CASE REPORT

Case of Autoimmune Hepatitis

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Abstract

Autoimmune hepatitis (AIH) accounts for cases of chronic liver disease with greater incidence in females than males. It has a bimodal distribution in the age group peaking around pubertal periods and later in the fourth to sixth decade of life. It is characterized by continual hepatocellular inflammation and necrosis which bears the potential to progress to fibrosis and cirrhosis. Approximately a third of the patients manifest with features of acute hepatitis while some patients may progress to chronic liver disease with acute liver failure manifesting in the form of jaundice and coagulopathy. Management has long involved administration of corticosteroids alone or in association with other immunosuppressants like azathioprine to achieve long-term remission. Response to therapy is significantly variable as few patients achieve remission while some may relapse, thereby becoming candidates requiring lifelong therapy. It can either present as insidious onset or acute with manifestations ranging broadly from fatigue malaise, lethargy right upper quadrant pain weight loss anorexia, and jaundice, where up to one-third of patients may have progressed to frank cirrhosis at the time of diagnosis. A 62-year female presented with complaints of facial puffiness more around the eyes, associated with profoundly reduced appetite, yellowish discoloration of the skin, conjunctiva since 1 month, and sudden onset generalized itching not associated with fever, joint pains, weight loss, vomiting, loose stools, rash, or bleeding manifestations. She was admitted for further evaluation and workup. Liver function test revealed predominant unconjugated hyperbilirubinemia with direct bilirubin of 0.7 mg/dL and indirect bilirubin of 1.6 mg/day and transaminitis. Further investigations showed significantly elevated immunoglobulin G (IgG) and 1:80 titer of antinuclear antibodies (ANAs). In view of the high suspicion of autoimmune etiologies, the patient was subjected to a liver biopsy that confirmed cirrhosis with moderate interface hepatitis in the background of negative viral serologies and substance abuse history. She was started on a steroid course on a monthly follow-up basis to ensure biochemical remission.

Keywords: Autoimmune hepatitis, Bilirubin, Biopsy, Case report, Cirrhosis of the liver.

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Background

Autoimmune hepatitis (AIH) accounts for cases of chronic liver disease with greater incidence in females than in males. It has a bimodal distribution in the age group peaking around pubertal periods and later in the fourth to sixth decade of life.

It can either present as insidious onset or acute with manifestations ranging broadly from fatigue malaise, lethargy right upper quadrant pain weight loss anorexia, and jaundice, where up to one-third of patients may have progressed to frank cirrhosis at the time of diagnosis.

It has three variants as discussed by Linzay et al. in the article "Autoimmune hepatitis" based on the autoantibodies positive AIH type 1, AIH type 2, and AIH type 3.[1] Furthermore, AIH type 1 accounts for 90% of the cases, which is variable in the age of onset and histology but stains positive for antinuclear antibodies (ANAs) antismooth muscle antibodies (ASMAs) and anti-soluble liver antigen/liver pancreas (anti-SLA/LP) antibodies. Furthermore, AIH type 2 accounts for only 10% of cases which is positive for anti-liver kidney microsomal (anti-LMK1) and anti-liver cytosol (anti-LC1) with rare anti-LMK-3 antibodies and has a presentation in early childhood or young adulthood.

The remaining 10% of cases belong to AIH type 3 which bears some resemblance to AIH type 1 but is different in that it is only positive for anti-SLA/LP antibodies. Among all three subtypes, AIH type 1 has an excellent prognosis while AHA types 2 and 3 require lifelong immunosuppression with frequent relapses upon drug withdrawal.

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Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

Case Presentation

A 62-year female presented with complaints of facial puffiness more around the eyes, associated with profoundly reduced appetite, yellowish discoloration of the skin, conjunctiva since 1 month, and sudden onset generalized itching not associated with fever, joint pains, weight loss, vomiting, loose stools, rash or bleeding manifestations.

