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AUTOIMMUNE HEPATITIS WITH AUTOIMMUNE HEMOLYTIC ANEMIA: A RARE ASSOCIATION

Gastroenterology

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ABSTRACT

Autoimmune hepatitis (AIH) is a clinical condition of progressive necroinflammatory disease of the liver. Its association with autoimmune hemolytic anemia (AIHA) is rare. It is usually diagnosed based on the presence of clinical presentations, laboratory findings of certain antibodies and characteristic histology. We report a young female aged 27 years with jaundice, loss of appetite and anemia which was diagnosed as AIH and AIHA. Treatment for both the indications was necessary to prevent further progression of disease and there was a good response to steroid therapy.

KEYWORDS

Autoimmune hepatitis (AIH), Autoimmune hemolytic anemia (AIHA), ANA, iron overload, steroids, jaundice.

INTRODUCTION

Autoimmune hepatitis (AIH) is a major immune mediated chronic liver disease characterized by hepatocellular inflammation and fibrosis causing liver failure (1). It typically affects young and middle-aged women regardless of age/ethnicity. The lack of alternative etiologies combined with a pattern of clinical and laboratory presentation remains a reliable method for practitioners to identify patients with this condition. Autoimmune hemolytic anemia is characterized by the production of auto-antibodies that bind to the surface of circulating erythrocytes, leading to haemolysis and decreased survival of the red blood cells. The estimated yearly incidence of AIHA is 1–3 cases per 100,000 persons in the general population; it is rarely associated with AIH (2).

Although autoimmune hepatitis is complicated by various autoimmune entities, association with autoimmune hemolytic anemia is limited to few case reports (3). Untreated autoimmune hepatitis can lead to scarring of the liver (cirrhosis) and eventually to liver failure. Treatment involves steroids with immunosuppressants, as the first line treatment. Early detection of AIH is a key, as early and effective treatment is associated with better patient outcome. Herein we present a case of AIH and AIHA which is rarely associated.

Case Study

A 27 year old woman with medical history of hypothyroidism, asymptomatic gallstones, solitary kidney, with past history of jaundice 10 years ago and presented with a two-week history of fever, yellowish discoloration of eyes, dark urine, shortness of breath, fatigue, loss of appetite admitted to our hospital. Her baseline investigations showed hemoglobin (Hb) levels-3.7 g/dL, total RBC 0.32 millions/cumm, WBC 10810/cumm (83% neutrophils,14.5% lymphocytes),platelet count 1.91lakhs/cumm. The red blood cells indices were elevated (MCV-134.2,MCH-53.8,MCHC-40.1) and peripheral smear was suggestive of hemolytic anemia. The direct Coombs test, antinuclear antibody (ANA) with IF was positive (1:100 titres) and prothrombin time 18.7 seconds, INR was1.41.

Rest of the laboratory tests revealed that LFTs were elevated AST,ALT,ALP (83 U/L,99 U/L, 87 U/L respectively) conjugated bilirubin- 34.9 mg/dL, unconjugated bilirubin 2 mg/dL, serum LDH 980 U/L(Normal 103-333 U/L),serum proteins 7.5 g/L with increased globulins (5.1g/L) and decreased albumin (2.9 g/dL).Serological markers for viral hepatitis were all negative. Evaluation of iron profile with transferrin saturation showed increased iron levels (191 µg/dL),TIBC was low(194),and elevated serum ferritin 19300 ng/mL. RFTs, thyroid function and blood sugar levels were within normal limits. Abdominal ultrasonography and CT scan showed an evidence of moderate hepatosplenomegaly, cholelithiasis and mild ascites.

In view of elevated liver enzymes, high ANA positive titre, increased immunoglobulins(IgG) levels, negative viral hepatitis screen probable diagnosis of type-I AIH associated with Autoimmune hemolytic anemia was made based on complex scoring system (IAHG). (Table 2) Patient was initially treated with 2 units of erythrocytes packed cells, O2 support in ICU.

Subsequently, patient was treated with IV hydrocortisone (steroids), iron chelators and B12 administration. She had significant clinical and laboratory improvement of anemia and liver functions and was discharged in hemodynamically stable condition and on follow up patient was stable on immunosuppression tapering dose with normal liver function.

