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CASE REPORT | LIVER

Postinfectious Autoimmune Hepatitis-Induced Liver Failure: A Consequence of Hepatitis A Virus Infection

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ABSTRACT

Autoimmune hepatitis (AIH) is a chronic inflammatory immune-mediated hepatic pathology of unclear etiology. The mechanisms initiating and driving autoimmune inflammation of the liver and the loss of hepatic tolerance are still elusive. Several studies have documented the involvement of genetic factors and triggering agents such as toxic injury, treatment with immune-modifying drugs, or previous viral infections with perhaps strongest evidence for the hepatitis C virus. Rarely, AIH has been reported to develop after hepatitis A virus infection. We describe a case of de novo AIH in a patient with a history of recent hepatitis A virus infection.

INTRODUCTION

Autoimmune hepatitis (AIH) is characterized clinically by autoantibodies in serum and hypergammaglobulinemia and histologically by interface hepatitis with periportal lymphoplasmacytic inflammation. Two types of AIH are recognized according to seropositivity: smooth muscle antibody or antinuclear antibody (ANA) defines AIH type 1 and antibodies to liver-kidney microsome type 1 or liver cytosol type 1 defines AIH type 2. The actual prevalence of AIH is unknown, but women are affected more frequently than men (female: male: 3.6:1).[1,2] Disease is seen in all ethnic groups and all ages.[2] The pathogenesis is not fully understood. Environmental triggers producing an immune response targeting liver autoantigen, failure of immunoregulatory mechanism, and a genetic predisposition collaborating to induce a T cell-mediated immune attack leading to a progressive necroinflammatory and fibrotic process in the liver have been postulated as possible mechanisms.[1,2] Described triggers include toxins, viral infections, immune-modulating drugs, liver transplantation, or can occur in conjunction and association with other autoimmune diseases.[3] Common viruses such as hepatitis A (HAV), hepatitis B, hepatitis C, hepatitis E (HEV), and Epstein-Barr virus have been described and reported as potential AIH triggers.[4–7] We describe a case of AIH triggered by the recent HAV infection.

CASE REPORT

A 45-year-old woman from Mexico presented to our hospital with icteric sclerae, headache, and confusion. She had been diagnosed with acute hepatitis A in Mexico 1 month before her presentation and had a full recovery with supportive management. On initial evaluation, her vital signs were normal; she had altered mentation, icteric sclerae, jaundice, and asterixis. Her alanine aminotransferase and aspartate aminotransferase were 2,869 and 1,469 U/L, respectively. Total bilirubin was 15.1 g/dL, with a direct component of 6.2 g/dL, international normalized ratio was 1.6, and ammonia was 55 μmol/L. Her initial Model for End-Stage Liver Disease was 22. Workup for etiologies of chronic liver disease showed elevated ferritin (1,657 ng/mL) and immunoglobulin G (IgG) (2,580 mg/dL). ANA, antimitochondrial antibody, antismooth muscle antibody, P-antineutrophil cytoplasmic antibody, C-antineutrophil cytoplasmic antibody, and antiliver-kidney microsomal type 1 antibody were negative. Ceruloplasmin and alpha-1 antitrypsin levels were normal. Anti-HAV immunoglobulin M (IgM), HEV IgG, and IgM were positive, but HEV ribonucleic acid

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was undetectable. There was no history of complementary and alternative medicine or herbal supplements intake. Abdominal ultrasound and computed tomography scan showed no significant abnormalities. Transjugular liver biopsy was performed, revealing a portosystemic gradient of 7 mm Hg and histology was consistent with AIH—panlobular hepatitis with bridging necrosis and abundant portal and perivenular lymphoplasmacytic infiltrate (Figure 1). She was started on oral prednisone and azathioprine. Her liver enzymes and liver synthetic function improved. After 1 week of therapy, her Model for End-Stage Liver Disease score improved to 16. She was discharged on a prednisone taper. At the 6-month follow-up, she had normal liver enzymes and synthetic function.

DISCUSSION

We describe a patient with features of AIH, including hypergammaglobulinemia, elevated transaminases, lymphoplasmacytic infiltration in liver histology, absence of persistent infection by a known virus, and a dramatic response to immunosuppressive therapy. Our patient acquired and was treated for HAV infection 1 month before her current presentation. Her IgM anti-HAV remained positive during our assessment, likely because of her recent infection. We hypothesize that her HAV infection was the inciting event leading to the development of AIH. Although anti-HEV IgM and IgG were positive, HEV ribonucleic acid was undetectable, and we suspect this was due to immune mimicry.

