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A Unique Conundrum: Unraveling Autoimmune Hepatitis in a Chronic Hepatitis B Patient

[1.]LALKRISHNA U -*SENIOR RESIDENT ,MD GENERAL MEDICINE ,DEP OF MEDICAL GASTROENTEROLOGY ,Govt MEDICAL COLLEGE ,KOTTAYAM*
[2.]GAURAV KHATANA - *SENIOR RESIDENT ,MD GENERAL MEDICINE ,DEP OF MEDICAL GASTROENTEROLOGY ,Govt MEDICAL COLLEGE ,KOTTAYAM*
[3.]GINO RONY PHILIP -*SENIOR RESIDENT , MD GENERAL MEDICINE ,DEP OF MEDICAL GASTROENTEROLOGY ,Govt MEDICAL COLLEGE ,KOTTAYAM*
[4.]SANDESH K -*PROFESSOR ,HOD ,DEP OF MEDICAL GASTROENTEROLOGY ,Govt MEDICAL COLLEGE ,KOTTAYAM ,DM MEDICAL GASTROENTEROLOGY*
[5.] SAJI SEBASTIAN -*ASSOCIATE PROFESSOR , DEP OF MEDICAL GASTROENTEROLOGY ,Govt MEDICAL COLLEGE ,KOTTAYAM ,DM MEDICAL GASTROENTEROLOGY*
[6.]RAMU M – *ASSISTANT PROFESSOR , DEP OF MEDICAL GASTROENTEROLOGY ,Govt MEDICAL COLLEGE ,KOTTAYAM ,DM MEDICAL GASTROENTEROLOGY*
[7.]DENI JOSEPH - *ASSISTANT PROFESSOR , DEP OF MEDICAL GASTROENTEROLOGY ,Govt MEDICAL COLLEGE ,KOTTAYAM ,DM MEDICAL GASTROENTEROLOGY*
CORRESPONDING AUTHOR
LAL KRISHNA U ,SENIOR RESIDENT,DEP OF MEDICAL GASTROENTEROLOGY AND HEPATOLOGY, Govt MEDICAL COLLEGE,KOTTAYAM ,unnikrishnalalkrishna@gmail.com ,Ph -7012895890

Abstract
There are only a few case reports in the literature regarding autoimmune hepatitis precipitated by chronic hepatitis B infection. Here, we present the case of a 61-year-old female who presented with excessive fatigue and transaminitis for one year. The patient had a prior history of jaundice (not previously evaluated), Graves disease three years ago, and a history of radioactive iodine ablation two years ago. Post-ablation, the patient developed hypothyroidism. Initial laboratory results showed SGOT at 512 U/L, SGPT at 334 IU/L, and ALP at 131. An extensive workup was conducted to evaluate the transaminitis. Her ANA (2+), ANTIHBc total, Anti SLA (1+), and Anti LC1 (1+) were positive. Further evaluation included HBV DNA quantitative PCR and liver biopsy. HBV DNA was not detectable, but the liver biopsy showed features of both autoimmune hepatitis (interphase hepatitis, lymphoplasmacytic infiltrates) and evidence of chronic hepatitis B (ground glass hepatitis) on underlying cirrhosis. After conducting a detailed literature search, we started her on both antivirals and immunosuppressants.
Key Words :*AIH -Auto immune hepatitis ,CHB -Chronic hepatitis B infection ,ANA -Anti nuclear Anti body Anti LC1-Liver cytosol .*

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I. Introduction

Auto immune hepatitis (AIH) is a rare cause of chronic inflammation of liver usually triggered by infections and other associated autoimmune etiology (hypothyroidism ,Vitiligo) with prevalence less than 0.02 % with female predominance[1].Usually AIH was associated with drug induced liver injury ,primary sclerosing cholangitis .Here we present a rare case of AIH triggered by chronic hep B infection .There are only few case reports in literature regarding this .

II. Case presentation

The patient was a 61-year-old female with a background of underlying mitral valve prolapse (diagnosed 10 years ago) and Graves' disease, who underwent radioactive ablation therapy two years ago. She presented with severe fatigue for one year. She had been evaluated at another center and was found to have severe hypothyroidism (Serum TSH - 40 mIU/L, normal range: 0.5 to 5.0 mIU/L) with decreased serum free T3 and serum free T4 levels, as well as altered liver function tests (SGOT - 734 U/L, SGPT - 512 U/L). She was started on thyroxine replacement and the transaminitis was considered to be due to hypothyroidism. The patient denied a history of

dyspnea, hematemesis, melena, edema, itching, weight loss, loss of appetite, and recent alcohol, alternative medicine, or other drug intake.

On examination, there was no pallor, icterus, cyanosis, clubbing, pedal edema, or lymphadenopathy. Her pulse rate was 88/min, and her blood pressure was 120/80. The abdominal examination was normal, and other systems were also normal. The results of her investigations are provided below:Hb / MCV (gm%)	9.6
TC	5800
DC	75/20/5
ESR	95
Plt	1.5 L
RBS(mg/dL)	120
Urea/Cr(mg/dL)	20/0/8
Na/K	138/4.2
TB/DB (mg/dL)	1.1/0.4
T Pr/ Alb g/dl	8.7/2.9
HIV	Negative
HbsAg	Negative (card)
Anti HCV	Negative (card)
Anti HBc total	Positive
HBV DNA quantitative PCR	Non detectable
ANA	1:80
Serum IgG Total	21ng/ml (up to 16 ng/ml)
Anti SLA	1+
Anti LC1	+
TPMT (Thiopurine methyl transferase acivitiy)genotyping	*1/*1 genotype (normal enzyme activity)
NUDT 15 (Nudix hydrolase)	Normal enzyme activity
Liver biopsy Findings	
Portal tracts	2-3 with lymphocytic infiltration
Plasma cells	Few
Interface hepatitis	Present
Fibrosis	Thick, predominantly macro and micro nodular steatosis (grade 2)
Hepatocytes	Some show ground glass appearance
Cholestasis	None observed
Eosinophilic infiltration	None observed
Diagnosis	Chronic hepatitis with steatosis (grade 2) and cirrhosis
Possibilities	(a) Post hepatitis (chronic hepatitis b related)
	(b) Associated autoimmune etiology
CECT abdomen	CLD with multiple regenerative hypodense modules
Upper GI endoscopy	Gastric antral vascular ectasia

After evaluation, the patient was diagnosed with chronic liver disease of mixed etiology, including both chronic hepatitis B and autoimmune hepatitis. The Child-Turcotte-Pugh score was 7, and the MELD score was 11.Revised Original Score for Autoimmune Hepatitis was 16 (Pre treatment). Our patient was initiated on a combination therapy, including antivirals for hepatitis B (entecavir 0.5mg) and Tab Azathioprine 50mg (after checking TPMT and NUDT 15 enzymes). Additionally, oral steroids in the form of tab prednisolone 40mg were prescribed once daily due to active hepatitis. All vaccinations, including hepatitis B, pneumococcal, and hepatitis A, were initiated. Steroids and Azathioprine were started one week after the initiation of antiviral therapy.

III. Discussion

Autoimmune hepatitis (AIH) is a chronic liver disease characterized by immune-mediated inflammation of the liver. The exact cause of AIH is not fully understood, but it is believed to involve a combination of genetic predisposition and environmental triggers[2]. AIH predominantly affects females more than males, with a peak incidence in middle-aged individuals. The disease can present with a wide range of symptoms, including fatigue, jaundice, abdominal discomfort, hepatomegaly, and elevated liver enzymes. However, some patients may be asymptomatic and are incidentally diagnosed through routine blood tests.,

Diagnosis of AIH involves a comprehensive evaluation, including clinical assessment, laboratory tests, imaging studies, and liver biopsy. Laboratory findings often reveal elevated liver enzymes, increased levels of certain autoantibodies (such as antinuclear antibodies and anti-smooth muscle antibodies), and elevated immunoglobulin levels. Liver biopsy helps confirm the diagnosis by demonstrating characteristic histopathological features, including interface hepatitis, lymphoplasmacytic infiltrates, and periportal fibrosis[3].

There are two main types of AIH: type 1 and type 2. Type 1 AIH is more common and is associated with the presence of antinuclear antibodies (ANA) and anti-smooth muscle antibodies (ASMA). Type 2 AIH is less common and is characterized by the presence of antibodies against liver kidney microsome type 1 (anti-LKM-1) and/or antibodies against liver cytosol type 1 (anti-LC1)[4].

