Lian-Sheng Ma, Editorial Office Director, Company Editor-in-Chief, Editorial Office，

According to the opinions of two reviewers and the chief editor, I revised and supplemented the original text. The point-to-point reply is as follows:

Reviewer #1: Two questions were raised:①Even Though the authors suggest that treatment with anti-hepatitis virus agents should be implemented, they do not show the data or literature supporting that. Reply: The data are the research results of this paper, and we have also cited the literature. Please refer to the original references 28-29. This time, another article 30 has been added. I think this expert did not take a good look at the original paper.② Hypersplenism can also be caused by Lymphoma, TB, Connective tissue and Inflammatory disease. Reply: Yes, but hypersplenism caused by these diseases will not lead to cirrhosis and portal hypertension. The first sentence of the control group in this paper is very clear.Control group: Surgical patients without hypersplenism associated with cirrhotic portal hypertension were used as controls.In order to highlight this meaning. I added a special sentence this timeThese patients have no history of hepatitis virus infection or cirrhosis caused by other reasons. The liver function is normal and the spleen volume is not enlarged.

Reviewer #2: He put forward five questions, which I replied to some time ago. Now, combined with the revised content, I will add the following answers:① The introduction is kind of irrelevant to the purpose of the study. Reply: I think it is good to introduce more basic knowledge of antibodies and complements to understand the full text. The basic knowledge published in recent magazines is easy to be cited by others. If you really want to delete it, I will delete it after you decide. And some errors appeared, which might be critical e.g., - the authors said that hypersplenism is often resulting from HBV infection: in fact, any causes of cirrhosis can cause hypersplenism, it depends on the degree of portal hypertension instead of the etiology. Reply: Actually, there is some misunderstanding in this sentence. In my paper, I listed the most

common clinical cases in which HBV infection can cause cirrhosis and hypersplenism, but did not deny that others can also cause cirrhosis and hypersplenism. To avoid misunderstanding, I added a sentence in the preamble this time:Liver cirrhosis caused by any reason may lead to hypersplenism related to portal hypertension[6], and possibly liver cancer.-Hepatitis B is an autoimmune disease <- HBV is NOT an autoimmune disease. Reply: In the preface, I have changed this sentence to a chronic infectious diseases. ② What is the inclusion and exclusion criteria of the patients enrolled in the study?, this detail is lacking. Reply: In the hypersplenism group, a paragraph "It is composed of hypersplenism caused by cirrhosis and portal hypertension of various reasons. Hyperplenism caused by non cirrhosis and portal hypertension, such as lymphoma, tuberculosis, connective tissue and inflammatory diseases, is excluded.". It should be clear. The content added in the control group this time is that "these patients have no history of hepatitis virus infection, nor any other cause that can cause cirrhosis, and the liver function is normal".③ What is the definition of hypersplenism in this study? Reply: I have published many articles on the definition of hypersplenism internationally. Afraid of repetition, they may be a little simple in the original discussion, and provide two references for readers to consult. However, this expert did not look at the references. This time, I used a long speech to make a detailed explanation in the first paragraph of the discussion.④ what is the hypothesis of this study, I cannot get it from the manuscript. Reply: Clinical research does not have to assume that what is is what. It is good to present objectively. Besides, the purpose of our research has been written in the preface of the original paper. Please see the last paragraph of the preface to make it clear. ⑤.How does the authors choose the control group? Is there any rationale to use this group of control patients?As far as I understand, selecting these hypersplenism group and control group does not help reflecting the effect of hypersplenism from cirrhosis. Reply: It is significant to select the control group for the study of the results of the hypersplenism group. However, people are not experimental animals, so we can not take normal people for blood sampling and testing. We can only replace them with surgical cases of hypersplenism with non

cirrhotic portal hypertension, which is also allowed. After the reviewer raised this question, I also made some modifications this time, which may be more specific.

Company Editor-in-Chief: Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. Reply: Highlights of this article: ① Antibodies and complements of liver cirrhosis have been reported, but there is little literature on antibodies and complements specifically studying hypersplenism in liver cirrhosis and portal hypertension, at least no report has been made in the past 30 years. ② Clinical studies have found that antibodies and complements are significantly related to liver function grading. ③ In terms of treatment, anti-virus and liver protection treatment are proposed. In the past, few people proposed antiviral therapy. We first proposed it as a whole. These highlights are reflected in the original text and the revised content. The current references can be found on Pubmed, and those that cannot be found have been deleted. The two newly supplemented literatures (18 and 29) are relatively new (the related literatures will not be found in the future). I input the keyword Impact Index Per Article, and 939 papers are displayed on Pubmed. I checked 300 papers, and found no one related to the content of this paper, which should be said to represent the latest frontier research achievements.

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