HEPATITIS B VIRUS ACUTE INFECTION AND FAST SELF-LIMITED RECOVERY: A RARE CASE REPORT

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ABSTRACT

Introduction: *Hepatitis B virus (HBV) causes acute/chronic disease which depends on age, immune level, characteristics of infected strain, etc. To our knowledge, very few people can remove HBV infection rapidly in less than 2 weeks, especially at the age of 78.*

Case Presentation*: A 78-year-old patient was hospitalized because of anorexia, naupathia and emesis for 2 days. It was diagnosed by sharp increase in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and positive HBV-associated markers. Magnesium isoglycyrrhizinate and reduced glutathione injection were administrated. Results: Without any anti-HBV therapy, about 10 days later, liver function was recovered miraculously, HBV antigens and DNA were positive-to-negative transformed, and kept HBV free in the latest follow-up.*

Discussion*: Our experience with this case highlighted the importance of healthy lifestyle, wholesome immunity and timely vaccination to combat HBV.*

Keywords: *Acute hepatitis, Hepatitis B virus, Liver injury.*

DOI: 10.19193/0393-6384_2022_5_519

Received *March 15, 2022;* ***Accepted*** *June 20, 2022*

Introduction

Hepatitis B virus (HBV), a hepatotropic, enveloped, coated, double-stranded DNA virus, contains hepatitis B surface/core/e antigen (HBs/c/eAg)[(1)], causes both acute and chronic hepatopathy[(2)]. HBV caused over 250 million people worldwide to be chronically infected, at least 880,000 deaths yearl[(3)]. The immunopathogenesis of HBV depends on a complex interplay of host and viral factors, such as age, gender, immune status, etc[(4)]. HBV-infected children under 6 years old tend to develop chronic infections, while less than 5% of adult cases will develop into chronic infections[(5)]. A tiny minority with HBV acute infection with 60-90 days incubation period in average can develop into acute liver failure[(6)], even death, it can occur at any age, but mainly between 20 and 40 years old[(4)].

HBV was classified into 8 genotypes, named A to H. A and D are prevailing in European countries, while B and C in China. Patients infected with genotype C showed longer immune clearance period, higher DNA level and ALT level, lower response to anti-HBV therapy than genotype B[(7)]. Immunocompetent adults infected HBV acutely could spontaneously clear the infection with 1-2 months duration[(8)]. Anti-HBV treatment or not depends on viral titer in serum.

Interferon or nucleoside analogs should implement as long as the HBV DNA copies exceed 1000 IU/ml. In addition, liver-preserving, aminotransferase-reducing, bland and digestible diet with enough nutrients and calories, adequate sleep and rest were recommended.

Case presentation

Clinical presentation: A 78-year-old male was admitted to Shaoxing People's Hospital (Zhejiang, China). He suffered epigastric discomfort, inappetence, sporadic belching and nausea 2 days before hospitalization. Past medical history included that he suffered from prostatic hyperplasia, calcification, and nephrectomy operation of left kidney because of inflammatory pseudotumor, but uninvolved hepatitis previously.

Lab findings: Lab tests indicated liver injury. ALT was strongly elevated to 3325 U/L, AST was 3093.5 U/L (Fig. 1A). Others including ALP, Gamma-glutamyltransferase (GGT), lactate dehydrogenase (LDH), total bilirubin total (TBIL), direct bilirubin (DBIL) and indirect bilirubin (IBIL) were all up-regulated in various degree (Fig.1). The reference range of liver function-related serum biochemical indicators was shown in table 1.

HBs/e Ag and HBc antibody (HBcAb) were all positive (Fig. 1C). Two weeks later, positive-to-negative transformation of HBs/eAg occurred, HBs antibody (HBsAb) and HBe antibody (HBeAb) were shifted from negative to positive. Positive situation of HBs/e/c antibodies lasted till the end of follow-up. HBV DNA in serum of the first examination after admission was 273 IU/ml, slightly elevated to 631 IU/ml one week later, and undetected about ten days later. Hepatitis A/C/E virus (HBV/HCV/HEV) antibodies, and Hepatitis D virus (HDV) RNA were all negative. Autoimmune liver disease was excluded based on the negative result of antinuclear antibody. Carbohydrate antigen 50 (CA50) was 67.1 IU/ml on admission, and then dropped to 20.9 IU/ml 9 days later. Besides CA50, other tumor markers were all within normal limits.

Lymphocyte subpopulation and lymphocytokines analysis showed that in the early stages of infection, $CD3^+$ T lymphocytes grew in number and percentage, especially cytotoxic CD8+/$CD3^+$ (Fig. 1D), which led to tissue inflammation and viral clearance through killing infected cells. During clearance period, $CD4^+$ and B T-cells (CD19+) reduced slightly, instead, $CD8^+$ and NK cells ($CD16^+/CD56^+$) increased. For cytokines, at the beginning IL-2, INF-γ and TNF-α were induced at a high level, and then declined gradually, while a slight drop in IL-4, IL-6 and IL-10 picked up again.

