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CASE STUDY

SARS-CoV-2 / HBV co-infection: case report

Hinde EL MOUHI [1, 2, 3,*], Leila BOUGUENOUCH [1, 2], Abdelhafid NATIQ [4], Brahim EL HEJJIOUI [1, 2, 3], Hind OUBIHI [4], Youssef EL KADIRI [4], Sana CHAOUKI [1, 5]

[1] Laboratory of Biomedical and Translational Research, Faculty of Medicine andPharmacy, Sidi Mohammed Ben Abdellah University of Fez, Morocco
[2] Unit of Medical Genetics and Oncogenetics, University Hospital Hassan II, 30070 Fes,Morocco.
[3] Engineering Science and Technology Doctoral Study Center, Faculty of Sciences andTechnologies, Sidi Mohammed Ben Abdellah University of Fez, Morocco
[4] Faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Morocco
[5] Department of Pediatrics CHU Hassan II, Fez, Morocco

Corresponding author e-mail : El Mouhi Hinde: Hinde.elmouhi@usmba.ac.ma

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SUMMARY

The disease COVID-19 caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has constituted a public health threat worldwide, and it is subsequently declared as a pandemic by WHO. Upper respiratory tract infections are the main manifestations of SARS-CoV-2. However, liver damage has also been reported during the course of the disease in severe cases. In addition to the recently emerged SARS-CoV-2, Hepatitis B Virus (HBV) also occupies a major place in terms of public health. Since both SARS-CoV-2 and HBV can cause hepatitis injury, it is urgent to further investigate SARS-CoV-2/HBV co-infection. In this paper, we studied the changes in markers of liver function, inflammation and injury in a patient with inactive HBV. And the possibility of reactivation of the latterafter infection with SARS-CoV-2.

Introduction

COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2), which firstly appeared in Wuhan, China, on December 31, 2019, and later on March 11, 2020, declared as a pandemic by the World Health Organization (WHO) (1). In addition to the recently appeared SARS-CoV-2, the Hepatitis B Virus (HBV), responsible for chronic liver disease, also ranks high in global public health, estimated at 257 million cases in 2015 (2). Worldwide, in 2018, HBsAg prevalence was estimated to be about 3.9% (3).

Since both SARS-CoV-2 and HBV can cause liver damage (4), a co-infection with SARS-COV-2 and Hepatitis B is expected to develop serious complications and have a poor prognosis. It is therefore urgent to have a better understanding of the risk of SARS-CoV-2 in an HBV-infected patient in order to design an optimized treatment strategy.

In the present study, we conducted a case study to evaluate the impact of SARS-COV-2 infection on liver biology characteristics in a patient with inactive HBV and confirmed COVID-19 positive. Furthermore, to understand the impact of pre-existing HBV infection on the progression of COVID-19, as well as HBV reactivation.

Material and methods

Conceptual framework and case studies

A 26-year-old patient with inactive hepatitis B virus has been recorded to Hassan II University Hospital, Fez, Morocco, to do RT-PCR analysis of COVID-19 after developing clinical symptoms, including: fever, exhaustive fatigue, myalgia and repertory symptoms. After SARSCoV-2 RNA analysis by RT- PCR, it was confirmed as COVID-19 positive. Therefore, an informed consent was signed by the patient. The inactive HBV carrier had a negative serum HBeAg, and a low serum HBV DNA (<2000 IU/ml). He had a normal abdominal ultrasound and liver FibroScan. As he received treatment with drugs like confirmed cases recommended by the National Health Commission of Morocco because of the suspicionof SARS-CoV-2 infection.

Virological tests for SARS-CoV-2 and HBV

According to the manufacturer's guidelines, the presence of SARS-CoV-2 RNA was detected by a real- time RT-PCR test recommended by the Moroccan Ministry of Health (QuantGene 9600, BIOER). In the same regard, Serum HBV DNA levels were measured by a real-time quantitative high-throughput PCR system on an ABBOTT system (m2000 RealTime System). While the levels of serum HBsAg, HBeAg, anti-HBsAc, anti-HBeAc, and anti-HBcAc were measured by an automated electrochemical luminescence immune analyzer (Elecsys 2010, Roche). An HBV viral burden > 2000 copies/ml is defined as activating hepatitis B virus.Results

Liver test parameters and abnormalities

According to the manufacturer's guidelines, Alanine aminotransferase (ALT), Alkaline Phosphatase (ALP), Aspartate Aminotransferase (AST), SGPT Transaminase (ALAT), SGOT Transaminase (ASAT), D-dimer, C Reactive Protein (CRP), Gamma-Glutamyl Transferase (GGT) Interleukin-6 (IL- 6), Lactate Dehydrogenase (LDH) and Total Bilirubin (TBIL) in plasma samples were measured by fully automated biochemical analysis (Cobas 4000, Roche).

Liver test abnormality was defined by the increase in the following liver enzymes in serum: ALP> 150 IU/L, ALAT> 55 IU/L, ASAT> 34 IU/L, GGT> 64 U/L, and TBIL> 26 μmol/L. An increase in ALT and/or ASAT more than 3 times superior limit units (SLU) and/or an increase in TBIL to more than 2 UL were defined as liver injury.

Thrombopenia was defined as a blood platelet count lower than 125×109 /L. Increased serum inflammation biomarkers, including D-dimer> 0.55 mg / L, CRP> 6 mg / L, IL-6> 5.4 pg / ml, and/or LDH> 250 U / L, were defined as an aberrant inflammatory response.

