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Case Report

Acute-on-chronic liver failure in an adult secondary to autoimmune hepatitis: a case report

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ABSTRACT

Autoimmune hepatitis (AIH) is a rare inflammatory liver disease mediated by the immune system and characterized by circulating autoantibodies. It can progress to cirrhosis and acute-on-chronic liver failure if the diagnosis is overlooked and treatment is delayed. A 35-year-old male was hospitalized for fever and jaundice. A liver ultrasound documented chronic liver disease with signs of portal hypertension and ascites. An evaluation for the etiology of chronic liver disease ruled out Hepatitis B and C, HIV, Type 2 diabetes mellitus, non-alcoholic fatty liver, alcohol, hepatotoxic drug use were denied, leading to the request for antinuclear antibodies (ANA) and anti-smooth muscle antibodies (SMA), which were positive, guiding us towards the diagnosis of autoimmune hepatitis, experiencing acute decompensation of chronic liver disease associated with the rapid onset of multiorgan failure secondary to urinary tract infection. AIH can progress to cirrhosis and terminal liver failure. In this case, our patient was asymptomatic before hospital admission, presenting with jaundice and fever, diagnosing chronic liver disease secondary to autoimmune hepatitis presenting acute-on-chronic liver failure secondary to complicated urinary tract infection. The treatment for AIH is oral corticosteroids. Broad-spectrum antibiotics were initiated without success, resulting in a fatal outcome. AIH is a disease that needs to be diagnosed by ruling out the main causes of chronic liver disease as it can initially present asymptomatically and, if untreated, can evolve into acute liver failure, chronic liver disease, and acute-on-chronic liver failure, which can be avoided with timely corticosteroid treatment.

Keywords: Autoimmune hepatitis, Acute-on-chronic liver failure, Characteristic autoantibodies

INTRODUCTION

Autoimmune hepatitis (AIH) is an inflammatory liver disease mediated by the immune system with circulating autoantibodies, characterized by a progressive and fluctuating clinical course.[1] The disease can be asymptomatic, begin as acute hepatitis, and progress to cirrhosis. Consequently, there is a wide spectrum of clinical presentations, from acute autoimmune hepatitis that progresses to severe acute liver failure to chronic autoimmune hepatitis that is progressive, causing cirrhosis and acute-on-chronic liver failure.[2] Autoimmune hepatitis can present at any age and in all ethnic groups, but it predominantly occurs in women. The worldwide pooled annual incidence and prevalence are 1.37 and 17.44 per 100,000 people, respectively.[3] A theory of AIH pathogenesis is based on autoreactive CD4 and CD8 T cells, which appear after the breakdown of self-tolerance due to environmental triggers in a genetically predisposed individual. The exact relationships between genes and the autoimmune process remain largely undefined, but at the molecular level, they are believed to involve the autoantigen, the major histocompatibility complex, and the T cell receptor.[4] The clinical presentation is very

heterogeneous, ranging from asymptomatic cases to acute liver failure. The most common clinical presentation includes mild nonspecific symptoms such as fatigue, arthralgias, malaise, anorexia, and weight loss. Extrahepatic autoimmune diseases can occur in 20-50% of cases. A minority of patients present with established liver cirrhosis and complications of portal hypertension; histological inflammation of the liver may be absent ("burnt-out cirrhosis").[5]

CASE REPORT

A 35-year-old male denies chronic use of drugs, alcohol, or herbal remedies. He has no tattoos or piercings and denies having chronic degenerative diseases. He also denies any history of blood transfusions. He has a history of laparoscopic cholecystectomy performed 10 years ago. The current condition began with an increase in abdominal girth over the past month. The clinical picture was further complicated by jaundice and a fever of 38.3°C for one week, prompting him to visit the emergency department. On physical examination, the patient presented with generalized jaundice, hydrated oral mucosa, lung fields with adequate air entry and exit, fine crackles in both bases of the hemithorax, a globular abdomen secondary to ascites, and lower extremities with edema ++/+++. Laboratory studies upon admission showed leukocytes of 8,270/ul, mild anemia: Hb 10.7, MCV 102, MCH 37.2, severe thrombocytopenia: platelets 33,000, normal renal function, Cr 0.99, BUN 17, urea 36, normal glucose: 86 mg/dl. Electrolyte imbalances: Na 133, Cl 97, K 3.3, Ca 7.6, Mg 1.59, P 2.6. Altered liver function with total bilirubin of 20.3 mg/dl (direct bilirubin 8.6 mg/dl and indirect bilirubin 11.7 mg/dl), AST 61, ALT 80, ALP 82, GGT 18, albumin 2.23, prolonged coagulation times: PT 33, INR 3.07, aPTT 88.

