American Journal of Case Reports

ISSN 1941-5923
© Am J Case Rep, 2017; 18: 170-172
DOI: 10.12659/AJCR.901688

Received: 2016.09.22
Accepted: 2016.12.05
Published: 2017.02.16

Dual Infection with Hepatitis B and Epstein-Barr Virus Presenting with Severe Jaundice, Coagulopathy, and Hepatitis B Virus Chronicity Outcome

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABDEF 1 Sirish C. Rao
ABDEF 2 Imran Ashraf
ABDEF 2 Fazia Mir
ABDEF 2 Sami Samiullah
ABCDEF 2 Jamal A. Ibdah
ABCDEF 2 Veysel Tahan

1 Department of Internal Medicine, University of Missouri, Columbia, MO, U.S.A.
2 Division of Gastroenterology and Hepatology, University of Missouri, Columbia, MO, U.S.A.

Corresponding Author: Veysel Tahan, e-mail: tahanv@health.missouri.edu
Conflict of interest: None declared

Patient: Female, 34
Final Diagnosis: HBV and EBV dual infection
Symptoms: Jaundice • fatigue • anorexia • subjective weight loss
Medication: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology

Objective: Rare co-existance of disease or pathology

Background: Hepatitis B virus (HBV) has been reported as a coinfection with hepatitis C virus (HCV), hepatitis D virus (HDV), cytomegalovirus (CMV), and human immunodeficiency virus (HIV).

Case Report: A 34-year-old female presented to our clinic with epigastric pain and severe acute hepatitis manifested as jaundice associated with hyperbilirubinemia, elevated transaminases, and coagulopathy. The patient was diagnosed with acute HBV with Epstein-Barr virus (EBV) coinfection leading to subsequent chronic hepatitis B.

Conclusions: To our knowledge, this patient case is the first reported case of HBV and EBV coinfection reported in the literature. HBV and EBV coinfection may cause severe acute hepatitis with HBV chronicity.

MeSH Keywords: Chronic Disease • Coinfection • Epstein-Barr Virus Infections • Hepatitis B Virus • Jaundice

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/901688

Background

The World Health Organization estimates that there are 400 million carriers of hepatitis B virus (HBV) in the world. The incidence of infection with Epstein-Barr virus (EBV) is estimated to range between 60–100 per 100,000 person years [1]. Dual infections of HBV with hepatitis C virus (HCV), hepatitis D virus (HDV), herpes simplex virus (HSV), cytomegalovirus (CMV), and human immunodeficiency virus (HIV) are possible and have been previously reported [2–8].

Individuals with dual infections of HBV and other viruses, including HCV, HDV, HSV, CMV, and HIV, have demonstrated worse clinical presentation and clinical course in comparison with individuals with mono-infections. Data on treatment of coinfections is limited, as studies have excluded patients with dual infections in HBV and HCV [2]. We aimed to present our HBV and EBV dual infection case of a patient who developed a severe acute course and chronicity of HBV. To the best of our knowledge, this case is the first published HBV and EBV coinfection report in the literature.

Case Report

A 34-year-old Caucasian female with no significant past medical history presented to our tertiary care facility with a four-day history of epigastric pain and jaundice that was sudden in onset, and was not associated with any fevers, chills, nausea, vomiting, or diarrhea. She denied utilization of excessive acetaminophen or alcohol use, illicit drug use, herbal preparations, or any toxin exposure. On further inquiry about sexual history, the patient revealed that she had a sexual partner with known chronic HBV and HCV infection. Physical examination was notable for scleral icterus, jaundice, and mild abdominal tenderness with deep palpation of the right upper quadrant. Initial laboratory testing revealed PT 18.5 seconds, INR 1.6, total bilirubin 28.13 mg/dL, direct bilirubin 19.2 mg/dL, AST 829 mg/dL, and ALT 485 mg/dL. An abdominal ultrasound showed a contracted gallbladder with spurious thickening without any intrahepatic biliary ductal dilation, mild ascites, and no portal or hepatic vein thrombosis. Her hepatitis panel was positive for HBs Ag, HBe Ag, HBc IgM Ab, EBV early antigen IgG antibody, EBV viral capsid antigen (VCA) IgM, and IgG Ab. Her test results for antibodies to EBV nuclear antigen and HBe Ab were negative. The patient was diagnosed with acute viral hepatitis secondary to HBV and EBV coinfection. The patient's clinical course was severe with jaundice, coagulopathy, and ascites during her acute infection but without symptoms of hepatic encephalopathy. During her hospital stay, the patient's transaminases and bilirubin levels gradually improved within two weeks, and she was discharged home. Her EBV DNA test was found negative within her three-week disease course. Her HBV DNA was positive (initial 1,320,000 IU/mL) and remained positive upon repeat testing at six months (24,400 IU/mL) with HBs Ag and HBe Ag positivity during her follow-up. These results confirmed chronicity of HBV infection following an acute HBV and EBV dual infection.

