography (NCCT) of head was done, which was normal. Her complete blood count, renal function tests, lipid profile, thyroid function tests and urine routine and microscopy were also within normal range. The erythrocyte sedimentation rate was 22 mm/1st hour. Total bilirubin level was mildly elevated [1.9 mg/dl (n - 0.2 - 1.2 mg/dl)] with indirect bilirubin of 1.3 mg/dl (n - 0.2 - 1.1 mg/dl). The serum alanine aminotransferase and aspartate aminotransferase were mildly elevated, i.e., 111 U/L (n - 15 - 50 U/L) and 81 U/L (n - 15 - 50 U/L) respectively. Her serum alkaline phosphatase (ALP) levels were also elevated [355 IU/L (n - 50 - 130 U/L)]. Her serum protein levels were low with albumin: globulin ratio reversal (S. albumin - 2.3 gm/dl, S. globulin - 4.1 gm/dl). In view of elevated serum alkaline phosphatase levels, serum Gamma-glutamyl transferase (GGT) level was done, which was elevated, i.e., 74 IU/L (n - 5 - 58 U/L). Her serum ammonia level was raised [67 umol/L (n - 11 - 32 umol/L)] too. Tests for viral hepatitis (Anti HAV, HBsAg, Anti HCV, Anti HEV) and HIV were negative. INR was 1.23 (n - ≤ 1.1). On ultrasonography of abdomen, liver was 8 cm in size, i.e., shrunken with coarsened echotexture; spleen was (12.6 cm) enlarged with portal vein measuring 11.5 mm (n - ≤ 13 mm). Endoscopy showed grade 3 oesophageal varices. Stool for occult blood was negative. No KF ring was observed on slit lamp examination. Her antinuclear antibody (ANA) was positive and S. IgG levels [2,790 mg/dl (n - < 200 mg/dl)] were elevated. Her Anti-mitochondrial antibody was positive. Anti-smooth muscle antibody, Anti LKM, p-ANCA and c-ANCA

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were negative. 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. So we came to a diagnosis of hepatic encephalopathy secondary to Autoimmune hepatitis-Primary biliary cirrhosis overlap syndrome (according to Paris criteria) with associated portal hypertension and grade 3 oesophageal varices. The patient was managed with lactulose, high bowel wash, ursodeoxycholic acid (UDCA) (15 - 20 mg/kg once a day), prednisolone (10 mg once a daily), azathioprine (50 mg once a day daily). Patient regained consciousness on the 3rd day after initiation of treatment. The patient was followed-up in outpatient basis and was doing well with treatment.

Discussion

Overlap syndrome is the term used for patients presenting with features of disorders within the spectrum of autoimmune liver diseases (i.e., AIH, PBC and PSC). It remains unclear whether these overlap syndromes form distinct disease entities or are only variants of the major immune hepatopathies[3,4].

AIH is a chronic inflammatory disorder characterised by periportal inflammation, hypergammaglobulinaemia, circulating autoantibodies and necrosis of the liver. It can affect any age group. In hypergammaglobulinaemia, mainly IgG levels are raised. On histopathological examination, interface hepatitis is hallmark of the disease. These cases have a favourable response to steroid therapy.

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 (which includes bile duct lesions). Treatment of the patient with UDCA can slow down the course of the disease, but till today, no drug is available which can stop the progression of PBC[5].

AIH-PBC Overlap syndrome lacks specific definition. Paris Diagnostic criteria of AIH-PBC overlap syndrome is widely recognised[6] (Table I).

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[7]. 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[8] (Table II). In end-stage disease, liver transplantation is the treatment of choice.

Table I: Paris diagnostic criteria of AIH-PBC overlap syndrome[6].

AIH (2 out of 3 criteria)	PBC (2 out of 3 criteria)
1. Alanine aminotransferase (ALT) levels > 5 × ULN	1. Alkaline phosphatase (AP) levels > 2 × or γ- glutamyltranspeptidase (GGT) levels > 5 × ULN
2. Serum immunoglobulin G (IgG) levels > 2 × ULN or a positive test for smooth muscle antibodies (ASMA)	2. Positive test for antimitochondrial antibodies (AMA)
3. Liver biopsy showing moderate or severe periportal or periseptal lymphocytic piecemeal necrosis	3. Liver biopsy specimen showing florid bile duct lesions
	(ULN: Upper limit of normal value).

The initial diagnostic dilemma in this case was because there was no clinical history suggestive of underlying chronic liver disease. But the liver biopsy led to the eventual of diagnosis.

Conclusion

Patients with overlap syndromes usually present with nonspecific symptoms, including fatigue, arthralgias and myalgias, thus the clinician has to be vigilant not to miss the diagnosis. Early diagnosis of overlap syndromes could have a noteworthy impact on the treatment of patients leading to decrease in the need of liver transplantation and improved survival.

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