The main goal of AIH treatment is to suppress the immune system and reduce liver inflammation. Immunosuppressive medications, such as corticosteroids (e.g., prednisone) and thiopurines (e.g., azathioprine), are commonly used as first-line therapy. Corticosteroids help control inflammation, while thiopurines modulate the immune response. Untreated or inadequately controlled AIH can progress to advanced liver disease, including cirrhosis, liver failure, and hepatocellular carcinoma. Therefore, long-term management and close follow-up are crucial to monitor disease activity, adjust medication dosages, and screen for potential complications. Liver transplantation may be considered for patients with advanced liver disease or those who fail to respond to medical therapy[5].

Chronic hepatitis B infection can occasionally precipitate autoimmune hepatitis, which is a condition where the body's immune system mistakenly attacks the liver cells. This coexistence of chronic hepatitis B and autoimmune hepatitis is known as "overlap syndrome." It is a relatively rare occurrence, but when it happens, it can present diagnostic and therapeutic challenges. In this condition, the immune system not only targets the hepatitis B virus but also attacks healthy liver cells, leading to inflammation and liver damage[6]. The exact mechanisms behind the development of autoimmune hepatitis in the presence of chronic hepatitis B are not fully understood. However, it is believed that a dysregulated immune response triggered by the hepatitis B virus may contribute to the development of autoimmune hepatitis.

Clinically, patients with chronic hepatitis B infection precipitated autoimmune hepatitis may exhibit features of both conditions. They may have elevated liver enzyme levels, signs of ongoing viral replication, as well as the characteristic autoimmune hepatitis markers, such as the presence of autoantibodies and increased immunoglobulin levels[7]. The diagnosis is made by assessing clinical symptoms, liver function tests, viral markers, autoantibodies, and liver biopsy.

Treatment for this condition involves a combination of antiviral therapy to control the hepatitis B virus and immunosuppressive medications to suppress the autoimmune response. The goal is to reduce liver inflammation, prevent further liver damage, and achieve long-term remission. However, the management approach needs to be individualized based on the patient's specific characteristics and disease severity. Regular monitoring of liver function, viral markers, and autoantibodies is crucial to assess treatment response and adjust the therapeutic regimen accordingly. It is important for individuals with chronic hepatitis B infection to work closely with healthcare professionals experienced in managing both hepatitis B and autoimmune hepatitis to ensure appropriate and optimal care. Anti virals also indicated after 6 months to one year of tapering steroids [8].

IV. Conclusion

Chronic Hepatitis B associated with autoimmune hepatitis is a challenging case for clinicians. Considering the concurrent evidence of CHB and AIH , we have initiated antiviral treatment due to the presence of ground glass hepatocytes (indicating evidence of HBSAg in liver biopsy). We have also started administering steroids and Azathioprine to prevent the progression of autoimmune hepatitis. It is crucial to frequently monitor the HBV DNA levels in this case. The patient's prior history of autoimmune disease (Graves disease) and past jaundice episodes suggest an autoimmune hepatic pathology. The primary challenge in this case is ensuring regular follow-up. Many patients who are prescribed steroids tend to continue taking them without proper monitoring.

FIGURE 1

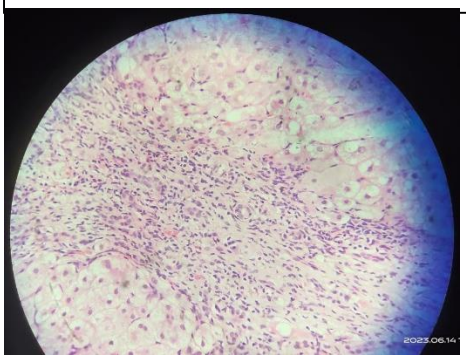

FIGURE 1 :LIVER BIOPSY (H &E STAINING SHOWING INTERPHASE HEPATITIS (PIECEMEAL NECROSIS) RED ARROW

FIGURE 2

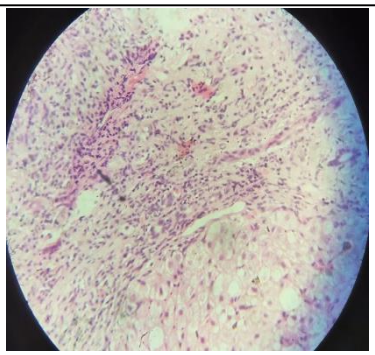

FIGURE 2:LIVER BIOPSY (H@E STAINING)SHOWING LYMPHOPLASMACYTIC

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