Family history was insignificant for bleeding diathesis, the patient was a homemaker by occupation and gave no history

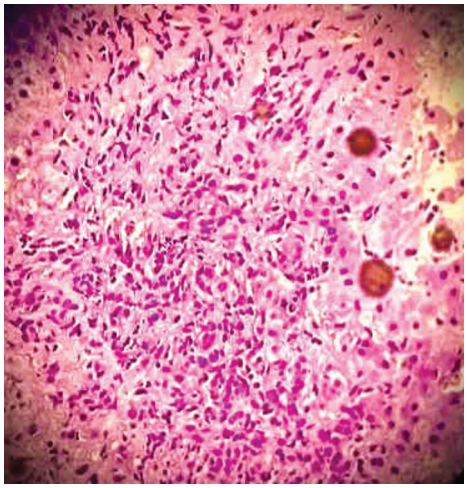

Fig. 1: Liver biopsy showing lymphoplasmacytic infiltrates

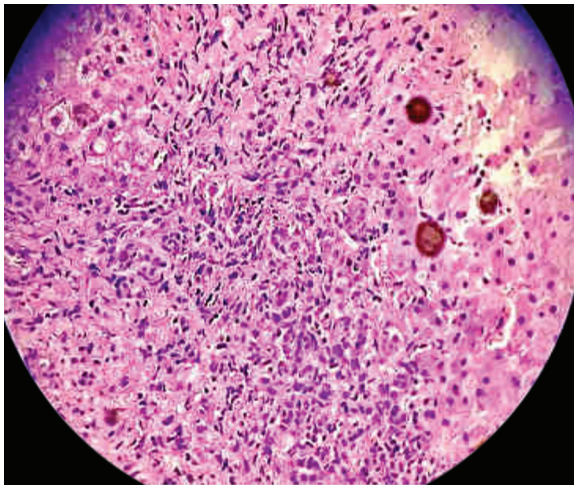

Fig. 2: Liver biopsy revealing mild interface hepatitis

of substance use, injection or needle sharing, prior blood transfusions, chemical or pesticide exposure, or medication abuse. Personal history was insignificant for any chronic illness or transplant and the patient consumed alcohol on a social basis only (<10 gm/day). On examination, the patient was oriented, with mild periorbital edema, and grade 2 pitting edema bilateral feet were present.

There were no stigmata of liver disease or portal hypertension, and no organomegaly or abdomen distension were found. The patient was admitted for further evaluation and workup. Liver function test revealed total bilirubin of 2.3 mg/dL and predominantly unconjugated hyperbilirubinemia with a direct bilirubin of 0.7 mg/dL and indirect bilirubin of 1.6 mg/day and transaminitis (AST 154 U/L, ALT 166 mg/dL and alkaline phosphatase of 207 U/L). The synthetic function of the liver was measured, and reports revealed serum albumin of 2.1 gm/dL and an international normalized ratio (INR) of 2.04.

The patient was evaluated for metabolic syndrome, [waist circumference, serum high-density lipoprotein (HDL), serum triglycerides, and blood pressure were found within reference ranges]. Ultrasound of the abdomen and pelvis showed mild surface irregularities. The patient for further subjected to contrast enhanced CT (CECT) abdomen that revealed caudate lobe hypertrophy,mild surface irregularities and normal branches of portal vein. Serologies were negative for viral markers and a workup for immune-mediated hepatitis and non-alcoholic steatohepatitis was performed. Results showed perinuclear antineutrophil cytoplasmic antibodies (pANCA) 0.66 (normal <20) anti-LMK1 10.20 (normal <20) and antinuclear antibodies significantly positive (3+) staining in centromere pattern with serum immunoglobulin G (Zachou et al.) (138.7 mg/dL) and serum α1 antitrypsin levels within the reference range.[2] A liver biopsy was performed that revealed distortion of acinar architecture with bridging fibrous septa enclosing few regenerating parenchymal nodules and the presence of moderate lymphomononuclear infiltrate shown in Figure 1 admixed with few plasma cells suggestive of mild hepatic interface activity shown in Figure 2 (see the article "Autoimmune hepatitis, one disease with many faces: etiopathogenetic, clinico–laboratory and histological characteristics, 2015).[3] Moderate ductular reaction along with increased portal fibrosis was also seen while the hepatocytes demonstrated macrovesicular steatosis, balloon degeneration shown in Figure 3, and occasional Mallory Denk bodies. Special

