Case Report

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Autoimmune manifestations in chronic hepatitis B

Abstract

The chronic hepatitis B infection (CHB) has been associated to a variety of autoimmune manifestations, including circulating non-organ-specific autoantibodies, membranous proliferative glomerulonephritis, mixed cryoglobulinaemia and polyarteritis nodosa. The diagnosis and treatment depend on the affected organs and demonstration of viral activity. However, we should initially assess the probable clinical diagnosis in which its outcome and long-term resolution depend on the proper use of antiviral drugs. Herein, we reported an unusual clinical presentation of hepatitis B reactivation in an antigen e-negative CHB patient.

Keywords: hepatitis B virus, chronic hepatitis B, autoimmune, hepatitis B reactivation, antiviral drugs, nucleos(t)de analogs

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Abbreviations: HBV, hepatitis B virus; CHB, chronic hepatitis B; ANA, antinuclear antibodies; anti-DNA, anti-double-stranded DNA antibodies; ANCA, anti-neutrophilic cytoplasmic antibodies; ENA, extractable nuclear antigens; anti-β2GCP, anti-β2 glycoprotein antibodies; CIC, circulating immune-complexes; IgG, total serum immunoglobulin class G IgM, total serum immunoglobulin class M; IgA, total serum immunoglobulin class A; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e-antigen; Anti-HBe, hepatitis B antibodies to e-antigen; anti-HAV IgM, hepatitis A virus antibodies class IgM; Anti-HCV, hepatitis C virus antibodies; Anti-HIV, human immunodeficiency virus antibodies

Introduction

Autoimmune manifestations could be observed in up to 20% of patients with acute or chronic hepatitis B virus (HBV) infection.[1] Serum-sickness-like disease is seen as a prodrome phase in 10 to 20% of patients with acute hepatitis, while polyarteritis nodosa and glomerulonephritis are the most described autoimmune extrahepatic disorders in chronic hepatitis B (CHB).[1,2] Herein, we reported an unusual clinical presentation of hepatitis B reactivation in an antigen e-negative CHB patient.

Case report

A 57 years-old Venezuelan woman was referred to the Immunology Institute because of the presence of pericarditis, mild bilateral pleural effusion and hematuria. At the time of consultation, she was prepared to receive intravenously methylprednisolone (1g daily). She started with general malaise, severe weakness, fever, hypotension and arthralgia in hands and knees 2 weeks prior to referral. On her past medical history, she was hospitalized with the diagnosis of endocarditis 4 years earlier. Relevant laboratory results on admission revealed decreased lymphocytes count (800/mm^3), C-reactive protein 42mg/L, ALT 143 IU/L, AST 78 IU/L, GGTP 111 IU/L, hematuria 2+ and negative serology markers for cytomegalovirus and Epstein-Barr virus. The immunological profile (depicted in Table 1) showed only mildly increase of serum C3 levels and positive lupus anticoagulant test. Renal function was within normal limits. We added the assessment of viral hepatitis immunological markers which were available 10 days later. During that period she did not respond to intravenously methylprednisolone, hydroxycloroquine sulfate and aspirin. Viral hepatitis immunological markers showed HBsAg positive, total anticore positive, anti-HBe positive, anticore IgM negative and HBeAg negative (Table 1). HBV viral load (HBV-DNA) by quantitative real-time PCR demonstrated 123,888 IU/mL. Antibodies to HAV (IgM), HCV and HIV were all negative. Methylprednisolone, hydroxycloroquine (200mg daily) and aspirin (100 mg daily) therapies were discontinued. The patient's clinical conditions were not suitable to perform liver biopsy at that time. Antiviral treatment with oral entecavir 0.5mg daily was initiated. Resolution of cardiac and pulmonary effusions and other symptoms improved progressively. Normalization of laboratory tests including liver enzymes values and negative lupus anticoagulant were also achieved. In addition, HBV-DNA decreased to <5IU/mL after 3 months of treatment. At present, she is currently asymptomatic, remains HBsAg positive but not presenting ALT flares or anti-surface antigen seroconversion after 3 years of follow-up with entecavir therapy.

Table 1 N=57; Epidemiological distribution of the pathological fractures, traumatic fractures, and nonunion

Marker	Result	Normal limits
ANA	Negative	
Anti-DNA	Negative	
ANCA	Negative	
ENA	Negative	
CH50	58	40-61U/mL
C3	202	90-180mg/dl
C4	19	10-40mg/dl
		Positive:>18GPL/ml
Anti-cardiolipins IgM	13	Undetermined:12-18
		Negative: <12GPL/ml
		Positive: >18MPLU/ml
Anti-cardiolipins IgG	9	Undetermined: 12-18
		Negative: <12MPLU/ml
Lupus anticoagulant	Positive	
Anti-β2GCP	Negative	
IgG	970	700-1.500mg/dL
IgM	85	48-380mg/dL
IgA	110	70-290mg/dL
Cryoglobulins	0.28	<0.500mg/mL

Table continued...