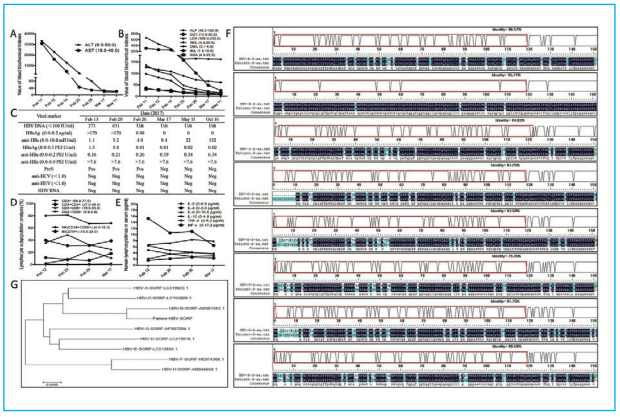

Figure 1: (***A***) The panel shows a timeline of the serum biochemical indicators after admission. ALT and AST were detected by biochemical analyzer. (**B**) ALP, GGT, LDH, TBIL, DBIL, IBIL and ADA in serum. (**C**) Clinical profile of hepatitis virus associated Markers. (**D**) Lymphocyte subpopulation of whole blood was analyzed by FCM (flow cytometry) at different points in time. (**E**) Six kinds of lymphocytokines including IL-2, IL-4, IL-6, IL-10, INF-γ and TNF-α in serum were detected by FCM based on cytometric bead array (CBA). (**F**) Segmented amplification and sequencing of HBV genome from the serum of patient. The gene of HBs was aligned with the amino acid sequence of genotype A-H. (**G**) Phylogenetic tree constructed by MEGA7. The HBs gene neighbor joining phylogenetic tree based on 1203 bp nucleotide sequences from GenBank and the isolated strain of patient. Reference ranges of all the lab test indexes were shown in relevant panal.

Test Items	AST	ALT	ALP	GGT	LDH	TBIL	DBIL	IBIL	ADA
Reference Range	9.0-50.0	15.0-40.0	45.0-125.0	10.0-60.0	109.0-245.0	3.4-20.5	0.1-6.8	1.5-18.0	4.0-22.0
Unit	U/L	U/L	U/L	U/L	U/L	μmol/L	μmol/L	μmol/L	U/L

Table 1: The reference range of liver function-related serum biochemical indicators.

HBV strain from patient: HBV sequence was analyzed by sequencing, and aligned with genotype A-H by DNAman (Fig. 1E), phylogenetic tree were constructed based on nucleotide sequence by MEGA7. HBV strain isolated from patient was highly homologous to genotype B (95.77%), while others were all between 80% and 90%. The genotype of HBV strain from patient was identified to B according to the cladogram (Fig. 1G).

Chemotherapy and antiviral therapy: All the tests showed that the patient was acutely infected by HBV which led to severe liver injury, mild skin scleral jaundice. After being hospitalized, he was

treated with first-grade nursing. The key measures involve magnesium isoglycyrrhizinate and reduced glutathione for liver protection, transaminase reduction, jaundice remove. It was then that low-fat diet was recommended.

Discussion

This report involves a patient diagnosed with HBV-associated acute hepatitis and high serum transaminase level, quick HBV clearance and recover. He was admitted to hospital because of abdominal discomfort, inappetence, sporadic belching eructation and nausea. HBV infection was proved to be the culprit of severe liver damage. Serum transaminase of the first time after enrollment in hospital reached the top, and then reduced gradually, went back to normalsingularly in two weeks. HBs/eAg and HBV DNA kept in line with transaminase, and on the decline until undetected. Anti-HBs, anti-HBe and anti-HBc were all positive, especially the value of anti-HBs had grown higher. In the latest follow-up, patient kept HBV free completely. Interestingly, individual tumorous marker may rise abnormally, for instance, CA50 was up-regulated sharply and then recovered after temporary elevation followed by repair of liver injury. Due to low HBV DNA level (<1000 IU/ml), anti-HBV therapy was not administered, only liver-preserving and aminotransferase-reducing jaundice. Multiple abnormal indexes triggered by HBV infection and strong immune response in the following had shown levels within normal range.

Till now, there're no effective methods for complete removal of HBV from patients[9]. According to lymphocyte subpopulation and lymphocytokines analysis, cellular immunity played a leading role in fighting with HBV. After viral clearance and liver repairment, it was the turn of humoral immunity to keep fighting. Our patient cleared HBV biweekly, much less than in general case with about 6 weeks. Fast HBV removal and recovery from severe liver injury may be attributed to the healthy and strong immune system, even though advanced age. It serves to show the importance of physical fitness and strong immunity. Actully, he didn't smoke or drink, never stay up late, always had a healthy and light diet and spent regular time on moderate exercise.