HAV, as an initiating factor in AIH, has been previously reported in the literature. In a prospective study of 58 healthy relatives of patients with AIH, Vento et al found that during a 4-year follow-up, subclinical acute hepatitis A was detected in 3 subjects.[4] Two of them developed AIH type 1 within 5 months. A defect in suppressor-inducer T lymphocytes, which control the immune response to the asialoglycoprotein receptor (an antigen expressed on the hepatocyte surface), was found in these patients before developing acute hepatitis A viral infection. Moreover, specific helper T cells and antibodies to the asialoglycoprotein receptor persisted and increased after acute hepatitis A. These authors suggest that in susceptible individuals, HAV can be a trigger for AIH.[4] Only very few cases of AIH triggered by hepatitis A viral infection have been reported.[5–7]

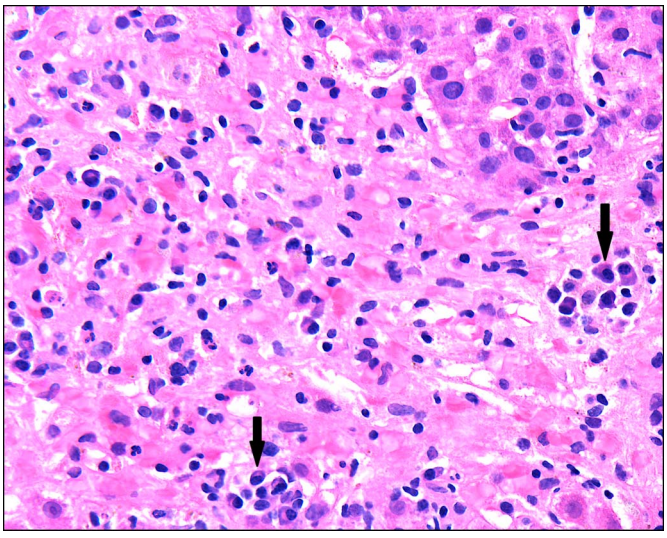

Figure 1. Liver biopsy showing bridging necrosis with extensive hepatocyte dropout and small aggregates of plasma cells (arrows).

Characteristic laboratory abnormalities in AIH include elevated transaminases, elevated IgG levels, and positive circulating autoantibodies including ANA, antismooth muscle antibody, antiliver-kidney microsomal type 1 antibody, and anti-liver cytosol-1. These autoantibodies are not specific for AIH and may be present in other liver diseases. A definitive diagnosis requires a liver biopsy. Interface hepatitis and plasma cell infiltration is the characteristic finding in liver biopsy. Neither histological finding is specific for AIH, and the absence of plasma cells in the infiltrate does not preclude the diagnosis. A diagnostic scoring system was established by the International Autoimmune Hepatitis Group for the diagnosis of AIH in patients with few or atypical features of AIH.[8] A score >15 before steroid treatment and >17 after steroid treatment is required for a definitive diagnosis. A score between 10 and 15 before steroid treatment and 12–17 after steroid treatment is considered as probable AIH with a sensitivity of 100% and specificity of 73% for diagnosing AIH.[1,2,8] Our patient had a score of 11 before and 13 after treatment with steroids, which is suggestive of probable AIH.

HAV infection is common, but the development of postviral hepatitis AIH is unusual. HAV infection can act as a trigger for AIH by initiating a self-perpetuating immune-mediated liver inflammation and can present acutely after the resolution of viral hepatitis.[3,9] Our case supports the hypothesis of a hepatotropic virus as a trigger for AIH.[4–7] Although we recognized positive HEV antibodies (IgG and IgM) in our patient, there was no active HEV viremia, excluding the possibility of coinfection. Because our patient had recent HAV infection and was still positive for anti-HAV IgM, relapsing hepatitis A was our major differential to AIH. It is crucial to differentiate between acute viral hepatitis and AIH beause their treatment is different. We should also recognize the potential for immune mimicry in acute immunologic flares.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. SK Subramanian is the article guarantor.

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Informed consent was obtained for this case report.

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