Autoimmune Hepatitis –SLE Overlap Syndrome

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Abstract
Autoimmune hepatitis also known as Lupoid hepatitis is an autoimmune liver disease characterized by the presence of autoantibodies including antinuclear antibodies (ANA) and hypergammaglobulinemia. SLE can be associated with hepatitis, which is referred to as lupus hepatitis. It is important to distinguish these two entities, as the course of the disease is different in both. It has also been noted that these two entities can co-exist when it is referred to as Autoimmune hepatitis-SLE overlap syndrome. We are reporting a case of Autoimmune hepatititis-SLE overlap syndrome in a 30 years old lady.

Introduction
Differentiating the hepatic involvement in Systemic lupus Erythematosis (SLE) and Autoimmune Hepatitis (AIH) has been challenging, as there are similarities in the clinical features and the biochemical parameters in both these entities. AIH is also known as Lupoid hepatitis, which is an autoimmune liver disease, caused by the presence of autoantibodies, including antinuclear antibodies (ANA) and hypergammaglobulinemia.

SLE can also have accompanying liver disease referred to as lupus hepatitis though it is rare. We are reporting a case of Autoimmune hepatitis- SLE overlap syndrome. This patient fulfilled the American College of Rheumatology (ACR) criteria for SLE and was proved to have AIH on liver biopsy.

Case Report
30 years old lady presented to our hospital with yellowish discoloration of sclera and abdominal distention for 1month. She was initiated on anti tubercular treatment for tuberculous lymphadenitis, 10 months prior to admission. She discontinued the medicines after 4 months as she developed jaundice following which her jaundice subsided. She also gave history of multiple blood transfusions in the past for anaemia. There was no history of obvious blood loss.

Clinical examination revealed icterus, pallor, clubbing, cervical lymphadenopathy and ascitis. There were no peripheral signs of liver cell failure. Probable diagnoses considered on her were Disseminated tuberculosis/ autoimmune hepatitis.

Investigations revealed anaemia (Hb 7g%), leucopenia with lymphopenia (TLC 3700/mm3, ALC 980/mm3), deranged PT and PTTK, direct hyperbilirubinemia and raised transaminases. Ascitic fluid examination was transudative. USG Abdomen showed liver cirrhosis with portal hypertension and ascitis. We further evaluated the patient for the various causes of liver cirrhosis.HBsAg and HCV Ag were not detected in serum. HEVAg was positive. KF rings were absent on slit lamp examination.

Prominent esophageal vein was noted on endoscopy. CT abdomen revealed nodular liver, dilated portal vein, multiple lymph nodes measuring 21x 12 mm in the mesentry, portal and aortocaval areas, ascitis and B/L pleural effusion.

Cervical lymph node biopsy and bone marrow aspiration were done considering a possibility of disseminated tuberculosis or lymphoma. Lymph node biopsy was reported as necrotizing lymphadenitis. Bone Marrow examination revealed plasmacytosis of 10-20 % with normal cell lines.

Serum protein electrophoresis revealed M band in γ region. IgG was1100 U/ml (650-1500), IgA was 488U/ml (50-450) and IgM was 260U/ml(24-332). ANA and AntiDsDNA were strongly positive [ANA 42.6 U/ml(0-1.4 ), AntiDsDNA 213 U/ml (0-40)] with decreased C3 and C4.

A diagnosis of SLE was made as she fulfilled ACR criteria. (Presence of ANA, AntiDsDNA, lymphopenia and serositis). Necrotizing lymphadenitis was attributed to SLE. However her advanced liver cell failure could not be explained by SLE alone. Hence we considered a possibility of Autoimmune Hepatitis – SLE overlap syndrome.

Meanwhile patient’s general condition worsened and she progressed to grade 4 encephalopathy. She was pulsed with methylprednisolone followed by oral prednisolone. However her general condition kept worsening and she succumbed to her illness eventually.

Postmortem liver biopsy was done which revealed large areas of necrosis and fibrosis replacing the normal lobular architecture. Liver cells were cord like and regenerative rosettes were present at other places. Macroversicular and micro vesicular steatosis with intense lymphoplasmacytic infiltrates was present in the fibrotic area. These findings were consistent with autoimmune hepatitis with submassive necrosis. So the final diagnosis was confirmed as Autoimmune Hepatitis-SLE overlap syndrome.

Discussion
Autoimmune Hepatitis (AIH) also known as Lupoid hepatitis is an autoimmune liver disease caused by the presence of auto antibodies, including antinuclear antibodies (ANA) and hypergammaglobulinemia. Systemic Lupus Erythematosis (SLE), which is an autoimmune disorder affecting multiple organs can have accompanying liver disease, which is also referred to as lupus hepatitis.

The difference between the hepatic involvement in SLE and AIH has not been clearly defined due to similarities in the clinical and biochemical features. Liver involvement in patients with SLE is well documented but is considered rare. It has been suggested that patients with AIH may be at an increased risk of developing systemic connective tissue diseases. Conversely, patients with systemic connective tissue disease may be at an increased risk of AIH. Therefore it is important to distinguish AIH from SLE since complications are different in the two conditions. SLE may result in end stage renal disease while AIH may lead to end stage liver disease.

Even though hepatic lesions due to pathogenic process of SLE have been thought to be rare; recent studies have indicated that liver involvement in patients with SLE is of a more significant importance than had been thought. The difference between AIH and hepatic lesions in SLE has long been an indistinct issue. Oka

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reported that 3% of patients with AIH satisfied the ACR criteria for SLE. Matsumoto et al., who surveyed 1,468 Japanese patients with SLE reported that only 1.1% of them had liver cirrhosis.

AIH-SLE overlap syndrome is considered when patients fulfill the ACR criteria for SLE and International Autoimmune Hepatitis group scoring for AIH. Although AIH and SLE are considered two different entities, both have features of an autoimmune disease with presence of various antibodies. However, histopathologically, they are quite distinct. Periportal piecemeal necrosis associated with lobular activity, rosetting of liver cells or dense lymphoid infiltrates is prominent in AIH, whereas in SLE, inflammation is usually lobular and occasionally periportal with paucity of lymphoid infiltrates.

Our patient fulfilled the ACR criteria for SLE. Her scoring as per the international Autoimmune Hepatitis group was 10. Her lower score was attributed to unavailability of other autoimmune antibodies and HLA typing. She also had Hepatitis E co-infection; which also contributed to negative scoring. However, the hepatotropic viruses are known triggers for AIH. In our patient, Hepatitis E virus infection would have been the trigger. However, rosetting of liver cells and dense lymphoplasmacytic infiltrate in our patient was consistent with AIH. The generalized lymphadenopathy in our patient involving cervical, mesenteric, portal, and aortocaval lymph nodes were attributed to SLE, as the biopsy was consistent with necrotizing lymphadenitis. The stormy course with liver cell failure was quite characteristic of AIH.

Antiribosomal P antibody is a useful marker to differentiate SLE associated hepatitis from AIH. Anti Sm antibodies are highly specific though relatively insensitive to SLE.

Corticosteroid therapy is the mainstay of therapy. Immunosuppressants like Azathioprine, mycophenolate mofetil, cyclosporine, and tacrolimus also have shown promising results.

**Conclusion**

Patients presenting with AIH-SLE overlap impose diagnostic and therapeutic dilemma on the physician. It is important to distinguish SLE-associated hepatitis (lupus hepatitis) from AIH associated with SLE since the course of the disease is different in both the entities.

Most of the biochemical parameters are inconclusive in differentiating the two entities. However, Liver biopsy is diagnostic.

**References**