

AUTOIMMUNE HEPATITIS AS INITIAL PRESENTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

Synopsis: This is a case of a 24 year old female with a strong family history of SLE who presented with autoimmune hepatitis and was eventually diagnosed to have SLE.

Clinical presentation: Two months history of intermittent jaundice, tea colored urine, anorexia, easy fatigability, pruritus, colicky right upper quadrant pain, intermittent diarrhea.

Physical findings: Normal Vital signs, fever of 38.3°C, jaundice, facial and bipedal edema, some tenderness over the right upper abdomen, no organomegaly.

Laboratory work up: hemoglobin of 72g/L, Serum bilirubin 26.4U/L, ALT 281U/L, AST 355U/L, alkaline phosphatase 275U/L, albumin 2.9mg/dL, globulin 4.2mg/dL. C3 0.62g/L, negative serology for viral hepatitis, urinalysis: urine protein 3+ (0.9g/24hours), RBC loaded/hpf, WBC 4-8/hpf, hyaline and granular casts. ANA 1:2560 speckled, anti-dsDNA 34.3IU/ml, moderately positive anti-Ro/SSA, anti-cardiolipin antibodies-negative.

Diagnosis: Systemic Lupus Erythematosus

Treatment: Prednisone and supportive therapy

Outcome: Improvement of hemoglobin, urinalysis, serum bilirubin, liver enzymes, serum creatinine levels 4 weeks after initiation of treatment.

Significance: This case illustrates SLE presenting as autoimmune hepatitis.

Recommendation: SLE should be considered in hepatitis when viral etiology has been ruled out.

Keywords: Autoimmune hepatitis, lupus hepatitis, systemic lupus erythematosus

INTRODUCTION

Systemic lupus erythematosus (SLE) presents in many ways, and can affect multiple organs including the liver. However, autoimmune hepatitis as a concomitant disease or a first manifestation of SLE is rare. In a prospective study of 260 SLE patients, 23% patients were found to have elevated liver enzymes and 8% may have been due to SLE itself.¹ We report a patient who presented with autoimmune hepatitis (AIH) prior to a full serologic diagnosis of SLE.

Case Report

A 24 year old female presented with a 2 month history of waxing and waning jaundice, tea colored urine, anorexia, easy fatigability and generalized pruritus. She also complained of intermittent diarrhea and colicky pain on the right upper abdominal quadrant; anti-spasmodics temporarily provided relief. Two months later, because of worsening jaundice and development of fever, she was admitted to the hospital.

There was no alopecia, oral ulcers, malar rash, discoid rash, nor photosensitivity. She never smoked, drank alcoholic beverages nor engaged in illicit drugs. There is no history of blood transfusion. Her mother died of cardiac complications of systemic lupus erythematosus (SLE) at age 42 years old. A younger sister has been on treatment for SLE with pulmonary hypertension in the last 4 years.

Physical examination showed a conscious, coherent patient with normal vital signs, except for a temperature of 38.3°C. She had icteric sclerae, generalized jaundice, facial and bipedal edema. The

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abdomen was soft with some tenderness over the right upper quadrant; there was no organomegaly. The rest of the physical examination was unremarkable. Laboratory tests showed hemoglobin of 72 g/L, white cell count (WBC) 9.2×10^9 /L, hypochromic red blood cells (RBC) with anisocytosis and poikilocytosis. Serum bilirubin was elevated at 26.4 U/L (indirect 8.2 U/L; direct 18.2 U/L), alanine aminotransferase (ALT) 281 U/L, aspartate aminotransferase (AST) 355 U/L, and alkaline phosphatase 275 U/L. Total protein was 7.1 mg/dl, serum albumin 2.9 mg/dl and globulin 4.2 mg/dl with an A/G ratio of 0.69, serum creatinine was elevated at 7.7 mg/dl. Arterial blood gases reported compensated metabolic acidosis, electrolytes were normal. Urine protein was 3+ (0.9 g/24 hours), RBC loaded/hpf, WBC 4-8/ hpf, with hyaline and granular casts. Serum complement (C3) was low at 0.62 g/L (NV 0.9-1.8). Serologies for viral hepatitis were all negative. Abdominal ultrasound showed normal liver, spleen and pancreas, with diffuse parenchymal changes of both kidneys; chest x-ray was normal. Further tests for autoantibodies disclosed high titer anti-nuclear antibody (ANA) 1:2560 with speckled pattern, anti-double stranded DNA at 34.3 IU/mL (normal value < 5 IU/mL), and moderately positive anti-Ro/ SSA; anti-cardiolipin antibodies (IgG and IgM) were negative.

The patient was started on prednisone 60 mg/day, plus supportive therapy. There was dramatic improvement, with prompt resolution of the fever and edema, lessening jaundice and a general sense of well-being. The hemoglobin, urinalysis, serum bilirubin, liver enzymes, as well as serum creatinine levels all returned to normal 4 weeks after initiation of therapy, and the prednisone was gradually tapered to 10 mg/day. She remained well on clinic visit 3 months later.

