Multiple Faces Of Autoimmune Hepatitis- A Case Series

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Key words-
Autoimmune liver disease, Acute hepatitis, Chronic liver disease , Transaminitis, Liver Biopsy, Endoscopy

Abstract

Introduction- Autoimmune liver diseases are mainly of three types: autoimmune hepatitis (AIH), primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC). Out of these three diseases, AIH is the most frequent, with a prevalence of 17 cases per 100,000 persons, followed by PBC and PSC. AIH and PBC mainly occur in women during menopause, AIH can also affect children and young adults. PSC mainly affects men from 20 to 40 years of age. In most cases, the three diseases can be reliably distinguished by serological analysis. However, overlap syndromes may occur in which patients present symptoms of two autoimmune liver diseases. The detection of specific autoantibodies allows precise differentiation between autoimmune liver diseases and infectious, toxic and other forms of hepatitis. AIH is often associated with chronic inflammatory rheumatic systemic diseases such as rheumatoid arthritis, Sjögren's syndrome and systemic lupus erythematosus. AIH usually present as chronic liver disease but in 20-30% of patients as acute hepatitis or even fulminant hepatic failure.

Case Series We report case series of three females who presented differently- one presented as acute hepatitis, second one as unexplained transaminitis and third one as chronic liver disease. All were proven on biochemical tests, serology and liver biopsy. All three had successful outcome with treatment. Our case series of three patients have different presentations- one presented as severe acute hepatitis, second one as unexplained transaminitis, and third one as cirrhotic. Moreover, cirrhotic one became pregnant and had successful outcome, like other two on timely starting of treatment and continuing as per scientific rationale. Many patients of acute severe hepatitis can land in fulminant hepatic failure but urgent treatment prevents the same, as occurred in our case. Second inference from our case series is that need of immunosuppressive decreases in pregnancy due to it being a immunocompromised state and once post-partum is over, then due to hormonal changes, need of immunosuppressive comes back and same happened in our case. Another inference from our case series is that before labelling any patient as MASH, autoimmune liver disease must be ruled out.

Conclusion- Autoimmune hepatitis can have wide spectrum of presentation like Wilson's diseases and it varies from asymptomatic stage with mild unexplained transaminitis to acute hepatitis, fulminant liver failure and cirrhosis.

INTRODUCTION- Autoimmune liver diseases involve a heterogeneous group of chronic inflammatory disorders, including autoimmune hepatitis, primary biliary cholangitis, and primary sclerosing cholangitis. [1-2] These conditions may present concurrently as an overlapping syndrome, which is characterized by the symptoms of two or more diseases [3-5]. The prevalence of AILD is

increasing, with an annual incidence of 1–2 cases per 100,000 people for each condition [6]. The pathogenesis of autoimmune liver diseases has yet to be fully defined, but it is believed to involve complex interactions between genetic predisposition, immune responses, and environmental factors [7-8]. Evidence of genetic predisposition includes familial clustering, high concordance rates in monozygotic twins, and an increased disease risk among first-degree relatives compared to the general population [9-10]. The etiology of the disease has not yet been clarified. However, a connection with infections with hepatitis, measles, cytomegalo or Epstein-Barr viruses have been discussed. While some patients show no to only mild symptoms, fulminant liver failure can also occur. The most frequent complaints encompass stomach ache, pruritus, nausea, anorexia and general malaise. AIH patients show elevated levels of transaminases and bilirubin as well as an increase in the total IgG titer. In at least 80 % of AIH patients, autoantibodies are also detected. These allow distinction of two AIH types. Delimitation from other chronic forms of hepatitis and consequently a clear diagnosis of AIH is essential since untreated AIH is associated with a five-year mortality rate of 50 %.

CASE SERIES- We report case series of three females who presented differently- one presented as acute hepatitis, second one as unexplained transaminitis and third one as chronic liver disease. All were proven on biochemical tests, serology and liver biopsy. All three had successful outcome with treatment.

