

## LIVER CIRRHOSIS FROM AUTOIMMUNE HEPATITIS IN A NIGERIAN WOMAN: A CASE REPORT

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### ABSTRACT

**Autoimmune hepatitis (AIH) is a rare cause of chronic liver disease (CLD). It presents with varied clinical features from acute hepatitis to CLDs like chronic viral hepatitis and alcoholic liver disease, making it difficult to diagnose in the absence of a high index of suspicion and adequate laboratory support. Autoantibody-mediated hepatocyte injury is the major feature of AIH.**

**We present a 44 year old woman with recurrent jaundice, ascites, splenomegaly, coagulopathy, negative chronic viral hepatitis screening, elevated IgG and positive anti-smooth muscle antibody. The patient responded well to immunosuppressive therapy.**

**This report brings to the fore the need for physicians to maintain a high index of suspicion and thoroughly evaluate all CLD cases of seemingly 'unknown' etiology for AIH in order to prevent progression to end-stage-liver-disease, since the disease is highly amenable to immunosuppressive therapy.**

**Keywords:** Autoimmune hepatitis, Autoimmune liver disease, Chronic liver disease, Nigeria

### INTRODUCTION

Autoimmune hepatitis (AIH) is a non-contagious chronic inflammatory disease that results from autoantibody-mediated hepatocyte injury. Autoimmune hepatitis, primary biliary cirrhosis and primary sclerosing cholangitis are together classified as autoimmune liver disease.<sup>1</sup>

AIH is classified into different types on the basis of the serum autoantibody profiles. The common denominator for all the types is the presence of hypergammaglobulinemia, precisely IgG.<sup>2</sup> Type 1 AIH is defined by the presence of antinuclear antibody (ANA), anti-smooth muscle antibody (Anti-SMA), or both and constitutes 80% of AIH cases.<sup>2</sup> It is also commonly associated with other autoimmune diseases like autoimmune thyroiditis, celiac disease and ulcerative colitis, with about 25% having cirrhosis at presentation.<sup>2</sup> Type 2 AIH is characterized by the presence of anti-liver kidney microsomal (Anti-LKM) 1 and/or anti-LKM 3 and/or anti-liver cytosol 1 (Anti-LC1) antibodies.<sup>2</sup> It is commoner in children, acute severe presentation does occur, and progression to cirrhosis commonly follows.<sup>2</sup>

The diagnosis of AIH is usually suspected when ongoing hepatocellular inflammation cannot be

explained on the basis of chronic viral infection, alcohol consumption, or exposure to hepatotoxic medications or chemicals.<sup>2</sup> As such, it is often a diagnosis of exclusion.

The incidence, prevalence and characteristics of AIH vary in different geographical regions. On a general note, it has a mean incidence of 1-2 per 100,000 and a point prevalence of 11-17 per 100,000.<sup>2</sup> It is commoner in women (especially young women) than men with a ratio around 4:1 but it occurs in all age groups, races and geographical areas.<sup>2-5</sup> The exact prevalence of the disease is not known in Nigeria as most studies on CLD focused on viral hepatitis, alcoholic liver disease and hepatocellular carcinoma. Only one case report of AIH in Nigeria was found in our literature search.<sup>6</sup> A case of a 9-year-old girl with co-occurring wild-type chronic hepatitis B and antinuclear antibody-positive autoimmune hepatitis was reported in Senegal, a West African country.<sup>7</sup> We present a young woman with liver cirrhosis that resulted from autoimmune hepatitis. The rarity of the disease, as well as the scarcity of reported cases in Nigeria, necessitated this effort.

## CASE REPORT

A 44-year-old woman with a 4-week history of jaundice was referred to our clinic for evaluation. She was initially being evaluated for obstructive jaundice by a Gastrointestinal Surgeon in our hospital before the referral.

She had a history of dark color urine and pruritus which was limited to the extremities for which she was given cholestyramine by the referring doctor. She no longer had pruritus at the time she presented at our clinic despite having stopped taking cholestyramine. There was abdominal pain but no fever or passage of pale stool. No history of vomiting, diarrhea, or abdominal swelling. No history of blood transfusion, intravenous drug abuse, surgery or multiple sexual partners. Her hemoglobin genotype is AA. She had a similar history of jaundice 7 months before her presentation to us which resolved after receiving unspecified treatment at another facility. She was not previously diagnosed with any chronic illness.

