Responds to the reviewer's comments:

Reviewer #1:

Specific Comments to Authors: This is an extremely interesting case report describing a patient with technically negative Hepatitis B viral titers, but occult Heptitiis B infection who presented with hepatocellular cancer (HCC). The article is well-written and the case is should be interesting for the readers of World Journal of Gastroenterology. I only have 2 questions 1. Why did the authors choose the expression "fast in and fast out" sign as opposed to the more commonly used "washout." 2. Do the authors ever use Des-γ-carboxyprothrombin (DCP) as a tumor marker for HCC? Several papers have noted that it is more accurate than AFP in diagnosing HCC. Could the authors comment on its utility as a screening tool and if they recommend any other tumor markers for the detection of HCC.

Response: We thank reviewer for these comments. For the first question, we would like to apologize for the wrong term used in here, we have changed it to "wash in and wash out". Please see line 16 of the first paragraph of the discussion in our revised manuscript. For the second question, AFP is routinely tested for liver cancer patients in Chinese hospitals, but the detection of DCP is not as common as AFP in China. Because the patient's clinical symptoms, laboratory test indexes and imaging results showed a clear diagnosis of liver cancer, we did not continue to test for DCP. As you mentioned, several papers pointed out that DCP was more accurate than AFP in the diagnosis of HCC, however, the patients did not have this result, the practicality of DCP as a tool for HCC screening and whether it should be recommended for the detection of HCC were not introduced in the discussion.

Reviewer #2:

Specific Comments to Authors: Major comments 1. There have been entire series published on the topic of HCC complicating occult HBV infection. This case report is therefore not particularly novel, just because there is a high titer of HBS AB. For a summary of these series see Pollicino T and Saitta C. World Journal of gastroenterology 2014; 20: 5951 Minor comments 1. In the abstract, "liver occupation" is an awkward term that could be replaced. 2. In the background section, it should be noted that HCC is also associated with any cause of cirrhosis in addition to the other conditions listed. 3. In the third paragraph of the background, it is misleading to state that the antiviral agents "eliminate" HBV from the host. That sentence could be revised. 4. In the case presentation, the term "floriform tremor" is used. That term generally means resembling a flower. Did the authors mean an absence of asterixis? 5. What were the tumor dimensions? 6. What was the HBV DNA value? 7. How was the diagnosis of cirrhosis established? 8. Surgery was mentioned. What was the histology of the tumor? What was the histology of the surrounding liver tissue? Was additional staining done? 9. It might be more valuable to state the world wide prevalence of hepatitis B rather than the annual incidence. 10. The authors mention poor specificity of serum alpha-

fetoprotein but do not mention the poor sensitivity, which is its major shortcomings. 11. The mechanism by which hepatitis B leads to HCC is duplicated in both the background and the discussion. It only needs to be mentioned only once in the manuscript. 12. The authors suggest routine measurement of serum HBV DNA after clearance of HBsAg to detect patients at risk for HCC. This might be reasonable but in order to propose this we would need to know the frequency of occult hepatitis B and the level of risk these patients have of developing HCC. Is it the same or is it less than in patients who have ongoing HBsAg positivity?

Response: We thank reviewer for these comments. We agree with this reviewer that a series of papers on HCC with occult HBV infection has been published. However, the focus of our paper is on the presence of very high serum anti-HBsAg antibody levels in a patient with undetectable HBsAg levels, represented a unique case which is very easy to be ignored by the doctor in clinical practice. We cite such an example to enable clinicians to improve their ability to predict HCC early, and thus achieve early diagnosis and treatment.

Response to minor comment 1: We thank reviewer for this suggestion. We have replaced "liver occupation " with " focal liver lesion ". Please see line 6 of the case summary.

Response to minor comment 2: We thank reviewer for this suggestion. In the introduction, we mentioned that liver cancer is related to genetic susceptibility factors and environmental factors (alcohol, aflatoxin B1, etc.), which are the reasons for the occurrence of cirrhosis. Then the cirrhosis develops into liver cancer.

Response to minor comment 3: We thank reviewer for this suggestion. We have modified this sentence to "Although several anti-HBV drugs that inhibit HBV replication of HBV in the host have been approved globally for clinical use, not all patients with HBV have access to these drugs. " Please see the beginning of the second paragraph of the introduction.