CASE 1- We report a case of fifty-two-year-old female, school teacher and a known case of thalassemia minor, moderately built with BMI of 26, presented with sudden onset fatigue, malaise and generalized weakness for last one month. On evaluation, her liver function tests were deranged with severe transaminitis i.e. ALT & AST of 686 I.U./ml and 733 I.U./ml, serum bilirubin was mild increased to 1.55 mg/dl, serum alkaline phosphatase and gamma glutamyl transferase were raised to 192.8 U/l & 96 U/l respectively but total serum proteins and serum albumin were essentially normal. The complete hemogram revealed anemia with hemoglobin of 9.2 gm/dl with normal total leucocytic and platelet count. This anemia was explained on basis of minor thalassemia. The rest renal function tests, serum electrolytes, lipid & thyroid profile, blood sugar, Electrocardiogram, Chest X-ray, urine complete examination, viral screen including HbsAg, anti HCV antibody, anti-HIV antibody, serum IgM HAV & HEV antibody were negative. The ultrasound abdomen showed slightly altered echotexture of liver with wavy outline and mildly prominent portal vein of 12.7 mm. Her upper gastro-intestinal endoscopy showed low grade oesophageal varices and Fibroscan score of 26 Kpa, suggestive of cirrhotic pattern. The triple phase CT scan abdomen also showed early cirrhotic pattern. The autoimmune profile showed strongly positive ANA Hep 2 titers of 1:100 but ASMA, anti LKM1 antibody & ASMA were negative. The serum alpha feto protein levels were also normal. The patient was subjected to liver biopsy which confirmed it to be autoimmune liver disease with classical interface hepatitis. The patient was already on ursodeoxycholic acid (UDCA) and multivitamins from beginning in view of acute hepatitis but transaminitis and serum bilirubin increased. Once diagnosis of autoimmune hepatitis was confirmed, she was put on budesonide 3 mg tid along with azathioprine 50 mg twice daily. Patient responded to treatment and within one month of above treatment, serum transaminases reduced to half and serum bilirubin became normal, her symptoms also decreased substantially. Her UDCA was stopped and immunosuppressive were continued in same dosage for next two months and repeat LFT showed normal liver function tests and clinical symptoms regressed almost completely. Her steroids were tapered and at present she is totally normal and performing her normal duties.

Figure 1- Liver Biopsy Showing Portal inflammation and Interface Hepatitis (H& E stain, 200 X)

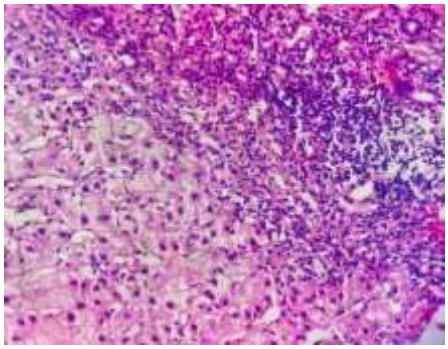


Figure 2- Liver Biopsy Showing Portal Inflammation and Interface Hepatitis (H & E stain, 100 X)

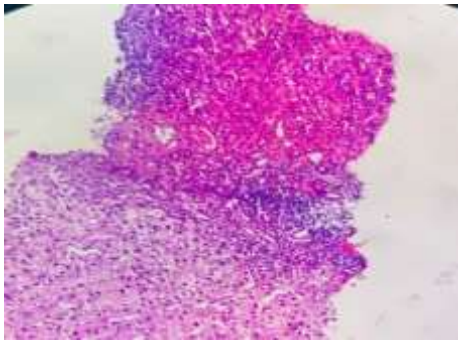


Figure 3- Liver Biopsy Showing Dense lymphoplasmacytic infiltrate in portal triad and peripheral area along with interface hepatitis

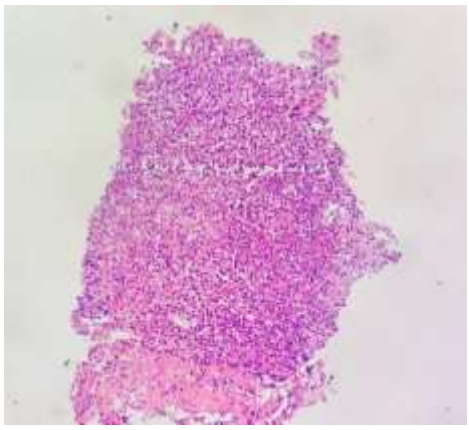


Figure 4- Liver biopsy showing lymphoplasmacytic infiltrate in portal area with interface hepatitis

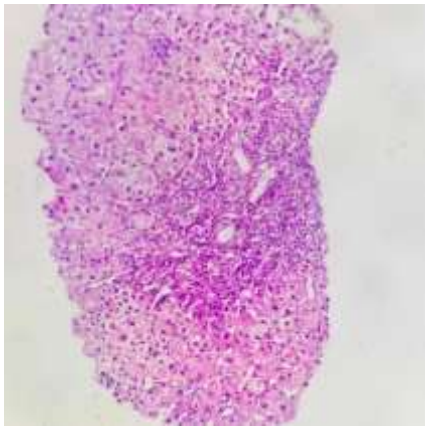
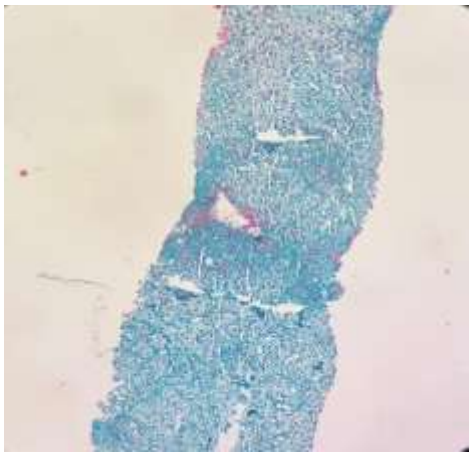


Figure 5- Liver biopsy showing no significant fibrosis in different stain

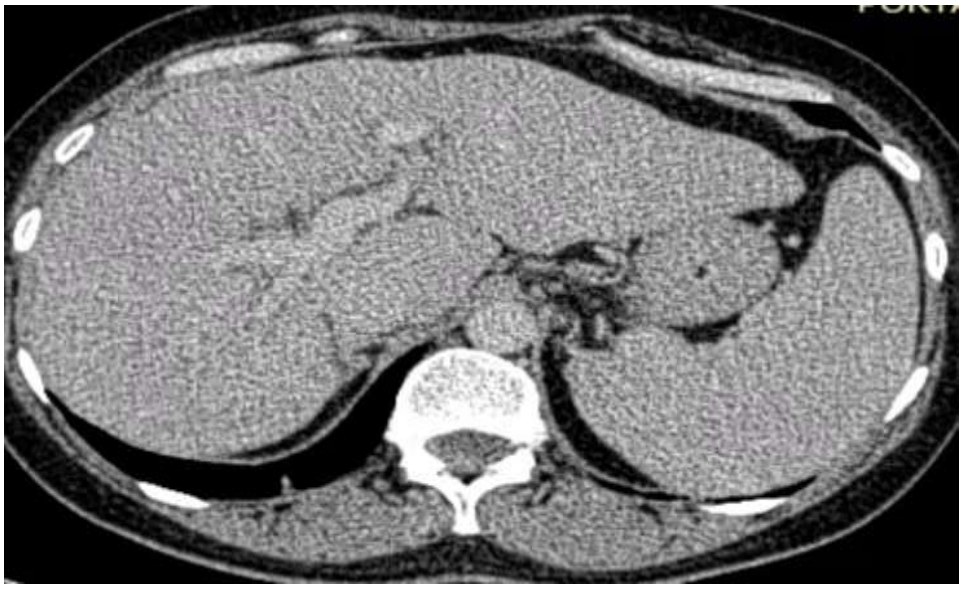
Figure 6- Liver biopsy showing no significant fibrosis in different stain.



