AN INTERESTING CASE OF JAUNDICE

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Abstract:
Overlap syndrome is used to describe variant forms of autoimmune hepatitis (AIH) which present with characteristics of AIH and primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC). Patients with overlap syndromes present with both hepatitic and cholestatic serum liver tests and have histological features of AIH and PBC or PSC. AIH-PBC is the most common form of overlap syndrome, affecting almost 10 of adults with AIH or PBC. Overlap syndromes show a progressive course without treatment, and therapy is empiric. Ursodeoxycholic acid is usually combined with immunosuppressive therapy but end-stage disease requires liver transplantation. We report a case of AIH-PBC overlap syndrome presenting with jaundice.

Keyword:
Overlap syndrome, AIH, PBC, jaundice

A forty six year old lady presented to us with fever, jaundice and abdominal distension for 2 weeks. Patient had history of myalgia, epistaxis, night blindness and loss of appetite and weight. There was no history of clay coloured stools, pruritis, malena, abdominal pain and arthralgia. She had past history of taking anti tubercular medications for cervical tuberculosis two years back. She was a teetotaller. No family of jaundice or native drug treatment history.

On clinical examination the patient had icterus with hyperpigmentation of face, hepatosplenomegaly, free fluid in abdomen. On investigation Hb- 11 g/dl, Total count –7200, Differential count - Neutrophils- 57, Lymphocytes - 40, Eosinophils - 3, ESR- 15/32 , Blood sugar 82mgs%, Urea 33 mgs%, Creatinine 0.9 mgs%, Total bilirubin 6.8 mg %, Direct 3.8 mgs% Indirect 3.3 mgs%, SGOT 389- IU/L, SGPT - 106 IU/L, SAP – 184 IU/L
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Total protein-6.8 gms%, Albumin-3.5 gms%, Globulin-3.3gms%. HbsAg and anti HCV were negative. BT 2’18 CT 3’15. INR 1.45, USG abdomen showed fatty liver with ascites. Ascitic fluid analysis showed protein -2.4gms%, albumin -1.2gms% [ High SAAG ,Low protein ]. Lymphocytes 2-4/hpf. Gastroscopy showed grade 1 oesophageal varices -3 columns with mild portal hypertensive gastropathy. Serum ANA 2+ positive. Autoimmune hepatitis markers were done. Anti SMA was positive. Anti LKM ,anti SLA/LP and anti LC-1 were negative. AMA M2 was strongly positive. The patient was suspected to have PBC- AIH overlap syndrome and hence liver biopsy was done to confirm the diagnosis.

Liver biopsy report:
Section showed liver tissue with smaller hepatic lobules separated by wide bands of fibrous tissue with dense sheets of lymphocytes and periportal creeping inflammatory reaction. Number of bile ducts appear reduced. The residual hepatocytes show intrahepatic cholestasis, intracytoplasmic greenish granules and bile canaliculi plugging.

HISTOPATHOLOGY OF LIVER- HIGH POWER VIEW
Impression- Bile duct destruction with inflammatory reaction with development of biliary cirrhosis and intrahepatic cholestasis - Features more in favour of autoimmune cholangitis.
Since the patient had features of both primary biliary cirrhosis and autoimmune hepatitis the diagnosis of overlap syndrome was considered. Patient was treated with ursodeoxycholic acid and listed for liver transplantation.
Conclusion: Overlap syndrome of primary biliary cirrhosis with autoimmune hepatitis is rare. Liver transplantation is the definitive treatment in end stage liver disease. This case is submitted for its rarity.

Discussion:
PBC and AIH are the most frequent autoimmune liver disease with a female preponderance. Clinical presentation depends on predominant component of disease. Patients with overlap syndromes usually present with nonspecific symptoms, including fatigue, arthralgia, myalgia, jaundice and pale stools. Serum liver tests typically show a hepatitic
pattern in AIH and a cholestatic pattern with marked elevation of AP and -GT, but mild elevation of serum transaminases in PBC. While serum IgG is the predominant immunoglobulin elevated in AIH, serum IgM is elevated in most patients with PBC. Patients presenting with clinical, biochemical, serological and histological features of both these diseases have been reported and described as “overlap syndrome”. Although there is no uniformly accepted criteria for diagnosis the diagnostic criteria defined by Chazouillères et al. are based on the presence of at least two of the following three types of features characteristic of each disease: biochemical (ALP levels at least twofold / GGT > at least five fold and ALT levels at least fivefold the upper normal PBC and AIH values, respectively); immunologic (presence of AMA in the case of BPC, and serum IgG levels at least twofold the upper normal values or the presence of ASMA in that of AIH); and histologic (florid bile duct lesions in the case of PBC and interface hepatitis in that of AIH). In the present case, the patient satisfied the aforementioned diagnostic criteria.

Autoantibodies are generally believed as a hallmark for the diagnosis of AIH. Serum ANA in patients with PBC are not a marker of AIH-PBC overlap syndrome, but often found in PBC patients without further signs of AIH. ANA with a specific immunofluorescence pattern of multiple nuclear dots directed against Sp100 or Coilin p80 are rather specific although less sensitive for PBC. Patients with AIH-PBC overlap syndrome show a predominant HLA type B8, DR3, or DR4 similar to AIH and a good response to corticosteroid treatment. The presence of soluble liver antigen (SLA) autoantibodies was found to be a marker of AIH-PBC overlap syndrome with a good response to immunosuppressive therapy. The time interval between the diagnosis of PBC and the diagnosis of AIH varied from 6 months to 13 years.

Recommendations for the treatment of PBC–AIH overlap syndrome have not yet been standardized owing to the low prevalence of this autoimmune liver disease. Because no randomized controlled therapeutic trials have been carried out so far, recommendations for treating PBC–AIH overlap syndrome are usually based on the methods used to treat the two main autoimmune liver diseases separately. It’s appropriate to start treatment with UDCA (13-15 mg/kg daily). However, if this therapy does not induce an adequate biochemical response in an appropriate time span (e.g. 3 months) or in patients with predominantly hepatitic serum liver tests, a corticosteroid should be added. Prednisone has been used at an initial dose of 0.5 mg/kg daily and should be progressively tapered once ALT levels show a response. The role of other immunosuppressants, (azathioprine) in the long-term management of patients with AIH-PBC overlap syndrome is unclear, but it’s an alternative to corticosteroids for long-term immunosuppressive therapy. Budesonide and cyclosporine A has also been used in patients with AIH-PBC overlap syndrome with success. Liver transplantation is regarded as the treatment of choice for end-stage disease. Recent studies have shown AIH-PBC overlap syndrome might have worse clinical outcomes compared to patients with PBC alone.
References:


