

## **Response letter**

1. The authors should clarify or discuss whether there is an evidence of a wider infiltration into the liver tissue or exclusively into the hepatocellular carcinoma

**Reply:** This needle biopsy specimen reveals patchy lymphoid infiltrated into portal area of normal liver tissue and tumor tissue. Contrast-enhanced CT reveals hepatomegaly ; So wider infiltrations of lymphoma into the liver tissue is suspected

2. Please state whether there was any evidence for a spread into the gastrointestinal tract and/or bone marrow

**Reply:** Repeat whole body contrast-enhanced CT before chemotherapy reveals no gastrointestinal tract involvement, and Core biopsy of bone marrow reveals no evidence of lymphomatous involvement. ( Page 6, Line 20-22)

3. Abstract: Avoid “huge”, please define it

**Reply :** we delete the word “ huge “ and use these words “ newly detected” ( Page 3, Line 5-6 )

4. Abstract: Please re-phrase, “7 cm liver mass”. “cm” is not a unit of mass. Maybe “a liver section in the size of ....” –

**Reply:** we will change it as “one hypodense mass of 7cm in diameter “ ( Page 3, Line 6-7 )

5. Introduction: “HBV has been suggested to be both lymphotropic and hepatotropic” – Please change. HBV is hepatotropic, and there may be some evidence that peripheral blood mononuclear cells (PBMCs) can serve as a reservoir

**Reply :** the sentence “ HBV has been suggested to be both lymphotropic and hepatotropic “ will be changed as “ HBV is hepatotropic, and there may be some evidence that peripheral blood mononuclear cells (PBMCs) can serve as a reservoir of HBV “( Page5, Line 5-7) and we add one reference.( reference No 5)

6. please mark the region of interests “low density mass” and “central

necrosis” with arrows and/or arrow heads

**Reply : we have add arrows and arrow heads. Please see Figure 1-4 and Figure 1-4 legend**

7. In the section “Diagnostic test”: Figure 5B listed before Fig 5A. Please keep the appropriate order

**Reply : we have changed and change the order , including Figure 5 , Figure 5 legends and text contents ( Page 6, Line 12 and 15)**

8. Section “Diagnostic test”: “.. that it was a HCC (Figure 5B). A right inguinal lymph ...” Context unclear. Possibly, following the assessment of the pathology of the liver tumor, the pathology for the enlarged lymph nodes were established. Please clarify

**Reply : the sentence “A right inguinal lymph node was excised by surgeons for confirmation, and the results showed mantle cell carcinoma” is changed to follow the pathology of the liver tumor ( Page 6, Line 18-19 )**

9. Please show in Fig. 5 (arrows, arrow heads) the localisation of the aggregates formed by the lymphoid cells

**Reply : we have added arrows in Figure 5b and Figure 5b legend**

10. Figs. 6: Control stain required, in the absence of primary antibody. Figure legend or text should provide the information, which primary and secondary antibodies were used (commercial provider), detection by immunoperoxidase staining?

**Reply : CD20 (L26; Dako; 1:1000), CD5 (4C7; Lieca; 1:200) and cyclin D1 (SP4; Zytomed; 1:25) (Figures 6A, 6B, 6C). The immunohistochemical study is performed using an automated immunostainer BOND-MAX (Leica)( Page 6, Line 12-13; Page 6 Line 16-17)**

11. Discussion: “ ... in patients with both HCV infection and liver cirrhosis” provide reference(s).

**Reply : we add three references ( No 3, 11, 12) and adjust the reference order**

**3. Tanaka H, Tsukuma H, Teshima H, Ajiki W, Koyama Y, Kinoshita N, Masaoka T, Oshima A. Second primary cancers following non-Hodgkin's lymphoma in Japan: increased risk of hepatocellular carcinoma. *Jpn J Cancer Res* 1997; 88: 537-542 [PMID: 9263530 DOI: 10.1111/j.1349-7006.1997.tb00416.x]**

- 11 **Suriawinata A**; Ye MQ; Emre S; Strauchen J; Thung SN Hepatocellular carcinoma and non-Hodgkin lymphoma in a patient with chronic hepatitis C and cirrhosis. Arch Pathol Lab Med. 2000; **124**:1532-1534 [PMID: 11035591]
12. **Ohtsubo K**; Oku E; Imamura R; Seki R; Hashiguchi M; Osaki K; Yakushiji K; Yoshimoto K; Ogata H; Nagamatsu H; Ando E; Shimamatsu K; Okamura T; Sata M Simultaneous hepatic relapse of non-Hodgkin's lymphoma and hepatocellular carcinoma in a patient with hepatitis C virus-related cirrhosis. Acta Haematologica. 2006; **116**:266-271 [PMID:17119328 DOI: 10.1159/000095878 ]

12. Discussion: “ In the present case, the patient had not received .... Moreover, two clinical or pathological evidences of HCV .... are found”. Unclear, please clarify. If HCV positive, please provide more details regarding the HCV infection, and the two clinical or pathological evidences.

**Reply : we change the word “ two “ to “ No “ , as “Moreover, no clinical or pathological evidences of HCV .... are found“ ( Page 7, Line 1)**

13. Discussion lists outcomes of individual published case reports, but summary would be required

**Reply: we add summary: These cases revealed the rare coexistence of HCC and NHL with or without extrahepatic involvement in hepatitis B carrier, but the role of HBV between HCC and NHL was not addressed. ( Page 7, line 21-24 )**

14. Discussion “HBV particles can then infect other lymphocytes ...” reference required which shows that lymphocytes are permissive for HBV

**Reply : we add two references ( No 5 , 22) :**

- 5 **Pontisso P**, Vidalino L, Quarta S, Gatta A. Biological and clinical implications of HBV infection in peripheral blood mononuclear cells. Autoimmun Rev 2008; **8**: 13-17 [ PMID: 18706529 DOI: 10.1016/j.autrev.2008.07.016]
22. **Feray C**, Zignego AL, Samuel D, Bismuth A, Reynes M, Tiollais P, Bismuth H, Brechot C. Persistent hepatitis B virus infection of mononuclear blood cells without concomitant liver infection. The liver transplantation model. Transplantation 1990; **49**: 1155-1158 [ PMID:2360255 DOI: 10.1097/

00007890- 199006000-00025]

15. Please introduce abbreviations when used for the first time in the manuscript, for instance Hematoxylin and eosin (H&E) stain

**Reply : we have introduce the abbreviations ( Page 15, Line 21 )**