

## List of Responses

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "**A three-in-one incidence of hepatocellular carcinoma, cholangiolocellular carcinoma, and neuroendocrine carcinoma: case report and literature review**" (ID: 74536). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1.However, unfortunately the text requires a major English polishing before any conclusion regarding scientific quality of the research.

Response: We polished the article again.



2.In addition, the titles of the tables must be revised accordingly to the contents.

Response: The title of the table have been revised and highlighted in blue in

the text.(line 278)

Reviewer #2:

1.According to the authors, their study aimed at improving the treatment of the disease (Introduction, last sentence). This aim is not reached and so the expectations raised in the reader are not fulfilled.

Response: Sorry, there is a problem with our expression. We aim to increase cognition and improve the treatment of the disease. And the sentences have been revised and highlighted in red in the text.(lines 50-51)

2.Please check all the dosages and units (e.g., "entecavir 0.5 g once daily"?) and provide the exact schedule.

Response: The unit have been revised and highlighted in red in the text.And the schedule have been provided in lines 52-53 .

3.The clinical descriptions should be shortened in order to become more concise. "Ranodermatin" (line 167): A PubMed search for "ranodermatin" retrieved no results.

Response: Sorry, there is a problem with our expression. The word is bombesin, and have been rebised in line 174.

4.In spite of editing, there are linguistic and stylistic problems; e.g., