Early Steroid Therapy in Seronegative Autoimmune Hepatitis: A Case Report

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Abstract

Classic autoimmune hepatitis (AIH) is a multifarious hepatic pathology of undefined etiology that leads to liver damage directed by the body's own immune system. In this case report, we described how the early diagnosis and treatment of seronegative autoimmune hepatitis (SAIH) with steroids could be beneficial.

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Informed Consent

A written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ABSTRACT

Classic autoimmune hepatitis (AIH) is a multifarious hepatic pathology of undefined etiology that leads to liver damage directed by the body's own immune system. In this case report, we described how the early diagnosis and treatment of seronegative autoimmune hepatitis (SAIH) with steroids could be beneficial.

Keywords : Steroid responsive; liver inflammation; immune liver diseases; immune-mediated injury; immune mediated hepatitis

Key Clinical Message

Delays in appropriate treatment of SAIH can lead to disease progression, which causes chronic inflammation in the liver, leading to cirrhosis and can end up with acute liver failure.

INTRODUCTION

Autoimmune hepatitis (AIH) is a chronic disorder characterized by continuing hepatocellular injury, which can progress to cirrhosis and liver failure. The current prevalence of AIH is estimated to be 24 per 100,000. Generally, AIH is seropositive with presence of auto-antibodies like antinuclear, anti-smooth muscle, anti-liver kidney microsomal antibodies among many others. But sometimes there are no autoantibodies detected in the serum when it is called seronegative AIH which presents with a course similar to classic AIH. This makes it a particularly challenging diagnosis that is made after excluding other causes of hepatitis like medication induced, toxin induced or infectious hepatitis. Seronegative AIH may be associated with other autoimmune diseases like Graves' disease concurrently.

In the United States, we see 1 in 200,000 cases occurring every year. Since this a treatable cause of liver disease, the progression can be stopped and even reversed with early institution of steroid therapy. The disease can manifest with all the symptoms and complications of chronic liver disease ranging from myalgia, nausea, vomiting to severe complications like portal hypertension with caput medusae and esophageal varices. Since this a treatable cause of liver disease, the progression can be stopped and life- threatening complications can be prevented and even reversed with early institution of steroid therapy.

CASE PRESENTATION

A 27-years old Southeast Asian female patient was admitted on 24/02/2021 with complaints of fever and yellowish discoloration for 2 months which were also associated with nausea, vomiting, constipation, and black stools. She had a medical history of asthma. The patient was non-alcoholic and was neither taking any prescription nor any non-prescription medications. Also, she had a negative travel history to areas endemic for hepatitis viruses and a negative family history of any liver disease. On clinical examination, fever, hepatosplenomegaly (HSM), and jaundice were noted. The initial laboratory examinations were remarkable for hepatic injury with LFT revealing Aspartate aminotransferase (AST) 2131 IU/L, Alanine aminotransferase (ALT) 1813 IU/L, Lactate dehydrogenase (LDH) 990 IU/L, Alkaline phosphatase (ALP) 263 U/L, Gamma- Glutamyltranspeptidase (GGT) 138 U/L, Albumin 3.33 g/dl, Prothrombin time/International normalized ratio (PT/INR) and total and direct bilirubin 6.96 mg/dl and 4.68 mg/dl respectively. USG revealed mildly altered echotexture of the liver with smooth borders, mild HSM with a liver span of 16 cm in the mid-clavicular line, and spleen size of 14 cm with pericholecystic edema and mild pelvic ascites. (Figure 1)

We ruled out acute viral hepatitis due to negative Anti-HAV Ab, HBsAg, Anti-HCV Ab, and Anti-HEV Ab. There was no Kayser-Fleischer ring seen on slit lamp examination. Now, although the entire picture was pointing towards autoimmune hepatitis, but serology was negative for the classic autoantibodies including ANA (via immunofluorescences), Anti-SM Ab, Anti-LKM-1 Ab, and also a negative Immuno 17 report. This raised suspicion of seronegative AIH. The patient was also admitted on 29/01/2021 with similar complaints of pyrexia of unknown origin and jaundice but responded to symptomatic treatment. However, she relapsed now. Due to a high clinical suspicion, the patient was advised to have a liver biopsy to confirm the diagnosis, but the patient's unstable condition didn't permit a biopsy. Still, she was diagnosed with seronegative AIH due to her clinical picture and prescribed methylprednisone (MPS) to which the patient responded with a visible improvement of her LFT as mentioned in Table 1.

This improvement in the clinical picture following steroids' administration confirmed the diagnosis of seronegative AIH in our patient.

DISCUSSION

AIH is characterized by an immune reaction directed towards liver tissue with autoantibodies being the culprit that not only commence, but also sustain the harm [2]. Clinically, it can have a variable presentation. There can be silent cases with no symptoms, but also there can be patients with significant symptoms related to hepatitis, which can rarely lead to acute liver failure as well.

AIH type 1, also known as Classical AIH, is known for the presence of ANA and/or smooth muscle autoantibodies (AMSA) and autoantibodies against actin and atypical perinuclear anti neutrophilic cytoplasmic

antibodies (p-ANCA). Type 2 AIH shows the occurrence of specific antibodies which are targeted against liver and kidney microsomal antigens (anti-LKM Ab) and/or liver cytosol type 1 antibody (ALC-1). For making a diagnosis, we need to rule out extrinsic causes of hepatitis such as drugs, alcohol, and viruses. Also, there should be satisfying inclusive criteria such as hyperglobulinemia, the presence of autoantibodies, and characteristic histologic features including interface hepatitis, plasma cells and rosettes. In about 70-80% of AIH cases, both ANA and ASMA can be found. Only in approximately 10% of patients of AIH, there are no circulating autoantibodies. Apart from a negative panel of autoantibodies, patients with SAIH are very similar to those of classical AIH in terms of their demographic, biochemical, and histological features. That is why they can be treated very successfully like classical AIH with corticosteroids. Also, they have similar prognosis after steroid therapy. SAIH has a favorable prognosis for patients who respond to

treatment. Most of the patients who receive appropriate treatment undergo remission, and the 10-year survival rate has approached from 83.8% to 94%. MIn the majority of cases we need to institute a maintenance therapy for their entire life, since discontinuation of the treatment can cause a reappearance of the disease in about 80% patients out of 100, over a term of 3 years.

In the past, there has been a case of seronegative autoimmune hepatitis reported by J.M. Sherigar et al. where a 58 y/o female patient came to the emergency department due to pain in her epigastrium along with nausea and vomiting, all the symptoms being there only for a day. That being an acute presentation of Seronegative autoimmune hepatitis is different from our patient who had chronic manifestations of fever and yellowish discoloration for 2 months. Also, in their case, the patient underwent a core liver biopsy which revealed that the portal tracts were penetrated with lymphocytes, plasma cells, and eosinophils. It also showed a severe grade 4 circumferential interface hepatitis, and steroid therapy was started after biopsy findings were confirmed, while in our case biopsy could not be performed as the patient was too unstable, so steroid therapy was started early based on clinical suspicion, showing how sometimes we have to start the therapy even in the absence of definitive diagnosis.

CONCLUSIONS

Like classical AIH, Seronegative AIH is also a diagnosis of exclusion but there can be a diagnostic dilemma due to a lack of serological autoimmunity evidence. Henceforth, the clinician should always keep this diagnosis in the list of differentials because diagnosing this condition and starting steroid therapy early in the course can lead to a substantial improvement in the liver pathology. Otherwise, the progression of the liver pathology in the absence of therapy can be detrimental, leading to stages requiring a liver transplant. The disease can also be recurrent if proper therapy is not instituted. Our case showed that the diagnosis can sometimes be made retrospectively if biopsy cannot be done.

Declarations

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D. Kriti Dhamija

Tables & Figures

Table 1**: Progression of LFTs**

LFT	First episode	2 days before steroid therapy	1 week after steroid therapy	2 weeks after steroi
SGOT/ SGPT (U/L)	125/180	2131/1813	105/174	120/210
S. Total Bil (mg/dl)	0.5	6.96	19.2	20
Alk Phosphatase (U/L)	130	263	64	85
INR	1.17		1.87	1.44
S. Albumin (g/dl)	3.0	3.33	4.0	4.0