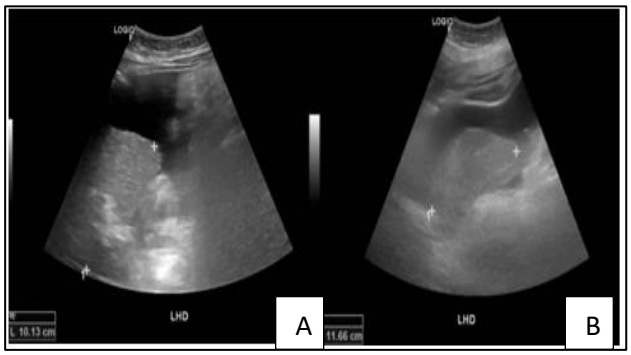

Figure 1 (A and B): Changes due to chronic liver disease with signs of portal hypertension.

Urinalysis was pathological, cloudy appearance, bilirubin>10 mg/dl, negative nitrites, leukocytes 30 per field, erythrocytes 10 per field, abundant bacteria. An abdominal ultrasound was performed, showing a liver with heterogeneous echogenicity, irregular serrated borders, measuring 117 mm in its largest longitudinal axis, without evidence of focal lesions. The intra- and extrahepatic bile ducts were normal, and the portal vein was 12 mm. The spleen (164 mm) was diffusely enlarged. Abundant free fluid was observed in all peritoneal spaces of the abdominopelvic cavity, concluding changes due to chronic liver disease with signs of portal hypertension and ascites (Figure 1).

During his hospital stay, management was initiated with IV ceftriaxone for 7 days for a urinary tract infection, which was the trigger for the decompensation. A therapeutic paracentesis was performed, draining 4 liters, and cytological, biochemical, and ascitic fluid culture were requested. The ascitic fluid was reported as yellow, clear, with leukocytes at 112 ul and a culture without bacterial growth, thus ruling out spontaneous bacterial peritonitis. An upper endoscopy was performed, revealing grade II esophageal varices according to Dagradi and severe hypertensive gastropathy (Figure 2).

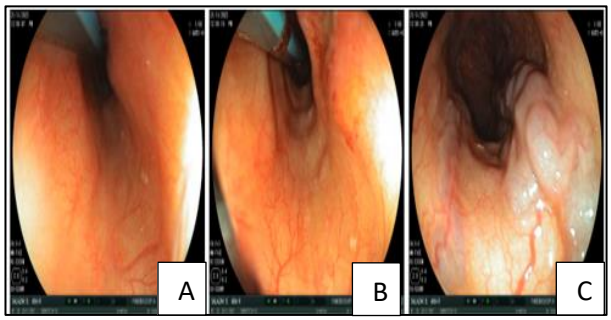

Figure 2 (A-C): Dagradi garde II esophageal varices.

Etiological evaluation of chronic liver disease was performed with negative hepatitis B and C tests, negative HIV, and negative TORCH profile. Type 2 Diabetes Mellitus was ruled out with hemoglobin A1c. Liver ultrasound showed no evidence of hepatic steatosis, and due to persistent decompensation and clinical suspicion, antinuclear antibodies (ANA) and anti-smooth muscle antibodies (SMA) were requested, reported at greater than 1:80 by indirect immunofluorescence, and a twofold elevation of the upper normal limit of serum immunoglobulin G. Drug-induced liver injury, alcohol-induced liver damage, and viral hepatitis were ruled out, leading to the management of the condition as autoimmune hepatitis. Treatment with prednisone 60 mg daily was initiated. The patient was not considered a candidate for liver biopsy due to the presence of chronic liver disease and the limited information that would be obtained from an invasive procedure. A thyroid profile was requested, showing TSH >14 and decreased free T4, documenting primary hypothyroidism as an extrahepatic autoimmune manifestation, so thyroid hormone replacement therapy was started. The patient showed elevated creatinine and azotemia (BUN 43, urea 92, creatinine 2.21), documenting acute kidney injury KDIGO III, as well as elevated total bilirubin levels of 30 mg/dl (direct bilirubin 13.5 mg/dl and indirect bilirubin 16.5 mg/dl), elevated transaminases (ALT 128, AST 120), West Haven grade I hepatic encephalopathy, and

prolonged coagulation times (INR 3.86), integrating the diagnosis of acute-on-chronic liver failure.

DISCUSSION

The diagnosis of AIH is based on histological abnormalities (interface hepatitis), characteristic clinical and laboratory findings (elevated ALT and AST levels, increased serum IgG concentration), and the presence of one or more characteristic autoantibodies.[6] Biochemical findings: The typical biochemical profile in AIH is a hepatocellular pattern, with bilirubin and aminotransferase concentrations ranging from just above the upper limit of normal (ULN) to more than 50 times these levels. Elevated GGT and IgG in 85% of patients with AIH.[7] In this case, our patient had aminotransferase levels twice the upper normal limit with a 2:1 ALT/AST ratio, a twofold elevation of serum immunoglobulin G, and normal GGT levels.

