CASE REPORT

A Rare Case of Autoimmune Hepatitis Overlapping with Autoimmune Haemolytic Anaemia and Immune Thrombocytopenic Purpura in a Male Patient

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INTRODUCTION

Autoimmune hepatitis (AIH), which predominantly affects women and usually responds to immunosuppressive therapy, is a disease characterized by hypergammaglobulinemia, increased titers of serum tissue autoantibody, and an immunogenetic background. This disease can present with a variety of coexisting non-hepatic disorders presumably caused by immune dysregulation. Here we present a male AIH patient with coexisting Idiopathic thrombocytopenic Purpura (ITP) and Autoimmune Hemolytic Anemia (AIHA) which is rarely reported.

CASE REPORT

Mr.K is a 46 year old ambulance driver, with no known medical illnesses. He was admitted to our hospital for evaluation of his progressive jaundice of 3 weeks duration and thrombocytopenia. He denied having fever, vomiting, loss of appetite or loss of weight. He does not consume alcohol and denied any history of blood transfusion in the past or illicit drug usage. He admitted taking capsules of Tongkat Ali and traditional "Viagra" which he bought in a night market one month prior to his admission. He had no family history of liver disease or autoimmune diseases.

On clinical examination, he was deeply jaundiced, no stigmata of chronic liver disease, and no features of hepatic encephalopathy. The liver was palpable at about 3 cm below the right costal margin, no palpable spleen or lymphadenopathy noted. No Kayser-Fleischer rings noted.

Ultrasound of the abdomen showed features of early liver cirrhosis with no splenomegaly. OGDS showed no varices or portal gastropathy. Laboratory data of this patient is as shown in Table I.

Other test results for HepBs Antigen, HepB c IgM antibody, anti Hepatitis C virus antibody and anti Hepatitis A virus were negative. Coombs Test (DAHG-Poly 2+, DAHG-Anti IgG 2+, DAHG-Anti-C 2+, DAHG positive), Antinuclear antibodies (ANA) was positive at titers 1:320 (homogenous), anti double stranded antibodies (anti dsDNA) negative, Anti smooth muscle antibody (ASMA) negative, Liver Kidney Microsome antibodies(LKM) negative, Anti mitochondrial antibodies(AMA) negative. Serum copper and ceruloplasmin were normal. Serum ferritin was normal.

Bone marrow aspiration showed hypercellular marrow with dysplastic changes in all the three cell lines with increased megakaryocyte count which was suggestive of accelerated peripheral platelet destruction. Liver biopsy was contraindicated in view of very low platelet counts and patient did not consent for transjugular liver biopsy.

On the basis of these results the patient was suspected to have Autoimmune Hepatitis (AIH) with coexisting Immune Thrombocytopenic Purpura (ITP) and Autoimmune Hemolytic Anemia (AIHA).

He was started on oral prednisolone 60mg/day and his liver function, platelet count and hemoglobin showed dramatic improvement after 1 month review. His serum bilirubin was 12umol/L, AST 43 IU/L, ALT 50 IU/L, hemoglobin 16.4g/dl, platelets 207x 104/mm. His prednisolone was tapered down and azathioprine 50mg daily was added. He was doing well on the last follow up.

DISCUSSION

Autoimmune hepatitis is an idiopathic hepatitis characterized by histological evidence of chronic liver inflammation, autoantibody and increased levels of gamma globulins. AIH is now recognized as a multisystem disorder that can occur in males or females of all ages. Although less common in men, AIH appears to have a higher relapse rate and younger age of disease onset in men. Despite this, men have significantly better long term survival and outcome than women[1].

A biphasic distribution for age at presentation has been noted with peaks between 10-30 years and above 40 years of age. This condition can coexist with other liver disease (e.g. chronic viral hepatitis) and may be triggered by certain viral infections (e.g. hepatitis A) and chemicals. In this case, there were no viral triggers, except for history of exposure to traditional "viagara" pills prior to his onset of symptoms

Usual presentation of AIH is as acute hepatitis, marked by fever, hepatic tenderness and jaundice. In some patients, the acute illness may appear to resolve spontaneously; however patients invariably develop signs and symptoms of chronic liver disease. Other patients experience rapid progression of the disease to acute liver failure, as marked by coagulopathy and jaundice. Ascites and hepatic encephalopathy also may

This article was accepted: 1 March 2012
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Table I: Laboratory Results

Investigations	Results
Liver Function Test	
Albumin	27 g/dl
Globulin	63 g/dl
Bilirubin	271umol/L (direct 107 / indirect 164)
Alanine amino transferase (ALT)	889 IU/L
Aspartate amino transferase (AST)	1498 IU/L
Gamma Glutamyl Transferase (GGT)	50 IU/L
Alkaline phosphatase	69 IU/L
Lactate Dehydrogenase (LDH)	459 IU/L (105-210 IU/L)
Full Blood Count	
Haemoglobin	10g/L
WBC	7.300/mm^3
Platelet count	20x 10^4/mm
Reticulocyte count	1.6%
Coagulation profile	Normal
Immunoglobulin	
IgG	31 g/dl (7-16g/dl)
IgM	1.90 g/dl (0.7-4.0g/dl)
IgA	5.03 g/dl (0.4-2.30g/dl)