DISCUSSION

The clinical data fulfilled a diagnosis of probable autoimmune hepatitis (AIH) with a score of 15 based on the criteria of the International AIH Group² (Table I). Notably, this relatively high score was obtained despite the absence of testing for gamma globulin or IgG level, anti-mitochondrial antibodies (AMA), HLA, other markers (Anti-SLA/LP, actin, LC1, pANCA), and liver biopsy. A concomitant diagnosis of SLE was also made, having met at least 4 of the 11 criteria by the American College of Rheumatology (ACR) classification criteria for SLE.^{3,4}

Table I. International Scoring System for Diagnosis of AIH²

Sex	Female	+2	HLA	DR3 or DR4	+1
AP:AST (or ALT) ratio	> 3 < 1.5	-2 +2	Immune disease/first degree relative	Yes No	+2 0
Gamma-globulin or IgG level above normal	> 2.0 1.5-2.0 1.0-1.5 < 1.0	+3 +2 +1 0	Other markers	Anti-SLA/LP, actin, LC1, pANCA	+2
ANA, SMA, or anti-LKM1 titers	> 1:80 1:80 1:40 < 1:40	+3 +2 +1 0	Histologic features	Interface hepatitis Plasmacytic Rosettes None of above Biliary changes Other features	+3 +1 +1 -5 -3 -3
AMA	Positive	-4	Treatment response	Complete Relapse	+2 +3
Viral markers	Positive Negative	-3 +3			
Drugs	Yes No	-4 +1	Pretreatment score Definite diagnosis: > 15 Probable diagnosis: 10-15		15
Alcohol	< 25 g/day > 60 g/day	+2 -2	Posttreatment score Definite diagnosis: > 17 Probable diagnosis: 12-17		17

Autoimmune hepatitis (AIH) is a generally progressive, chronic hepatitis of unknown cause that occurs in children and adults of all ages. It may have a fluctuating course, with periods of increased or decreased activity. The diagnosis is based on characteristic clinical and biochemical findings, histological abnormalities, and abnormal levels of serum globulins, including autoantibodies.⁵ Pathogenesis of this disease is believed to be due to environmental agents that trigger a cascade of T cell-mediated events directed at liver antigens in a host genetically predisposed to this disease, leading to a progressive necro-inflammatory and fibrotic process in the liver. Susceptibility to AIH is reportedly associated with tumor necrosis factor (TNF) genes, the loci of which are in the class III region of the major histocompatibility complex (MHC), although this finding has been disputed.⁵

Though rare, AIH has been found in patients with SLE.⁶⁻⁹ The incidence of AIH in SLE patients is unclear because not all patients will have diagnosis confirmed by liver biopsy. Pistiner *et al.* found evidence for autoimmune hepatitis among 22 of 464 patients with SLE (4.7%) who fulfilled the ACR

criteria for SLE.¹⁰ Another study reported 4 out of 131 (3%) SLE patients had a clinical picture of chronic active hepatitis. There was no evidence for viral infection and only 1 patient had low-titer smooth muscle antibodies (SMA), however SLE patients with AIH were more likely to have autoantibodies against dsDNA, Sm, ribosomal P compared to SLE patients without AIH.¹¹ In our case, the suspicion of SLE was definitely strengthened by the strong family history of SLE in the mother and sister.

Patients with AIH usually present with nonspecific symptoms of fatigue, malaise, and anorexia. Jaundice is present in fulminant hepatitis.¹² In SLE, nonspecific liver enzyme elevations are seen in a minority of patients and usually are of little significance. Liver function tests usually are obtained incidentally as part of blood chemistry panel and most of the liver function abnormalities in SLE result from the administration of aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), azathioprine or methotrexate, or because of increased muscle enzyme levels.^{12,13} Pathologic changes also are nonspecific and mild.¹²

Autoimmune hepatitis (lupoid hepatitis) is a form of chronic active hepatitis presenting with malaise, arthralgia, fever, anorexia, jaundice, and negative viral hepatitis studies. Anti-mitochondrial and anti-SMA are often present, along with abnormalities associated with SLE, such as LE cell, and ANA. Most of these patients should be classified as being a subset of chronic active hepatitis, since only 10% fulfill the ACR criteria for SLE. Biopsy findings include piecemeal necrosis and are identical to chronic active hepatitis B and C.¹²

Laboratory tests in AIH shows elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) usually less than two to threefold but in severe cases up to a ten-fold elevation, with mild increase in alkaline phosphatase and bilirubin. In our case, the ratio of AST/ALT was 1.26, which distinguishes it from viral hepatitis (where ALT is higher or at least similar to AST and both of them usually more than 500 U/L), or from alcoholic hepatitis (AST/ALT ratio =2, with AST level not exceed than 300 U/L).¹⁴

The therapy of lupus hepatitis remains high dose prednisone alone or a lower dose prednisone in conjunction with azathioprine, which is the mainstay treatment of AIH.^{13,15} Remission can be achieved in the majority of patients within the first 3 years of diagnosis. Maintenance therapy with low dose prednisone and azathioprine is preferred for patients with multiple relapses.¹³

The prognosis of AIH varies depending on the patients included in the survey. The 5 year survival was reported by Mackay to be 65% in 1968 but 80% in 1988 with prednisone and azathioprine therapy.^{16,17}

CONCLUSION

This case illustrates a rare presenting manifestation of SLE as autoimmune hepatitis. Although the strong family history prompted further work-up for SLE, it is important to consider SLE in hepatitis when viral etiology has been thoroughly ruled out.

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