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Autoimmune Hepatitis: An unusual presentation.

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CASE REPORT

Autoimmune Hepatitis: An Unusual Presentation

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Abstract

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease that occurs in a bimodal age distribution in the second and fifth-sixth decade of life. The disease is more prevalent in females and presents with variable clinical manifestations ranging from being asymptomatic to acute liver failure. AIH is often overlooked and not worked up in elderly patients who present with liver failure. This can lead to increased morbidity and mortality in elderly patients. AIH should be considered as a differential diagnosis in patients who present with elevated transaminases regardless of age or gender as early recognition and treatment leads to improved outcomes. In this article, we present a unique case of AIH in a male patient in his eighth decade of life who presented with acute liver failure without any obvious cause and had no history of autoimmune diseases.

Keywords: Autoimmune Hepatitis, Acute Liver Failure, Jaundice, Transaminitis, Anti-smooth muscle antibodies, Anti-liver/kidney microsomal-1 antibodies, Ascites, Autoimmune diseases

1. Introduction

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease that occurs across a bimodal age distribution in the second and fifth-sixth decade of life with a predominance in females[1] but can occur in both genders and all ages. There are few studies that have investigated the epidemiology of AIH. AIH is a rare disease with prevalence rates of 10–17 per 100 000 in Europe.[2] The exact etiopathogenesis of the disease is unknown but it is hypothesized that a loss of tolerance against liver antigens is the main pathophysiological mechanism. Due to the large heterogeneity of disease manifestation patients may be asymptomatic or can present with acute liver failure.[1] It is a diagnosis of exclusion and should always be considered in all patients who present with elevated transaminases once other common etiologies of liver diseases are ruled out. We present a unique case of AIH diagnosed in a male patient in his eighties who presented with acute liver failure without an obvious cause.

2. Case presentation

An 83-year-old male with a past medical history of hypertension and type 2 diabetes mellitus was admitted to our hospital for complaints of fatigue, jaundice, and abdominal distention. He reported that his fatigue started many months ago however; recently he noticed yellowing of his skin and sclera with abdominal distension prompting him to seek care. On presentation, his vital signs were within normal limits. Physical examination revealed scleral icterus, jaundice, asterixis, palmar erythema and a distended abdomen with a positive fluid thrill. Laboratory workup showed white blood cell (WBC) count of 6.3 K/uL (normal: 3.3–8.7 K/uL), thrombocytopenia with platelet count 122 K/ul (normal 150K/ul - 450 K/ul), aspartate transaminase (AST) 194 U/L (normal 8 U/L - 33 U/L), alanine transaminase (ALT) 64 U/L (normal: 29 U/L - 33 U/L), alkaline phosphatase (ALP) 157 U/L (normal 44 U/L - 147 U/L), lactate dehydrogenase (LDH) 329 U/L (normal 140 U/L - 280 U/L), gamma-glutamyl transferase (GGT) 300 U/L (normal 9 U/L - 48 U/L), total bilirubin 3.3 mg/dl (normal 1.2 mg/dl), direct bilirubin 1.9 mg/dl (normal 1.2 mg/dl), serum albumin 2.4 g/dl (normal 3.4 g/dl - 5.4 g/dl), international normalized ratio (INR) of 1.7 (normal 1.0) and ammonia levels of 87 umol/L (normal 11 umol/L - 32 umol/L). Serum iron and ferritin levels were within normal limits. Serum thyroid stimulating hormone (TSH) and free

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thyroxine (T4) levels were within normal limits. Screening for hepatitis A, B, and C viruses, human immunodeficiency virus (HIV), Ebstein-Barr virus (EBV) and cytomegalovirus (CMV) panel were negative. A review of potential exposure to hepatotoxins like alcohol and medications was negative. Due to abdominal distension and positive fluid thrill an abdominal ultrasound was performed that revealed ascites. A diagnostic paracentesis was performed and 200 ml of straw-colored ascitic fluid was removed. Analysis of ascitic fluid revealed 225 WBCs/mm^3 (55 % neutrophils) with total protein 2.4 g/dL, albumin 1.2 g/dL, and serum ascites albumin gradient (SAAG) of 1.2. Bacterial cultures of the fluid were negative. Cytology did not reveal any malignant cells. The patient's hospital course was complicated by hepatic encephalopathy and worsening liver function. At this point autoimmune serologies for workup of autoimmune hepatitis were sent. Autoimmune serology revealed elevated antinuclear antibodies (ANA) 1:1280 (normal 1:40 or less), anti-smooth muscle antibodies (ASMA) 87 units (normal less than 20 units), anti-ds (double stranded) DNA antibodies of 1247 IU/mL (normal less than 200 IU/mL) and elevated serum IgG 2317 mg/dL (normal range less than 1741 mg/dL) levels. AIH was diagnosed based on positive ASMA, anti-ds DNA antibodies, elevated IgG levels and a simplified AIH diagnostic score of 6. Patient and his family refused liver biopsy and wanted to pursue a more conservative and noninvasive treatment approach. Patient denied any family or personal history of autoimmune diseases. Workup for other autoimmune diseases commonly associated with AIH such as primary sclerosing cholangitis, primary biliary cholangitis, ulcerative colitis, rheumatoid arthritis and celiac disease was negative. Patient was started on prednisone 40 mg oral daily and within a week of starting steroid therapy his clinical condition markedly improved and transaminases and total bilirubin levels decreased. He was discharged and outpatient follow up revealed his scleral icterus had improved, AST, ALT and IgG levels had normalized and he was doing well. He was started on azathioprine in addition to prednisone and prednisone dose was tapered down.