She is the fifth of five children in a polygamous family setting. She has five children. No family history of a similar illness.

On physical examination, she was cachectic, deeply jaundiced but not pale. She had bilateral pitting pedal edema. The liver span was 8cm by percussion. She had moderate ascites, the blood pressure was normal but there was tachycardia (pulse was 112 per minute). The remainder of the examination was normal.

An abdominal ultrasound scan at our facility showed a normal sized liver (12.6cm) with mildly accentuated echotexture. The intrahepatic ducts and the biliary tree were within normal limits. The spleen was enlarged (14.4cm) with normal echogenicity, both kidneys were normal in shape, size and outline, and there was moderate ascites.

Viral markers of hepatitis B and C (HBsAg, HBeAg, Anti-HBe, Anti-HBc total, and Anti-HCV) were negative. The results of other laboratory tests are as depicted in Table 1.

A diagnosis of liver cirrhosis secondary to autoimmune hepatitis was made at the end of the evaluation. She was commenced on 60mg of Prednisolone which was to be tapered off to 20mg over 4 weeks. She unilaterally stopped the Prednisolone 12 days after commencement because she developed facial swelling. At clinic presentation after the stoppage of Prednisolone, jaundice had cleared. She was later placed on Budesonide 3mg TID and Azathioprine 50mg daily. Budesonide was discontinued after 4 weeks. She also had oral spironolactone, furosemide and propranolol in the course of treatment. She is currently on only Azathioprine 50mg daily.

One year since commencement of treatment, she is stable with no jaundice, ascites or pedal edema. She has also gained some weight despite the loss of previously accumulated fluid. Her weight at first presentation was 45kg while her current weight is 49kg.

**Table 1:** Results of relevant laboratory tests of a Nigerian female with autoimmune hepatitis

Tests	Before Treatment	After one year of treatment
ALT (0-22 IU/L)	347 IU/L	18 IU/L
AST (0-18 IU/L)	162 IU/L	13 IU/L
ALP (0-35 IU/L)	-	18 IU/L
Total Bilirubin (up to 20umol/L)	272 umol/L	45 umol/L
Conjugated Bilirubin (up to 5umol/L)	250 umol/L	21 umol/L
Total Protein (58-80g/L)	101g/L	71g/L
Albumin (35-50g/L)	36g/L	45g/L
Platelet	122,000/mm <sup>3</sup>	
Prothrombin Time	Test-24s; Control-16s	Test-17s; Control- 16s
INR	1.54	1.06
Urine Bilirubin	+	-
HBsAg	Negative	Negative
HBV-DNA	Undetectable	-
ANA	Negative	-
SMA	Positive	-
Serum IgG (700-1600)	2230mg/dl	-
Alfa fetoprotein	81.7ng/ml	-

## DISCUSSION

Autoimmune hepatitis is a chronic inflammatory disease of unknown etiology that is characterized by the presence of hypergammaglobulinemia, circulating autoantibodies, necroinflammatory changes on hepatic histology and a dramatic response to immunosuppressive therapy.<sup>2,8</sup>

The exact pathophysiologic mechanism of AIH is unknown.<sup>5</sup> The dominant hypothesis is that AIH is a disease that develops in a genetically predisposed person, who is also exposed to environmental triggering factors.<sup>2,5,8</sup> Subsequently, the autoimmune attack is perpetuated possibly via molecular mimicry and is favored by the impaired control of regulatory T-cells.<sup>2,5,8</sup> Several triggers have been identified which include- drugs, viral antigens (hepatitis A, B and C) and herbal agents.<sup>2</sup>

The clinical manifestation of AIH can range from asymptomatic, acute hepatitis and rarely to fulminant hepatic failure, chronic hepatitis or well-established cirrhosis. About 25–34% may be asymptomatic.<sup>2</sup> However, asymptomatic patients commonly become symptomatic and thus need to be monitored.<sup>2</sup>

The immunologic tests that are indispensable for the diagnosis of AIH are serum ANA, SMA, anti-LKM1 and IgG.<sup>2,5,8</sup> Other immunological tests that may be relevant include anti-actin antibody, anti-LKM3, anti-liver cytosol 1, perinuclear antineutrophil cytoplasmic antibodies (pANCA), and antibodies to soluble liver antigen (SLA) or liver pancreas antigen (LP).<sup>2,5,8</sup>

The case at hand had features of chronic hepatocyte inflammation as evidenced by the moderate elevation of the transaminases, lower limit serum albumin and high total protein (indicating hypergammaglobulinemia). Although the patient had a negative ANA, the presence of elevated serum IgG and a positive SMA is enough to diagnose AIH, precisely type 1, in a patient that had no history of alcohol ingestion and any serological marker of hepatitis B and C. The initial dramatic response to prednisolone therapy was quite encouraging despite the adverse effect. More reassuring is the fact that the patient's albumin had improved significantly; the globulin component of the total protein, ALT, AST and INR have normalized and the bilirubin levels nearing normal after one year of immunosuppressive therapy (Table 1).

The presence of conjugated hyperbilirubinemia and the initial pruritus could have caused a diagnostic dilemma but the disappearance of the pruritus even after cholestyramine was stopped and the finding of a normal biliary tree on abdominal ultrasonography

were reassuring. AIH may have cholestatic features that can resemble primary sclerosing cholangitis or primary biliary cirrhosis and overlap with these diseases have been described in 10%-20% and 2%-8% of cases, respectively.<sup>5</sup>

Features like past history of jaundice, pedal edema, ascites, coagulopathy, splenomegaly and coarsened liver on ultrasound in this patient all indicate that the disease was long standing and that she had developed liver cirrhosis. While a histological finding of interface hepatitis is desirable in the diagnosis of AIH, liver biopsy could not be performed on this patient because of coagulopathy at the time of evaluation.

Anti-inflammatory or immunosuppressive therapy has been the mainstay of treatment of both type 1 and type 2 disease.<sup>2,5</sup> When treated adequately, the 20-year survival rate for all treated patients exceeds 80%, and life expectancy is similar to that of age and sex-matched normal subjects from the same geographical area.<sup>2,5</sup> The treatment is divided into two phases: (i) induction of remission, and (ii) remission maintenance.<sup>2,5,9</sup> Prednisolone monotherapy and Prednisolone in combination with Azathioprine (AZA) are alternative induction therapies for AIH; for maintenance, Prednisolone in combination with AZA and AZA monotherapy are superior to Prednisolone monotherapy.<sup>2,5,9</sup> The combination therapy has an advantage in the reduction of Prednisolone related side effects. Budesonide may be used as an alternative to Prednisolone in order to reduce steroid specific side effects.<sup>2,5,9</sup> We opted for the Budesonide/AZA therapy because our patient reacted to the Prednisolone monotherapy.

Remission of previously symptomatic patients is defined as a complete normalization of all inflammatory parameters, including AST, ALT, bilirubin, IgG, recovery from symptoms and inactive liver histology for at least 2-3 years.<sup>9</sup> Some patient could relapse after cessation of therapy. The ideal thing to do after the first episode of relapse is to use a Prednisolone/AZA combination therapy.<sup>2</sup> Alternative therapies for subsequent relapse include tacrolimus, mycophenolate mofetil, cyclosporine, methotrexate, cyclophosphamide, ursodeoxycholic acid, infliximab and rituximab. Although there are some encouraging results with each of the medications, the treatments have not been standardized due to lack of randomized controlled trials' data.<sup>2,3</sup>

Liver transplantation is the ultimate rescue treatment for all liver diseases but has only a minor role in AIH.<sup>9</sup> Approximately 4% of liver transplantations in both the US and Europe are due to AIH.<sup>9</sup> The cornerstone

of AIH management is, in fact, the avoidance of liver transplantation by timely diagnosis and adequate immunosuppressive therapy.<sup>9</sup> Liver transplantation is, however, required in patients who are refractory to or intolerant of immunosuppressive therapy and in whom end-stage liver disease develops.<sup>2,5,9</sup>

## CONCLUSION

To the best of our knowledge, this is the second case report of AIH in Nigeria. There is a need to maintain a high suspicion index for the disease and to thoroughly evaluate all CLD cases of apparently unknown etiology for AIH in order to prevent progression to end-stage-liver-disease, since AIH is highly responsive to immunosuppressive therapy.

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