Table II: Diagnostic scoring system for atypical autoimmune hepatitis in adults

Category	Factor	Score
Sex	Female	+2
Ratio of ALP to AST or ALT	>3	-2
	<1.5	+2
Gamma-globulin or immunoglobulin G level (times above upper limit of normal)	>2.0	+3
	1.5-2.0	+2
	1.0-1.5	+1
	<1.0	0
ANA, ASMA, or anti-LKM1 titers	>1:80	+3
	1:80	+2
	1:40	+1
	<1:40	0
Antimitochondrial antibodies	Positive	-4
Viral markers of active infection	Positive	-3
	Negative	+3
Hepatotoxic drugs	Yes	-4
	No	+1
Alcohol consumption	<25 g/day	+2
	>60 g/day	-2
Concurrent immune disease	Any nonhepatic disease of an immune nature	+2
Other autoantibodies*	Anti-SLA/LP, actin, LC1, pANCA	+2
Histologic features	Interface hepatitis	+3
	Plasma cells	+1
	Rosettes	+1
	None of the above	-5
	Biliary changes**	-3
	Atypical features***	-3
Human leukocyte antigen	DR3 or DR4	+1
Treatment response	Remission alone	+2
	Remission with relapse	+3
Pretreatment score	Definite diagnosis	>15
	Probable diagnosis	10-15
Post treatment score	Definite diagnosis	>17
	Probable diagnosis	12-17

ensue. About 20 % of patients present initially with sign of decompensated cirrhosis.

AIH is associated with wide variety of other immune mediated diseases and the list of reported autoimmune disorders are Autoimmune thyroiditis, Graves disease, Ulcerative colitis, Autoimmune Hemolytic Anemia, Idiopathic thrombocytopenia[2], Systemic lupus erythematosus, Sjogren Syndrome, Polymyositis, Mixed connective tissue disease, Coeliac Disease and Myasthenia Gravis. Patients with AIH may present with overlapping syndromes such as primary biliary cirrhosis and primary sclerosing cholangitis.

In this patient, two associated disorders i.e. AIHA and ITP were discovered. Overlapping syndromes were unlikely in this patient as AMA was negative, IgM and the serum alkaline phosphatase and serum gamma glutamyl transferase were normal.

Autoimmune hepatitis type 1 is characterized by positive test results for ASMA and ANA, type 2 disease positive for anti–LKM-1 antibody and type 3 diseases is marked by positivity for anti-SLA antibody. An immunoglobulin G (IgG)–predominant polyclonal hypergammaglobulinemia is a common finding in patients with untreated autoimmune hepatitis.

Serum aminotransferases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) are elevated in 100% of patients at initial presentation, with average values of 200-300 U/L. Aminotransferase values correlate poorly with the degree of hepatic necrosis; however, values in the thousands may indicate acute hepatitis or a severe flare of preexisting disease.

Liver biopsy remains essential for diagnosis and evaluation of disease severity in patients with AIH. This procedure can be preformed percutaneously with ultrasound guidance or by the transjugular route. The latter is preferred if the patient has coagulopathy or severe thrombocytopenia. Histologically AIH is characterized by a chronic inflammatory cell infiltrate, plasma cells being the predominant cell type. Biopsies may show evidence of interface hepatitis, bridging necrosis and fibrosis. The presence or absence of cirrhosis on liver biopsy is an important determinant of the patients' prognosis.

Even though our patient was a male and we had no histological evidence, he had all other inclusion criteria for a definitive diagnosis of AIH i.e. indolent onset of clinical features, concurrent immune mediated diseases, predominant transaminase abnormality, marked elevation of IgG levels(>1.5x normal), presence of ANA(>1:80). Although this patient did admit to taking traditional medications the presentation with multiple autoimmune diseases and biochemical resolution with steroid therapy did not support this diagnosis.

A scoring system for quantitative diagnosis of autoimmune hepatitis has been proposed by International Autoimmune Hepatitis Group (Table II)[3].

Prednisolone and Azathioprine have been the mainstays of drug therapy for patients with AIH. Approximately 65% of patients respond to initial therapy and enter histologic remission; however 80% of these patients relapse after drug withdrawal. The 10-year life expectancies for treated patients with and without cirrhosis at presentation are 89% and 90%, respectively.

The prognosis of autoimmune hepatitis depends primarily on the severity of liver inflammation. Patients with a severe initial presentation tend to have a worse long-term outlook than patients whose initial disease is mild. Similarly, the inability to enter remission or the development of multiple relapses, either during therapy or after treatment withdrawal, implies a worse long-term prognosis.

In conclusion although autoimmune hepatitis is rare in males, it should be suspected in those who present with acute hepatitis with or without underlying cirrhosis and with coexisting autoimmune disorders.

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