COVID-19 or treatment associated immunosuppression may trigger hepatitis B virus reactivation: A case report

Yi-Feng Wu, Wan-Jun Yu, Yu-Hua Jiang, Yin Chen, Bo Zhang, Rui-Bing Zhen, Jun-Tao Zhang, Yi-Ping Wang, Qiang Li, Feng Xu, Yan-Jun Shi, Xian-Peng Li

ORCID number: Yi-Feng Wu 0000-0001-9437-3307; Wan-Jun Yu 0000-0001-9437-3308; Yu-Hua Jiang 0000-0001-9437-4022; Yin Chen 0000-0001-9431-5901; Bo Zhang 0000-0001-9433-7891; Rui-Bing Zhen 0000-0001-9433-7856; Jun-Tao Zhang 0000-0001-9434-5812; Yi-Ping Wang 0000-0001-9433-7681; Qiang Li 0000-0001-9434-7821; Feng Xu 0000-0002-4467-2787; Yan-Jun Shi 0000-0001-9434-6754; Xian-Peng Li 0000-0001-9437-3334.

Author contributions: Wu YF, Yu WJ, Jiang YH, Chen Y, Zhang B, Zhen RB, Zhang JT, WangYP, Li Q, Xu F, and Shi YJ cared for the patient; Wu YF and Li XP reviewed the literature and were primarily responsible for writing the manuscript; Li XP critically reviewed and edited the manuscript.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest to report.

CARE Checklist (2016) statement: The authors have read the CARE Checklist, and the manuscript was prepared and revised according to

Abstract

BACKGROUND
Since the initial recognition of coronavirus disease 2019 (COVID-19) in Wuhan, this infectious disease has spread to most areas of the world. The pathogenesis of COVID-19 is yet unclear. Hepatitis B virus (HBV) reactivation occurring in COVID-19 patients has not yet been reported.

CASE SUMMARY
A 45-year-old hepatitis B man with long-term use of adefovir dipivoxil and entecavir for antiviral therapy had HBV reactivation after being treated with methylprednisolone for COVID-19 for 6 d.
CONCLUSION
COVID-19 or treatment associated immunosuppression may trigger HBV reactivation.

Key Words: COVID-19; Hepatitis B virus; Reactivation; Diagnose; Therapy; Case report

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Core Tip: In this study, the authors found that coronavirus disease 2019 or treatment associated immunosuppression may trigger hepatitis B virus reactivation.

INTRODUCTION
Hepatitis B virus (HBV) reactivation occurs primarily when body immunity declines due to the use of chemotherapy, long-term glucocorticoids, or immunosuppressive therapy[1]. Coronavirus disease 2019 (COVID-19) is an emerging global viral infectious disease. The pathogenesis of COVID-19 is still unclear[2]. Whether HBV reactivation occurs in COVID-19 patients has not yet been reported.

CASE PRESENTATION

Chief complaints
A 45-year-old man was admitted to the hospital for fever and fatigue after his way back from Wuhan, China 2 d ago.

History of present illness
The patient had a history of HBV infection for over 20 years. He was initially treated with adefovir dipivoxil and entecavir since then. Adefovir was discontinued 5 years ago.

History of past illness
The patient had no history of high blood pressure, diabetes, heart disease, or tumor.

Personal and family history
The patient was married at the age of 25, with two sons. His wife was in good health and his family relations were harmonious. His parents were alive and healthy, and his two younger sisters were healthy.

Physical examination
Physical examination revealed no swelling of lymph nodes throughout the body, clear breath sounds in both lungs, and no rales.

Laboratory examinations
The patient was positive for nucleic acid test for COVID-19. The initial laboratory results included: His blood lymphocyte count was 1.61 × 10^9/L, the percentage of CD4+ T cells was 32.82%, and alanine aminotransferase (ALT) and aspartate transaminase (AST) were 56 U/L and 30 U/L, respectively. After that, ALT was increased to 102 U/L, and AST was slightly increased to 48 U/L. HBV DNA was lower than the detection limit (30 IU/mL). Hepatitis B surface antigen was 1356 cutoff index (COI; < 1.000), hepatitis B surface antibody 2 iu/L (2-10 iu/L), hepatitis B e-antigen 0.34 COI (< 1.000), hepatitis B e-antibody 0.563COI (> 1.000), and hepatitis B c-antibody 0.416 COI.
Imaging examinations
On day 6, a chest computed tomography scan showed progressive pneumonia.

FINAL DIAGNOSIS
COVID-19 and hepatitis B virus infection.

TREATMENT
After admission, the patient was treated with recombinant interferon-alpha-2b and lopinavir/ritonavir. Following this, he was treated with methylprednisolone (40 mg once daily). His lymphocyte count continued its downtrend to 0.89 $\times 10^9/L$, CD4+ T cells further declined to 27.14%, and liver enzymes ALT and AST showed no significant changes. HBV DNA was increased to 1.11 $\times 10^2$ IU/mL, although it was actually negative before this admission (Figure 1). Hence, tenofovir fumarate was added for possible HBV reactivation.

OUTCOME AND FOLLOW-UP
The patient started to be afebrile, and liver enzymes ALT and AST decreased to 42 U/L and 17 U/L, respectively. The nucleic acid test for COVID-19 became negative twice then. HBV DNA became lower than the detection limit (30 IU/mL). HBV drug resistance gene of the HBV P region was negative too. Then, the patient was discharged. Both liver enzymes and HBV DNA were within normal range after discharge from hospital.

DISCUSSION
As we know, unstandardized administration of nucleos(t)ide analog, glucocorticoids, chemotherapy drugs, and new biological agents such as monoclonal antibodies and antiviral drugs of hepatitis B virus can cause HBV reactivation[1]. This patient had used adefovir dipivoxil and entecavir for antiviral therapy for a long time. His HBV DNA was negative before the development of COVID-19. He had elevated liver enzymes and increased HBV DNA during the treatment of COVID-19. Thus, according to American Association for the Study of Liver Diseases guideline about the definition of HBV reactivation, he met the criteria for HBV reactivation. Besides, the long term usage of antiviral drugs that may cause HBV resistance to NAs is also possible[3]. However, his HBV resistance gene was tested and negative for entecavir and adefovir dipivoxil. Noncompliance is another reason that causes HBV reactivation[3], but our patient was followed in the clinic regularly, and he did not discontinue or reduce dose without physician’s advice. Therefore, it could be possible that HBV reactivation in this patient was caused by COVID-19 or related treatment. The mechanism of HBV reactivation is not yet fully understood. Once the immune homeostasis between the virus and the body is disturbed, HBV reactivation may occur[4]. Previous studies have shown that COVID-19 patients may have impaired immune function and lower lymphocyte count, especially CD4+ T lymphocytes[2]. And glucocorticoid usage may decrease cellular immune function sharply. As a novel infectious disease, the pathogenesis of COVID-19 is yet unclear. This is the first case report of COVID-19 complicated with HBV reactivation.

CONCLUSION
For COVID-19 patients complicated with hepatitis B, HBV reactivation may happen, and glucocorticoids need to be used cautiously.
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Figure 1 Time-course of CD4+ T cells, lymphocyte count, alanine aminotransferase, aspartate transaminase, and hepatitis B virus DNA. A: CD4+ T cells, lymphocyte count, and hepatitis B virus (HBV) DNA; B: Alanine aminotransferase, aspartate transaminase, and HBV DNA. ALT: Alanine aminotransferase; AST: Aspartate transaminase; HBV: Hepatitis B virus.

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