Table 1: Initial Laboratory Findings

MCV	134.2
MCH	53.8
MCHC	40.1
Platelet count	1.64 l/cumm
Total WBC	9430 cells/cumm
Creatinine	0.5mg/dL
Reticulocyte production Index (RPI)	3 %
PT	18.7 secs
INR	1.41
aPTT	35 secs
ESR	100mm
Direct Coombs test	Positive (4+)
Aspartate aminotransferase (AST)	83 U/L
Alanine aminotransferase (ALT)	99 U/L
Alanine phosphatase	87 U/L
Direct bilirubin	34.9 mg/dL
Indirect bilirubin	2 mg /dL
Serum proteins	8.2 g/dl
Albumin	3.1 g/dL
Globulin	5.1 g/dL
Peripheral smear	Neutrophilic leukocytosis
LDH	980 U/L
ANA with IF	+ titre (1:100)

Table 2: Simplified Diagnostic Criteria For Autoimmune Hepatitis

Variable	Cutoff	Points
ANA or SMA	1:40	1
	≥ 1:80	2
or LKM	≥ 1:40	2*
or SLA	Positive	2
lgG	≥ Upper normal limit ≥ 1.10 times upper normal limit	1 2
Liver histology (evidence of hepatitis is a necessary condition)	Compatible with AIH Typical AIH	1 2
Absence of viral hepatitis	yes	2 6: probable AIH ≥ 7: definite AIH

*Addition of points achieved for all auto antibodies (maximum, 2 points).

DISCUSSION

Autoimmune hepatitis is an immune-mediated inflammatory liver disease characterized by histopathological evidence of inflammation and fibrosis (4). AIH may be asymptomatic, or causes chronic non-specific symptoms (fatigue, malaise, arthralgias and amenorrhea) or present with an abrupt onset of symptoms including jaundice, hepatic tenderness, loss of appetite. The pathophysiology of AIH is unclear and is more common among women. There is scanty literature about the association between AIH and AIHA. The rarity of AIH in men compared to females is demonstrated by epidemiological studies (11).There are very few case reports with association of AIH and AIHA (4).Liver enzymes are usually elevated in the majority of the patients at the initial presentation. Our patient had marked jaundice and anemia with all other manifestations for diagnosis of AIH overlapping with AIHA i.e. simplified criteria for AIH along with hemolysis (DCT positive).

In our patient, ANA was positive, IgG elevated and all the other etiologies for liver disease like alcohol, viruses and metabolic causes were negative. Liver biopsy was not performed as the patient was unstable and unfeasible on presentation. Additionally our patient had low hemoglobin, elevated reticulocyte count, coombs direct positive and normal hemoglobin electrophoresis. This was confirmatory for hemolytic anemia. But additionally, she had high MCV and low serum B12 levels which were corrected promptly. Iron overload which was due to inadvertent iron infusions prior to admission was treated with deferoxamine. Immunosuppressive therapy, with corticosteroids and azathioprine, can achieve sustained remission in more than 80% of patients with AIH (10).

Our patient was treated with steroids, iron chelators, vitamin B12 administration and nutritional supplements. There was a significant improvement in the general condition and biochemical analysis.

Quality of life is commonly decreased in patients with AIH and symptoms of fatigue, stress and anxiety are significantly more common than in the general population and targeted counseling may be necessary. In summary, the presence of these uncommon associations in the patient provokes us to further understand the pathophysiology underlying these two autoimmune conditions. It is essential to continue monitoring the course in order to reveal the mechanisms involved. An improved comprehension of the diagnostic and clinical significance of autoantibody reactivity will assist the healthcare professional in selecting the most pertinent tests and properly interpreting the laboratory's report.

Fortunately, immunosuppression with steroids and azathioprine in particular is very effective and the outcomes for patients are now excellent, given proper diagnosis and prompt treatment. Untreated mortality from severe disease is considerable. Approximately, 80% of treated patients obtain remission (11, 12).

Although autoimmune hepatitis with autoimmune hemolytic anemia is rare, it should be suspected in those with a compatible clinical presentation.

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