CASE 2- A fifty-eight-year-old female, senior nursing officer and not a known case of any chronic illness, moderately built with BMI of 28, presented with persistent dyspepsia symptoms for last two

months. She was put on proton pump inhibitors with pro-kinetic agent. The ultrasonogram abdomen revealed grade 2 fatty liver. On evaluation, her liver function tests were mildly deranged with transaminitis i.e. ALT & AST of 102 I.U./ml and 80 I.U./ml, serum bilirubin was normal, serum alkaline phosphatase and gamma glutamyl transferase were borderline raised to 104 U/l & 68 U/l respectively but total serum proteins and serum albumin were completely normal. The complete hemogram, renal function tests, serum electrolytes, lipid & thyroid profile, blood sugar, Electrocardiogram, Chest X-ray, urine complete examination, viral screen including HbsAg, anti HCV antibody, anti-HIV antibody, serum IgM HAV & HEV antibody were negative. She was started on ursodeoxycholic acid 300 mg tid, thinking on lines of metabolic syndrome associated Steato hepatitis (MASH) but despite two months on treatment, transaminitis persisted. Thus, further evaluation was done. Her upper gastro-intestinal endoscopy was normal and Fibroscan score was 9 Kpa, suggestive of moderate fibrosis. The triple phase CT scan abdomen showed only fatty liver early, as seen on ultrasonogram abdomen. The autoimmune profile showed positive ANA titers of 1:80 but ASMA, anti LKM1 antibody & ASMA were negative. The serum alpha feto protein levels and Wilson's profile were normal. The patient was subjected to liver biopsy which confirmed it to be autoimmune liver disease with classical interface hepatitis. The patient was already on ursodeoxycholic acid (UDCA) and multivitamins from beginning in view of MASH which were stopped and she was put on wysolone 30 mg daily once along with azathioprine 50 mg twice daily. She received wysolone, instead of budesonide due to financial constraints. Patient responded to treatment and within one month of above treatment, serum transaminases became normal. Later on, her wysolone was tapered over next six months and stopped, in view of persistent normal liver function tests but after one month of stopping oral steroids, serum transaminases again increased. Hence, she was started on low dose of wysolone 5 mg daily in addition to azathioprine 50 mg twice daily which she was receiving from starting. She responded to treatment within next two months and serum transaminases became absolutely normal. Now after six months on follow up, on same treatment, she is totally asymptomatic with normal liver function tests.

Figure 7- Triple Phase CT Scan abdomen showing mild altered liver echotexture with wavy margins in Autoimmune Hepatitis Patient



CASE 3- A twenty-five-year-old female, housewife, not a known case of any chronic illness, presented with fatigue and generalized for last few months. She was moderately built with BMI of 24. She was seen by local practitioner who got routine biochemical tests and ultrasonogram abdomen. The ultrasonogram abdomen revealed cirrhosis of liver with splenomegaly and increased portal vein diameter, suggestive of portal hypertension. On biochemical evaluation, liver function tests were mildly deranged with transaminitis i.e. ALT & AST of 80 I.U./ml and 68 I.U./ml, serum bilirubin was normal, serum alkaline phosphatase and gamma glutamyl transferase were borderline raised to 92 U/l & 58 U/l respectively, total serum proteins (6.2 gm/l) and serum albumin (2.8 gm/l) were low. The complete

