

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 59733

**Title:** Clinical cure and liver fibrosis reversal after postoperative antiviral combination therapy in hepatitis B-associated non-cirrhotic hepatocellular carcinoma: A case report

**Reviewer's code:** 04105237

**Position:** Peer Reviewer

**Academic degree:** MD, MSc, PhD

**Professional title:** Assistant Professor, Doctor

**Reviewer's Country/Territory:** Mexico

**Author's Country/Territory:** China

**Manuscript submission date:** 2020-09-28

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2020-10-12 05:05

**Reviewer performed review:** 2020-10-12 20:25

**Review time:** 15 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

This is the presentation of a clinical case showing the evolution of a patient with HBV infection after several drug treatments, and after partial hepatectomy secondary to HCC development. However, some inconsistencies render this case presentation difficult to follow, and understand its relevance: 1) in the discussion, it is written: ...patient with HBeAg-negative chronic hepatitis B, however, in the description of the case it is written HBeAg-positive. Despite it is obvious that it is the evolution of the HBeAg through the time, as described, it is difficult to follow the case. 2) the authors state that there was a reversal of over fibrosis (from G1S3 to G2S1), however, they did not explain why there is an increase in inflammation despite seroconversion, and apparently no other risk factors for other liver diseases (such as MAFLD). 3) it is not clear why in the presentation of the case the findings in the US are mentioned, but the image actually corresponds to MRI. 4) The figures regarding histology don't show the described changes, and also there is no special staining for evaluating liver fibrosis.

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**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 59733

**Title:** Clinical cure and liver fibrosis reversal after postoperative antiviral combination therapy in hepatitis B-associated non-cirrhotic hepatocellular carcinoma: A case report

**Reviewer's code:** 00697631

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2020-09-28

**Reviewer chosen by:** Jia-Ping Yan

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**Review time:** 6 Days and 18 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

Comments to the authors RE: Manuscript NO: 59733 Yu X et al, Clinical cure and liver fibrosis reversal after postoperative antiviral combination therapy in HBV-associated non-cirrhotic hepatocellular carcinoma: case report Yu et al reported a case of chronic hepatitis who achieved HBsAg/Ab seroconversion and resolution of fibrosis after the resection of HCC and antiviral treatments. The reported case showed a rare clinical course among the chronic HBV-infected patients and could provide important information of management of HBV carriers. However, there are several concerns to be addressed. 1. The resolution of fibrosis after antiviral therapy in HBV-infected patients has been reported previously and not so rare observation(Chang T et al, Hepatology 2010;52:886, Marcellin P et al, Lancet 2013;381:463 etc). Previous reports should be cited adequately. 2. In Fig 3B, the picture of liver puncture biopsy is shown but the picture does not include portal area of liver lobule. It is difficult to evaluate the presence of fibrosis from the picture. The picture including portal region should be provided. 3. The changes of biological marker indicating liver fibrosis should be provided, for example by calculating Fib-4 index. 4. As shown in the report, the development of HBs Ab in chronic HBV infection is rare, however, the HBV Ag/Ab seroconversion after antiviral treatment has been reported even in immunosuppressive state such as patients coinfecting with HIV/HBV and patients receiving hemodialysis. What is the incidence of HBs Ag/Ab seroconversion in the natural course of chronic HBV infection? 5. The reported case received IFN, oral antivirals and HBV vaccination. What is the treatment recommendation of authors for these kind of chronic HBV patients? 6. Fig 2 and Table 1 include same data. Table 1 is not necessary if Fig 2 is provided.

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**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 59733

**Title:** Clinical cure and liver fibrosis reversal after postoperative antiviral combination therapy in hepatitis B-associated non-cirrhotic hepatocellular carcinoma: A case report

**Reviewer's code:** 00038362

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** China

**Manuscript submission date:** 2020-09-28

**Reviewer chosen by:** Jia-Ping Yan

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**Reviewer performed review:** 2020-10-28 15:45

**Review time:** 14 Days and 22 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

This manuscript describes a case study of a patient with a HBV-related non-cirrhotic hepatocellular carcinoma (HCC), his treatment and prognosis outcome. Overall, this is an interesting case, generally well-presented and supportive of the therapeutic regimen utilized as a managed care approach that prolong patient's HCC recurrence-free survival. There are various grammatical errors that need correction. The authors must carefully revise the English for correctness. Here are several points that need attention and/or clarification:

1. The summary statement states that lamivudine was administered two years after treatment. It is unclear what treatment took place two years prior to lamivudine.
2. The relationship between HBsAg titers and ALT values is not clearly explained. Also, the concept of ALT elevation by host immunity would not be obvious to potential readers of the article. This should be better addressed. The authors also state that: "Acute elevation of ALT levels is mainly immune-mediated". What does this mean? No context is provided for such statement.
3. Another unclear point is provided by the following statement: "Several factors can affect the postoperative HCC recurrence, with HBsAg as the main factor". Does this imply a cause-effect relationship? Is so, how? How does HBsAg itself drives HCC recurrence?
4. The paper could benefit of a graphical depiction of the patient's timeline of illness and treatment.