3. Discussion

AIH is a chronic inflammatory liver disease predominantly affecting females[1] with a male to female ratio of around 4: 1.[3] In women a bimodal age pattern with disease presentation in second decade and fifth-sixth decade is usually seen, however, it should be stressed that this disease can develop in both genders and in all age groups[4,5] from as early as the first year of life up until the eighties as in our patient who was 83 years old, had no history of prior liver disease and no history of autoimmune disease.[6,7]

Clinical manifestations of AIH may vary. Patients can be asymptomatic or have a subclinical course of mildly elevated liver enzymes accompanied with nonspecific symptoms of arthralgia, fatigue, jaundice (mimicking hepatitis), or have fulminant hepatic failure.[8–10] In our case our patient presented with acute liver failure. Likely when he developed fatigue months prior to presentation was when AIH started developing and he sought attention only when the disease reached the stage of acute liver failure.

AIH is a diagnosis of exclusion. Physicians should keep AIH as a differential diagnosis in all patients who present with elevated transaminases once other common etiologies of liver damage have been ruled out regardless of their age, gender or past medical history.

Autoantibodies constitute an important part of the diagnostic workup of AIH. Antibodies associated with AIH are ANA, ASMA, and anti-liver/kidney microsomal-1 (anti-LKM-1) antibodies. Anti-ds DNA antibodies are most commonly associated with systemic lupus erythematosus (SLE) but can be found in patients with AIH. ANA are commonly found in a large variety of diseases and are nonspecific for AIH.[1] ASMA and anti-LKM-1 are more specific for AIH.[1] AIH is sub classified into type 1 AIH (AIH-1) and type 2 AIH (AIH-2). AIH-1 is characterized by the presence of ANA and/or ASMA. It accounts for about 75–80 % of all cases of AIH.[2] AIH-2 is characterized by the presence of anti-LKM-1. It accounts for less than 10–15 % of all cases of AIH.[2] Our patient likely had AIH-1 as he had elevated ANA and ASMA.

The simplified criterion for AIH is also used to establish the diagnosis of AIH. It consists of a scoring system with scores calculated based on presence of autoantibodies, IgG, histology, and exclusion of viral hepatitis. The score was found to have 88 % sensitivity and 97 % specificity for AIH if it was greater than or equal to 6 and 81 % sensitivity and 99 % specificity if greater than or equal to 7.[11] Our patient had elevated ANA, ASMA, anti-ds DNA antibodies and a simplified AIH diagnostic score of 6 satisfying the diagnosis of AIH.

Treatment strategies for AIH consist of induction therapy with prednisone as monotherapy or combined with azathioprine.[1] In about 10 % of patients, treatment with prednisone and azathioprine is unsuccessful, due to intolerable side effects or lack of clinical response.[1,4] In these patients, alternative immunosuppressive treatments can be used

including cyclosporine, tacrolimus, methotrexate, cyclophosphamide, mycophenolate mofetil, and 6-mercaptopurine that yield varying degrees of success.[1] Treatment is indicated in every patient and is generally life-long. Treatment should be aimed at biochemical remission which is the normalization of ALT, AST and the IgG levels.[12] Our patient responded well to steroid therapy and was later transitioned to a combination therapy with steroids and azathioprine.

4. Conclusion

AIH is more common in females. It occurs in a bimodal age distribution in second decade of life and then in the fifth to sixth decade of life. However, clinicians should have a high index of suspicion for this clinical entity in anyone presenting with elevated transaminases regardless of age as early recognition and treatment are keys to improved outcomes. Clinical manifestations of AIH vary widely and can range from being asymptomatic to fulminant hepatic failure.

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