

Dear editor and reviewers:

Thank you very much for all the helpful suggestions. We have extensively revised the whole manuscript.

**Reviewer #1:**

**Scientific Quality: Grade C (Good)**

**Language Quality: Grade B (Minor language polishing)**

**Conclusion: Accept (General priority)**

**Specific Comments to Authors:** - references should ordered in the text (e.g. ref [4] appear before ref [2] and [3]). - **Abstract: Should add more details about the case** - **Discussion: need to add more discussion about the case** - **Figures 1 and 2: what is the meaning of Y-axis? Also, not mention in the text.**

**R:** We thank the reviewer's constructive comments. We have reordered the references in the text; We have added more details about the case in the abstract and discussion; In figure 1, the left Y-axis means the value of CD4+ and HBV DNA, the right Y-axis means the value of Lymphocyte. In figure 2, the Y-axis means the value of ALT, AST and HBV DNA; We have mentioned the figures in the text.

**Reviewer #2:**

**Scientific Quality: Grade D (Fair)**

**Language Quality: Grade B (Minor language polishing)**

**Conclusion: Major revision**

**Specific Comments to Authors:**

**-There is no recommendation to combine adefovir plus entecavir for HBV treatment unless there is entecavir resistance, you " may" add adefovir [ although shifting to tenofovir is the recommended approach], however, you excluded drug resistance in the case history? how can you justify?? -we need baseline PCR to accurately define reactivation? -what was the status of HBsAg at baseline? -As long as HBV resistance genes was tested and negative for entecavir and adefovir dipivoxil, why retreatment with tenofovir was initiated?**

**R:** We thank the reviewer's constructive comments, and apologize for the unclear description. The patient began his treatment with adefovir dipivoxil 10 mg/d and entecavir 0.5 mg/d as advised in other hospital, the reason remained unclear, and Adefovir was discontinued five years ago as advised by another doctor. The detection of HBV drug resistance gene of the HBV P region was negative on February 3. As a strong first-line antiviral drug, tenofovir was selected to use when the COVID-19 pneumonia was aggravated and HBV reactivation, which could control the virus more quickly and reduce liver damage. On March 3, laboratory reexamination showed that the level of HBV DNA was below the detection limit (30 IU/mL), ALT was 29 U/L, and AST was 15 U/L. Then, the patient was off tenofovir fumarate and was administered only

entecavir for antiviral therapy. the level of HBV DNA was lower than the detection limit (30 IU/mL) on April 16 and August 14. HBsAg was 1356 COI. These indicated no HBV resistance and the usage of entecavir was only effectively to control the virus.

**-We think elevation before methylprednisolone is due to lopinavir/ritonavir not covid-19 treatment? -what was the dose of Methylprednisolone? -Are 6 days being sufficient for steroids to cause reactivation of HBV? usually occurs at 4-6 weeks -based on the lack of evidence of the role of steroids in the possible reactivation, we think the title and the conclusion should only raise the question about the possible role of COVID-19 in reactivation, not the COVID treatment**

**R:** We thank the reviewer's constructive comments, and apologize for the unclear description. The dose of Methylprednisolone was 40 mg once daily, and was added in the manuscript. HBV reactivation may occur, once the immune homeostasis between the virus and the body is disturbed. As a novel infectious disease, the pathogenesis of COVID-19 is yet unclear, which may cause a lower cellular immune function, and glucocorticoid usage may also decrease cellular immune function sharply. In our case, the duration time of Methylprednisolone usage was 6 days, which might be too short to cause reactivation of HBV. However, it was an extremely special case(HBV plus COVID-19), the pathogenesis and mechanism is unclear, and deserving further study. So in the conclusion, we thought: For COVID-19 patients complicated with hepatitis B, the possibility of HBV reactivation can happen, and glucocorticoids may need to be used cautiously.

**Reviewer #3:**

**Scientific Quality: Grade D (Fair)**

**Language Quality: Grade B (Minor language polishing)**

**Conclusion: Minor revision**

**Specific Comments to Authors: The authors describe a case of HBV reactivation in a patient with chronic HBV who was hospitalised for COVID19. This is a short and focused report of an important new observation and could inform clinical care of patients with HBV and Covid19. I would suggest that the authors provide more details about the patient with HBV including: 1. serology results for surface antigen and antibody and e antigen and antibody 2. any details for the severity of liver disease - did the patient have a liver biopsy in the past, ? what was the fibrosis stage? did the patient have any non-invasive assessment with liver stiffness measurement, ELF test, FIB4 or other non-invasive test.**

**1. serology results for surface antigen and antibody and e antigen and antibody.**

**R:**We thank the reviewer's constructive comments. We have added the serology results for surface antigen and antibody and e antigen and antibody in the text.

HBsAg was 1356COI(<1.000), HBsAb 2iu/l(2-10iu/l), HBeAg 0.34COI(<1.000), HBeAb 0.563COI(>1.000), HBcAb 0.416COI (>1.000).

**2. any details for the severity of liver disease - did the patient have a liver biopsy in the past, ? what was the fibrosis stage? did the patient have any non-invasive assessment with liver stiffness measurement, ELF test, FIB4 or other non-invasive test.**

**R:** We thank the reviewer's constructive comments. The patient had no liver biopsy before. His liver Shear Wave Elastography(SWE) was 6.5kPa, wthic indicating no liver fibrosis.