Discussion

HBV coinfections with HCV, HDV, HSV, CMV, and HIV have been reported. However, our current knowledge is still limited pertaining to viral interaction, clinical presentation, and clinical course of HBV coinfections with any other virus, and there were no reported cases of HBV and EBV coinfection in the literature. Previous studies have shown that dual infection with HBV and HCV leads to more extensive liver damage than infection with HBV or HCV alone, and dual infection may lead to necrotic inflammatory changes, cirrhosis, and progression to hepatocellular carcinoma [4]. Reciprocal inhibition has also been observed with HBV and HCV coinfection, with varying opinions on which virus, HBV or HCV, possesses a greater degree of viral suppression between the two [5,6]. Coinfection with HBV and HIV has exhibited greater chronicity of HBV infection, which may be secondary to the immunosuppressive effect of HIV hindering the immune system's ability to clear the acute infection [7].

Optimal treatment of HBV coinfections is still in flux. Current recommendations for HBV coinfections entail determining the dominant virus and treating accordingly [9]. Given the concern for reciprocal inhibition, treating one virus may in turn allow the suppressed virus to become more active and worsen the clinical course. EBV has been treated with multiple antivirals (acyclovir, ganciclovir, and vidarabine) with some success; however, antiviral therapy is generally ineffective for the treatment of chronic EBV [10]. EBV DNA can be determined in patients with primary infection within two weeks of symptom onset. It decreases rapidly in plasma/serum and it becomes undetectable after three to four weeks [11,12]. Our patient's EBV DNA was negative three weeks after the onset of symptoms, which would be secondary to the disease course or we can speculate that it may have been secondary to HBV/EBV viral interaction induced EBV suppression. The higher AST/ALT ratio in our case of coinfection would be consistent with severe zone 3 liver disease. However, we have seen a higher AST/ALT ratio with EBV infection in our clinical experience [13].

Liu et al. [14] studied the occurrence and association between CMV and HBV among 117 patients receiving allo-hematopoietic stem cell transplantation (allo-HSCT). In 91.8% of the allo-HSCT cases, both donor and recipients were CMV positive and 13.7% of cases had HBs Ag positivity. When the patient had either CMV pp65 antigenemia or two consecutive CMV PCR

positive results, ganciclovir 5 mg/kg twice daily for two weeks was administered, and it was followed by 5 mg/kg once daily until two consecutive negative results for CMV PCR and CMV pp65 antigenemia. Of the eight CMV patients, two died secondary to CMV disease and the other patients responded to ganciclovir therapy. The CMV mortality rate was 1.7% (2/117 patients). HBs Ag positivity was found in 13.7% (16/117) of recipients and 11.1% (13/117) of donors. No HBV treatment was used. No patient had clinically significant HBV infection. Even the HBs Ag positive CMV infection group had particularly better survival compared to the HBs Ag negative CMV infection group.

Bayram et al. [15] reported a virus-virus interaction between CMV and HBV. HBV replication was inhibited by the local induction of cytokines produced during CMV-induced hepatitis and this inflammation likely contributed to viral clearance of HBV [15].

Standard treatment of HBV and EBV coinfection has not yet been evaluated; however, treatment goals will most likely be aimed at suppression of HBV given the transient nature of EBV.