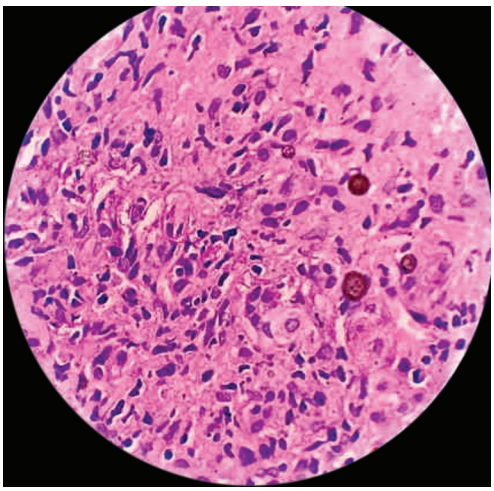

Fig. 3: Liver biopsy showing balloon degeneration of hepatocytes

stains for copper were also performed that turned out to be negative. Fibrosis was graded using a modified histology activity index score (HAI) of 4–5.

The review article by the International Autoimmune Hepatitis Group (IAIHG) "Unanswered clinical and research questions in autoimmune hepatitis: Conclusions of the International Autoimmune Hepatitis Group Research Workshop, 2019" score was calculated which was found to be 15.[4] The patient was diagnosed with autoimmune hepatitis and according to the American Association for the Study of Liver Diseases (AASLD) revised guidelines 2019, the patient was started on prednisone 40 mg/day (cirrhotic dose) with a tapering dose weekly and followed with repeat liver function tests every 3 monthly to look for response to therapy and potential achievement of biochemical remission.

Discussion

Autoimmune hepatitis is characterized by continual hepatocellular inflammation and necrosis which bears the potential to progress to fibrosis and cirrhosis. Approximately a third of the patients manifest with features of acute hepatitis while some patients may progress to chronic liver disease with acute liver failure manifesting in the form of jaundice and coagulopathy. Lab evaluation usually

shows markedly elevated serum aminotransferases 1.5–5 times the upper normal limits, raised serum immunoglobulin IgG levels along with bilirubin and alkaline phosphatase levels in association with compromised synthetic function of the liver (low serum albumin and elevated INR). Markers of autoimmunity in the form of ANAs, ASMAs, antiliver kidney microsomal antibodies, antisoluble liver antigen antibodies, and anti-LC1 cytosol antibodies may be positive. Hematological abnormalities in the form of coombs positive autoimmune hemolytic anemia, and leukopenia can be found in some individuals.

Nevertheless, a biopsy is an important requisite for diagnosis that commonly reveals histological findings of interface hepatitis, lymphoplasmacytic infiltrates, rosette formation and biliary changes that are assigned a separate score each to facilitate the identification of the disease severity.

Management has long involved administration of corticosteroids alone or in association with other immunouppressants such as azathioprine as discussed by Komori to achieve long-term remission.[5] Response to therapy is significantly variable as few patients achieve remission while some may relapse with withdrawal, thereby becoming candidates requiring lifelong therapy.

The 2019-AASLD (American Association for the Study of Liver Diseases) criteria indicate that only those patients who have a >10-fold rise in the upper limit of aminotransferases (AST) or a more than 5-fold rise in AST along with a more than 2-fold increase in γ-globulins from their upper limit or with histological evidence of interface hepatitis require immunosuppressive therapy in both initial and maintenance regimen forms to achieve remission.[6] It should however be noted that usage of azathioprine in acute severe AIH should be done once after jaundice resolves and thiopurine methyltransferase tests (TPMTs) results are negative.

It is worth noting that some patients may also present with overlap syndromes of primary sclerosing cholangitis (PSC) and PBC primary biliary cholangitis (PBC) where the addition of ursodiol to the treatment regimen should be considered as most become steroid resistant.

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