Respond to minor comment4: We thank reviewer for this suggestion. We mean that in the physical examination of the patient, the test of Hepatic encephalopathy asterixis was negative. It is our inaccurate wording that caused you to have doubts. We have revised it to "hepatic encephalopathy asterixis "in the article. Please see the last sentence of physical examination.

Respond to minor comment 5: We thank reviewer for this suggestion. It was our mistake not to introduce the dimensions of the tumor. The CT results showed that the tumor was about 10cm*12cm in cross-section.

Respond to minor comment 6: We thank reviewer for this suggestion. Novartis screening test results of patient blood indicated a positive HBV DNA result (detection

sensitivity: 3 IU/ mL). In addition, due to the low viral load of the patients, we failed to amplify the full HBV-DNA fragment from the patient and the Novartis screening test only give positive or negative for HBV test, so it was not possible to quantify and sequence it, which is the regret of this article.

Respond to minor comment 7: We thank reviewer for this suggestion. The patient had advanced HCC from outpatient to hospitalization and was not diagnosed with cirrhosis.

Respond to minor comment 8: We thank reviewer for this suggestion. The patient did not receive surgical treatment in our hospital, so the tumor tissue was not presented. The original intention of this paper is not to focus on liver cancer, but to enable clinicians to make prediction of latent hepatitis B virus infection and liver cancer in future OBI patients with the help of this case.

Respond to minor comment 9: We thank reviewer for this suggestion. In the second paragraph of the discussion, we mentioned that "about 80% of primary liver cancers worldwide are associated with chronic hepatitis B virus infection. " Please see the first sentence of the second paragraph of the discussion.

Respond to minor comment 10: We thank reviewer for this suggestion. We have realized the mistake and changed the sentence to "Although AFP is the most widely used serum marker for HCC, its specificity as a marker for early diagnosis of HCC is 87-93%, and its sensitivity is only 45.3%-62%, and its use needs to be explained by experts combined with analysis of imaging results. " Please see line 6-9 in discussion.

Respond to minor comment 11: We thank reviewer for this suggestion. We have deleted in the introduction the mechanism by which hepatitis B causes HCC. Please see the introduction.

Respond to minor comment 12: We added the passage " The prevalence of OBI varies greatly across the world and We thank reviewer for this suggestion. across patient populations, with higher rates reported in Asia. The prevalence of OBI is higher in patients with chronic liver disease and may be as high as 40% to 75% in those with HBsAg-negative HCC. It is almost equivalent to a persistent HBsAg positive HCC patient." to the discussion section of the article. Please see the first sentence of the last paragraph of the discussion.

Reviewer #3:

Specific Comments to Authors: 1. Congratulations to the authors for presenting a difficult case scenario of very high serum anti-HBsAg antibody levels in a patient with undetectable serum HBsAg levels. Though it has been described very well in literature by various studies the issue needs to be deliberated upon. 2. The authors can consider significantly reducing the word count in the case report for a more impactful presentation specifically addressing the issue possibility of viral replication in spite of anti-HBsAg antibody levels. 3. Specific literature search for

the titers of anti-HBsAg antibody in similar cases/cohorts which can be presented as a table for easy comparison and understanding. 4. As mentioned if the gene sequencing of HBV DNA is under process and expected in a short time, its result would be added credibility to the report. 5. The conclusion may be modified to help clinicians make a better decision about the levels of anti-HBsAg antibody above which further evaluation may be indicated in a patient (This would warrant a further literature search to address this specific issue)

Response to comment 1: We thank this reviewer for the appreciation of this manuscript.

Respond to comment 2: We thank this reviewer for this comment. We have reduced the number of words, referred to the comments of the review and editorial department, and revised it in accordance with the format requirements of the magazine.

Response to comment 3: We thank this reviewer for this comment. We have added a recent meta-analysis in our manuscript, please see the last sentence of the last paragraph of the discussion.

Response to comment 4: We thank this reviewer for this suggestion. However, due to the low HBV viral load of the patient, we failed to successfully amplify HBV DNA fragment of the patient and are still working on that.

Response to comment 5: We thank this reviewer for this suggestion. We also hope to use more cases like this to conduct future studies. To learn more about the levels of anti-HBsAg antibody above which further evaluation may be indicated in a patient.