However, in contrast to previous CMV-HBV interaction causing HBV replication inhibition, it was active HBV replication and inhibition of EBV replication in our HBV+EBV dual infection case.

Acute HBV and EBV coinfection can present as severe liver disease and can cause HBV chronicity. Given the worsened disease state and the HBV chronicity, treatment goals and options prompt the need for further investigation.

Conclusions

To the best of our knowledge, this is the first reported case with HBV and EBV dual infection. Our patient's acute HBV and EBV dual infection course was very severe, and although HBV chronicity rate was lower than 5% and the patient's development of jaundice was a sign of a strong immune response to clear the HBV infection, our patient still developed HBV chronicity. In the absence of data from the literature on HBV and EBV coinfection, we may speculate that EBV coinfection or superinfection may lead to a severe acute HBV infection course with subsequent development of HBV chronicity even after a prominent immune response with jaundice.

Conflict of interest statement

All the authors state that they have no conflicts of interests to declare.

References:

1. Hjalgrim H, Friborg J, Melbye M: The epidemiology of EBV and its association with malignant disease. In: Arvin A, Campadelli-Fiume G, Mocarski E et al. (eds.), Human Herpesviruses: Biology, Therapy, and Immunoprophylaxis. Cambridge: Cambridge University Press; 2007. Chapter 53
2. Senturk H, Tahan V, Canbakan B et al: Chronic hepatitis C responds poorly to combination therapy in chronic hepatis B carriers. Neth J Med, 2008; 66: 191–95
3. Sagnelli E, Coppola N, Scolastico C et al: Virologic and clinical expressions of reciprocal inhibitory effect of hepatitis B, C, and delta viruses in patients with chronic hepatitis. Hepatology, 2000; 32: 1106–10
4. Park JS, Saraf N, Dieterich DT: HBV plus HCV, HCV plus HIV, HBV plus HIV. Curr Gastroenterol Rep, 2006; 8: 67–74
5. Tsai SL, Liaw YF, Yeh CT et al: Cellular immune responses in patients with dual infection of hepatitis B and C viruses: Dominant role of hepatitis C virus. Hepatology, 1995; 21: 908–12
6. Wang YM, Ng WC, Lo SK: Suppression of hepatitis C virus by hepatitis B virus in coinfected patients at the national university hospital of Singapore. J Gastroenterology, 1999; 4: 481–85
7. Phung BC, Sogni P, Launay O: Hepatitis B and human immunodeficiency virus co-infection. World J Gastroenterol, 2014; 20: 17360–67
8. Liu Z, Hou J: Hepatitis B virus (HBV) and hepatitis C virus (HCV) dual Infection. Int J Med Sci, 2006; 3: 57–62
9. Martin P, Lau DT, Nguyen MH et al: A treatment algorithm for the management of chronic hepatitis B virus infection in the United States: 2015 update. Clin Gastroenterol Hepatol, 2015; 13: 2071–87
10. Cohen JI: Optimal treatment for chronic active Epstein-Barr virus disease. Pediatr Transplant, 2009; 13: 393–96
11. Kimura H, Hoshino Y, Hara S et al: Viral load in Epstein-Barr virus-associated hemophagocytic syndrome. Microbiol Immunol, 2002; 46: 579–82
12. Balfour HH, Holman CJ, Hokanson KM et al: A prospective clinical study of Epstein-Barr virus and host interactions during acute infectious mononucleosis. J Infect Dis, 2005; 192: 1505–12
13. Tahan V, Ozaras R, Uzunismail H et al: Infectious mononucleosis presenting with severe cholestatic liver disease in the elderly. J Clin Gastroenterol, 2001; 33: 88–89
14. Liu YC, Lu PL, Hsiao HH et al: Cytomegalovirus infection and disease after allogeneic hematopoietic stem cell transplantation: Experience in a center with a high seroprevalence of both CMV and hepatitis B virus. Ann Hematol, 2012; 91: 587–95
15. Bayram A, Ozkur A, Erkilic S: Prevalence of human cytomegalovirus co-infection in patients with chronic viral hepatitis B and C: A comparison of clinical and histological aspects. J Clin Virol, 2009; 45: 212–17