HBV/HDV coinfection could result in an increased risk of chronicity, HCC and mortality compared to mono-infection of HBV[10]. Genotype B HBV was proved to have more mild clinical consequences than genotype C. The secondary cause of quick clear and recovery is that our patient infected by genotype B HBV without HDV infection. HBV can be prevented by a safe, available and effective vaccine, which could offer a 98-100% protection, avert the development of complications including the development of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. Patient in present study was not vaccinated and had no specific immunity.

Conclusion

Nowadays, because of large survival pressure, good living conditions, polluted environment, it's becoming more and more difficult to maintain a healthy lifestyle which would help ourselves be healthier. For the good of strong immunity and health, people should stay away from smoking, drinking, greasy diet, staying up late. There is, in addition, we must pay much attention on preliminary vaccination.

References

1) Mysore KR, Leung DH. Hepatitis B and C. Clinics in liver disease. 2018; 22(4) :703-22. doi: 10.1016/j.cld.2018.06.002.
2) Yip TC, Wong VW, Chan HL, Tse YK, Lui GC, Wong GL. Tenofovir Is Associated With Lower Risk of Hepatocellular Carcinoma Than Entecavir in Patients With Chronic HBV Infection in China. Gastroenterology. 2020; 158(1): 215-25 e6. doi: 10.1053/j.gastro.2019.09.025.
3) Zhuang X, Forde D, Tsukuda S, D'Arienzo V, Mailly L, Harris JM, et al. Circadian control of hepatitis B virus replication. Nature communications. 2021;12(1):1658. doi: 10.1038/s41467-021-21821-0.
4) Wu J, Han M, Li J, Yang X, Yang D. Immunopathogenesis of HBV Infection. Advances in experimental medicine and biology. 2020; 1179: 71-107. doi: 10.1007/978-981-13-9151-4_4.
5) Pei Y, Wang C, Yan SF, Liu G. Past, Current, and Future Developments of Therapeutic Agents for Treatment of Chronic Hepatitis B Virus Infection. Journal of medicinal chemistry. 2017; 60(15): 6461-79. doi: 10.1021/acs.jmedchem.6b01442.
6) Sun D, Liu F. Modeling and Control of a Delayed Hepatitis B Virus Model with Incubation Period and Combination Treatment. Interdiscip Sci. 2018; 10(2): 375-89. doi: 10.1007/s12539-017-0275-y.
7) Sumi H, Yokosuka O, Seki N, Arai M, Imazeki F, Kurihara T, et al. Influence of hepatitis B virus genotypes on the progression of chronic type B liver

disease. Hepatology. 2003; 37(1): 19-26. doi: 10.1053/jhep.2003.50036.
8) Lin CL, Kao JH. Natural history of acute and chronic hepatitis B: The role of HBV genotypes and mutants. Best practice & research Clinical gastroenterology. 2017; 31(3): 249-55. doi: 10.1016/j.bpg.2017.04.010.
9) Yang YC, Chen YH, Kao JH, Ching C, Liu IJ, Wang CC, et al. Permanent Inactivation of HBV Genomes by CRISPR/Cas9-Mediated Non-cleavage Base Editing. Molecular therapy Nucleic acids. 2020; 20: 480-90. doi: 10.1016/j.omtn.2020.03.005.
10) Koh C, Da BL, Glenn JS. HBV/HDV Coinfection: A Challenge for Therapeutics. Clinics in liver disease. 2019; 23(3): 557-72. doi: 10.1016/j.cld.2019.04.005.

Abbreviations

HBV, hepatitis B virus; HDV, hepatitis D virus; HBcAb, hepatitis B core antibody; HBeAb, hepatitis B e antibody; HBeAg, hepatitis B e antigen; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HBx, HBV X gene encoded protein; BCP, basal core promoter; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HEV, hepatitis E virus; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyltransferase; LDH, lactate dehydrogenase; TBIL, total bilirubin; DBIL, direct bilirubin; IBIL, indirect bilirubin; ADA, adenosine deaminase; CA50, carbohydrate antigen 50; FCM, flow cytometry; CBA, cytometric bead array; IL-2, interleukin 2; IL-4, interleukin 4; IL-6, interleukin 6; IL-10, interleukin 10; INF-γ, interferon γ; TNF-α, tumor necrosis factor α. CD, cluster of differentiation.

Author contributions: Bo Qin designed the research and provided fundamental support; Bo Qin, Minjun Xu and Jiefeng Ding performed the research; Bo Qin analyzed data and wrote the paper. All authors have read and approved the manuscript.

Funding

This work was supported by the Science Technology Department of Zhejiang Province, China (LGF22H190009) and Health Commission of Zhejiang Province, China (2020KY325, 2022KY411).

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