Marker	Result	Normal limits
CIC	<1	0-4.4mEq/mL
HBsAg	Positive	
Anticore IgM	Negative	
Total anticore	Positive	
HBeAg	Negative	
Anti-eHB	Positive	
Anti-HAV IgM	Negative	
Anti-HVC	Negative	
Anti-HIV	Negative	

Discussion

At the time of her referral, the patient was an unrecognized HBsAg carrier. It is highly probable that she acquired HBV infection during her past hospitalization. Therefore, based on her nosocomial background, clinical features and negative immunological profile except for a lupus anticoagulant positive, we decided to assess her viral hepatitis B and C status. Liver enzymes values and immunological/virological markers confirmed the existence of HBV reactivation in an HBe-negative CHB patient. Nosocomial HBV risk infection in Venezuela remains as an unsolved problem.[3] Furthermore, we have previously reported that approximately 12% of our chronic hepatitis B population is HBe-antigen negative. This implies that they are harbouring precore/core HBV variants such as our patient.[3,4] Autoimmune manifestations in HBV might be mediated by immune-complexes deposits of viral proteins and antibodies which activate the complement cascade and also recruit inflammatory cells to extrahepatic organs.[1,5] This pathogenic mechanism has been mostly investigated in patients with HBV-related glomerulonephritis.[6] Although, at the beginning, our case might resemble a probable antiphospholipid syndrome, the presence of a transient positive lupus anticoagulant in HBV has been already described.[7] Thus far, the patient has remained negative for anti-phospholipids antibodies and lupus anticoagulant.

Another pathogenic mechanism implies active viral replication which induces extrahepatic organ inflammation contributing to the autoimmune manifestations.[1,5] In this regard, the majority of CHB patients who develops autoimmune manifestations and/or HBV reactivation are HBe-positive a marker directly correlated to active replication of the B virus.[5,8,9] Clinically, HBV reactivation is associated with ALT flare and simultaneously increase of viral replication.[8,9] These events explain spontaneously reactivation or reactivation associated to immunosuppressive states.[10,11] Control of HBV induced-liver necro-inflammation and symptoms resolution are usually achieved by decreasing the viral load (HBV DNA) with the use of nucleotides/nucleosides analogs (NA).[8-11] Our HBe-negative CHB patient showed a viral load >100,000 IU/mL (5,0 logs) and responded favorably to the NA therapy.

Conclusion

Our case report represents a rare instance of a patient with spontaneously HBe-antigen negative chronic B hepatitis reactivation whose extrahepatic autoimmune manifestations prevailed. This was mainly mediated by active viral replication and successfully treated with a nucleoside analog.

Conflicts of interest

None.

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References

1. Cacoub P, Terrier B. Hepatitis B-Related Autoimmune Manifestations. *Rheum Dis Clin of N Am*. 2009;35(1):125–137.
2. Carneiro de Moura M, Marinho R. Historia natural y manifestaciones clínicas de la hepatitis B crónica. *Enferm Infecc Microbiol Cli*n. 2008;26(Supl 7):11–18.
3. Alexopoulou A, Karayiannis P. HBeAg negative variants and their role in the natural history of chronic hepatitis B viral infection. *World J Gastroenterol*. 2014;20(24):7644–7652.
4. Machado IV, Fortes MP, Vargas-Lovelle B, et al. Genotype F prevails in Venezuelan urban patients with chronic hapatitis B. *Ann Hepatol*. 2010;9(2):172–176.
5. Liang TJ. Hepatitis B: The Virus and Disease. *Hepatology*. 2009;49(5 Suppl):S13–S21.
6. Chao TM. Hepatitis B and Renal Disease. *Curr Hepatitis Rep*. 2010;9(2):99–105.
7. Huh JY, Yi DY, Hswang SG, et al. Characterization of antiphospholipid antibodies in chronic hepatitis B. *Korean J Hematol*. 2011;46(1):36–40.
8. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol*. 2017;67(2):370–398.
9. González SA, Perillo RP. Chapter 14. Immunopathogenesis of Chronic Hepatitis B and the Clinical Events That Shapes its Natural History. In: Gershwin E, Vierling JM, editors. *Liver Immunology*. 2nd edn. New York, USA. Springer; 2014. p: 191–206.
10. Loomba R, Liang TJ. Hepatitis B Reactivation Associated With Immunosuppressive and Biological Modifier Therapies: Current Concepts, Management Strategies, and Future Directions. *Gastroenterol*. 2017;152(6):1297–1309.
11. Nordeen F. Hepatitis B virus infection: An insight into infection outcomes and recent treatment options. *Virus Dis*. 2015;26(1-2):1–8.