hemogram revealed pancytopenia with hemoglobin level of 9.6 gm/dl, total leucocyte counts of 4500/mm3 and platelet count of one lakh/mm3. The complete lipid profile was below normal which was suggestive of cirrhotic pattern. The renal function tests, serum electrolytes, thyroid profile, blood sugar, Electrocardiogram, Chest X-ray, urine complete examination, viral screen including HbsAg, anti HCV antibody, anti-HIV antibody, serum IgM HAV & HEV antibody were normal. Her upper gastro-intestinal endoscopy revealed grade 2 oesophageal varices. Fibroscan score was 29 Kpa, suggestive of cirrhotic pattern. The triple phase CT scan abdomen confirmed findings of cirrhosis of liver with splenomegaly, portal hypertension and collaterals. The autoimmune profile showed positive ANA titers of 1:120 but ASMA, anti LKM1 antibody & ASMA were negative. The serum alpha feto protein levels and Wilson's profile were normal. The patient was subjected to ultrasound guided liver biopsy which confirmed it to be autoimmune liver disease with classical interface hepatitis. The patient was put on wysolone 30 mg daily, azathioprine 50 mg twice daily and tablet Carvedilol 3.125 mg twice daily, in addition to supportive therapy with multivitamins and calcium & vitamin D3 combination. She received wysolone, instead of budesonide due to financial constraints. Patient responded to treatment and within two months of above treatment, serum transaminases became normal and clinical symptoms got relieved. Later on, she became pregnant and his immunosuppressive were tapered and stopped. There were no complaints during pregnancy and routine biochemical labs remained well under control. She underwent caesarean section at term due to fetal distress. She was discharged on fifth post-operative day and new born was asymptomatic, accepting breastfeeding normally. After post-partum period, his transaminases started to increase with mild hyperbilirubinemia, hence she was restarted on low dose wysolone 20 mg daily once, along with tablet azathioprine 50 mg twice daily with carvedilol 3.125 mg twice daily with symptomatic multivitamins and calcium +vitamin D3 combination. She again responded to treatment and LFT became normal on follow up after one month. Now after four months on follow up, on same treatment, she is totally asymptomatic with normal liver function tests.

DISCUSSION - Hepatocellular necrosis and inflammation are the hallmarks of autoimmune hepatitis (AIH), a chronic, progressive immune- mediated liver disease that can lead to fibrosis and, ultimately, cirrhosis. It is a multifactorial illness, with a prevalence three times higher in females than in males, often followed by other autoimmune disorders such as vitiligo, insulin-dependent diabetes, nephrotic syndrome, urticaria pigmentosa, haemolytic anemia, idiopathic thrombocytopenia, and celiac disease [11]. A diagnosis of AIH can be confirmed according to certain criteria: female preponderance, elevated levels of immunoglobulin G (IgG), the presence of autoantibodies, and pathohistological verification suggesting interface hepatitis—laboratory findings that suggest fluctuations in a patient's aminotransferase level. There are two types of autoimmune hepatitis i.e. AIH-1 & AIH-2 and both have different presentation. AIH-2 has an earlier age of onset, present with fulminant hepatic failure and is connected with IgA deficiency, while AIH-1 is associated with a more subtle beginning, with symptoms such as malaise, fatigue and arthralgia; however, a significant number of patients are asymptomatic and only exhibit increased transaminase levels after biochemical screening [12-14]. Severe AIH is life threatening condition, hence merits rapid diagnosis and institution of immunosuppressive therapy. Despite successful treatment, cirrhosis can develop in many patients, being often already present at time of the diagnosis. The therapy is, however, still useful because it can reduce the activity of the disease [15]. Immunosuppressive treatment may be considered in asymptomatic adult patients with mild laboratory and histological changes, but the decision must be individualized and balanced against the possible side effects of the therapy.7Patients with minimal or no disease activity or in-active cirrhosis should not be treated, but must continue to be followed closely, i.e., 3-6 months [16]. Our case series of three patients have different presentations- one presented as severe acute hepatitis, second one as unexplained transaminitis, and third one as cirrhotic. Moreover, cirrhotic one became pregnant and had successful outcome, like other two on timely starting of treatment and continuing as per scientific rationale. Many patients of acute severe hepatitis can land in fulminant hepatic failure but urgent treatment prevents the same, as occurred in our case. Second inference from our case series is that need of immunosuppressive decreases in pregnancy due to it being a immunocompromised state and once post-partum is over, then due to hormonal changes, need of immunosuppressive comes back and same happened in our case. Another inference from our case series is that before labelling any patient as MASH, autoimmune liver disease must be ruled out.

CONCLUSION- Autoimmune hepatitis can have wide spectrum of presentation like Wilson's diseases and it varies from asymptomatic stage with mild unexplained transaminitis to acute hepatitis, fulminant liver failure and cirrhosis. Hence early diagnosis and initiation of treatment play significant role in successful outcome.

CONFLICT OF INTEREST- No conflict of interest and prior permission from patient and relatives was taken before publishing the case report.

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