Results

Clinical characteristics

The case study was confirmed COVID-19 positive, and was an inactive HBV carrier (HBsAg positive, HBeAg negative, HBcAg positive with an HBV viral load < 2000 IU/ml). This patient was not co- infected with hepatitis C (HCV) or HIV. The patient was 26 years old and had mild symptoms of COVID-19 including fever, cough, myalgia, sputum and other superior respiratory symptoms. The patient received oral antibiotic therapy, without antiviral therapy for hepatitis B, with vitamins C and Dand Zinc.

The patient was treated at home because his conditions did not require hospitalization. Abdominal ultrasound and FibroScan, before and after SARS-CoV-2 infection, showed no abnormalities in the liver or other organs, and clinical, biological, and histological information showed inactive HBV carriage.

Dynamic changes in liver function after SARS-COV-2 infection

To assess the relationship between SARS-CoV-2/HBV coinfection and liver function, we compared dynamic changes in clinical indicators associated with liver injury before and after SARSCoV-2 infection in this patient. Pre-infection tests were performed 2 months before the onset of COVID-19 symptoms (with a follow-up every 6 months), and post-infection tests were analyzed 1 month after the disappearance of COVID-19 symptoms. The results showed ALT, AST, and TBIL above normal, but still below the values that were defined as liver injury (an increase in ALT and/or AST to more than 3 times the superior normal limit (SLU) units and/or an increase in TBIL to more than 2 SLU).

To better understand the influence of these increased values on liver function, The values of the liver inflammation markers were found to be normal even after infection with SARS-CoV-2. In addition, we further analyzed the levels of serum GGT, GOT, and GPT, which are the diagnostic biomarkers of cholangiocyte injury. The GOT value remained in the normal range, with an elevation in the level of GGT and GPT.

Dynamic changes in biomarkers of inflammation

The inflammatory response may play an important role in liver injury in patients with COVID19 after SARS-CoV-2 infection. And a proven SARS-CoV-2 / HBV co-infected patient may have an unfavorablediagnosis.

In our research, we found that the platelet count was normal (between 150 x 10^9 / L and 400x10^9 /L) for this SARS-Cov-2 / HBV co-infected case study 1 month after resolution of COVID-19 symptoms. To investigate possible mechanisms of immune-mediated liver injury, we further analyzed the dynamic change of representative biomarkers of inflammation, including LDH, D-dimer, IL-6, and C-reactive protein.

Serum levels of LDH, and IL-6 are revealed normal. Protein C reagent and D-dimer show higher values than normal.

Change in HBV viral load

The immune system reacted normally against HBV during SARS-CoV-2 infection, and the HBV viral load was not significantly altered (still <2000 IU/ml).

As SARS-CoV-2 did not reactivate the HBV virus, and it did not influence the serum levels of HBsAg, HBeAg and HBcAg.

Discussion

The present study is a descriptive study extended on the biological and clinical characteristics of a 26- year-old patient, co-infected with SARS-CoV-2 / HBV. This patient was referred to Hassan II University Hospital, Fez, Morocco, after the development of COVID-19 symptoms, to be tested for SARS-CoV-2by RT-PCR.

Currently, information on HBV/SARS-CoV-2 co-infection is limited (5–9). Previous studies have found that liver injury in SARS-CoV-2 / HBV co-infected patients was related to disease severity and worse prognosis (10,11). In this context of COVID-19, Zou et al, reported that 14 patients co-infected with SARS-CoV-2 and chronic HBV developed liver injury, and the proportion of severe COVID-19 was higher in patients with liver injury. (12)

Referring to previous studies, up to 60% of patients showed liver failure after infection with SARS- COV-2 (8).

Our study showed that the patient studied, who is an inactive carrier of HBV, presented an increase in liver biological markers, but still below the values that have been defined as liver damage, which suggests a lower risk of liver damage.

To confirm this segregation, and further to the evaluation of liver damage in this patient, we analyzed the results obtained from the inflammatory factors: D-dimer, CRP, LDH and IL-6, these factors showed a slight increase compared to the normal but still not pathological and therefore, a normal liver function is maintained in our patient.

Abdominal ultrasound and FibroScan, before and after SARS-CoV-2 infection, showed no liver or other organ abnormalities, and clinical, biological, and histological information showed inactive HBV carriage.

In the context of HBV co-infection with another virus, HBV can be reactivated or suppressed (13). Since HIV and HBV share similar infecting means, there is a high frequency of co-infection. Studies show that HIV immunosuppression can lead to loss of hepatitis B surface antibodies and reactivation of chronic hepatitis B (14). For HBV and HCV co-infection, HBV replication is suppressed by the HCV- induced innate immune response (12). Other studies have already shown that SARS-CoV-2 is able to induce a variety of cytokines, including IL-6 and TNF-α, and some of these are known to inhibit HBV infection (19,20).

By measuring, this patient, the replication marker of HBV, HBeAg is not activated after infection with SARS-CoV-2, there was therefore, no evidence of increased risk of liver injury compared to HBV- uninfected patients, we suppose that there was no risk of HBV reactivation in this co-infected patient. Our study did not report a significant difference in the results of liver test before and after infection with SARS-CoV-2. The patient did not use virotherapy or steroids or other drugs used to treat SARS-CoV-2 patients that can also cause liver damage (17). The patient's viral load has been well controlled for the past 6 years, and has been steadily decreasing, without using antiviral therapy. Liver function parameters remain relatively well controlled after SARS-CoV-2 infection because he has not used steroidal or non-steroidal anti-inflammatory drugs or immunosuppressants that can facilitate HBV reactivation. To accomplish this, it is important to use HBV antivirals such as entecavir or tenofovir before starting immunosuppressive therapy in COVID-19 patients with chronic hepatitis B. By decreasing viral

load, the likelihood of hepatitis B relapses may be reduced (13).

Conclusion

This should clearly explain the main conclusions of the study, highlighting its importance and relevance.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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Ethical Approval statement

The patient has read and signed the informed consent for this study.

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