Characteristic autoantibodies: Increased total IgG levels and/or serological markers (antinuclear antibodies (ANA), anti-smooth muscle antibodies (ASMA) at a titer of at least 1:40 by indirect immunofluorescence, anti-liver/kidney microsomal-1 antibodies (anti-LKM-1), anti-liver cytosol-1 antibodies (ALC-1), or anti-soluble liver antigen/liver pancreas antibodies anti-SLA/LP).[8] For our patient, ANA and SMA were requested, reported as greater than 1:80 by indirect immunofluorescence. When a liver biopsy is obtained, the diagnosis can be confirmed by histology showing interface hepatitis and/or a predominantly lymphoplasmacytic infiltrate.

Although a liver biopsy can confirm the presence of autoimmune hepatitis, some patients can be diagnosed based on strong clinical suspicion and laboratory results.[6] In this case, our patient was not a candidate for liver biopsy as he was in a stage of chronic liver disease and the risks outweighed the benefits. Exclusion of diseases with similar presentation, particularly viral hepatitis, drug-induced liver injury, and alcoholic liver disease.[6] The patient was ruled out for viral hepatitis, recent medication intake, and alcohol consumption, thus integrating the diagnosis of autoimmune hepatitis. There are two types of AIH, based on characteristic autoantibodies. Type 1 is characterized by antinuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA)/anti-soluble liver antigen/liver pancreas (anti-SLA/LP) antibodies, and type 2 is characterized by anti-liver kidney microsome type 1 (anti-LKM1) antibodies and anti-liver cytosol-1 (ALC-1) or anti-soluble liver antigen/liver pancreas (anti-SLA/LP) antibodies.[9]

Based on the positive characteristic autoantibodies (ANA and SMA), our patient has type 1 autoimmune hepatitis. The International autoimmune hepatitis group (IAIHG) proposed a scoring system that has been validated in several studies and is used in clinical practice. In 2008, a simplified version was published based on the presence of autoantibodies, IgG levels, compatible liver histology, and the absence of viral hepatitis. This system is simpler and, although less sensitive (95% vs. 100%), has higher specificity (90% vs. 73%).[10] Our patient scored a total of 6 points on the simplified version, with a high probability of autoimmune hepatitis. The following elements are critical components for the definition of acute-on-chronic liver failure (ACLF), acute onset with rapid deterioration of clinical condition, the presence of liver failure defined by elevated bilirubin levels and elevated INR in patients with chronic liver disease with or without cirrhosis, and the presence of at least one extrahepatic organ failure (neurological, circulatory, respiratory, or renal).[11]

It is a clinical syndrome of acute hepatic decompensation with superimposed acute injury observed in patients with preexisting cirrhosis characterized by the presence of extrahepatic organ failure.[9] Our patient presented with acute deterioration of clinical conditions, elevated bilirubin levels (total bilirubin of 30 mg/dl), elevated INR (INR 3.86), and extrahepatic organ failure with acute kidney injury KDIGO III (BUN 43, urea 92, creatinine 2.21), integrating the diagnosis of acute-on-chronic liver failure. The presentation of AIH-ACLF is often unusual, as nearly half of the patients are seronegative.[14] The primary goal of AIH treatment is to induce a complete biochemical response, defined as normalization of transaminase and IgG concentrations.[15] Glucocorticoids are the first-line treatment; prednisone alone, 40-60 mg daily in adults, or a lower dose of prednisone, 20-40 mg daily, in combination with azathioprine 50-150 mg daily.[6,12]

In patients with AIH and cirrhosis, induction treatment with prednisone at 20-40 mg daily is recommended. Azathioprine should not be used in patients with decompensated cirrhosis.[7] Exacerbation of AIH as a cause of ACLF is a crucial diagnosis that, if delayed, can result in unfavorable scenarios. Corticosteroid therapy (prednisone 1 mg/kg) appears to be beneficial in improving 90-day survival, although the response may vary.[13] In this case, our patient was started on oral corticosteroid therapy with prednisone at 80 mg daily; however, there was no response, and he passed away due to multiorgan failure. Patients with severe acute AIH who do not improve laboratory tests or clinically worsen within 1-2 weeks of glucocorticoid therapy, acute liver failure, or acute-on-chronic liver failure should be evaluated for liver transplantation.[12]

CONCLUSION

Autoimmune hepatitis is a rare disease that needs to be diagnosed after ruling out the main causes of chronic liver disease, as it can initially present asymptomatically. If not treated in time, it can progress to acute liver failure, chronic liver disease, and acute-on-chronic liver failure, which can be avoided with timely treatment using corticosteroids. With induction and maintenance therapy, a complete biochemical response is achieved, as it not

only halts the progression of fibrosis but also allows for its regression.

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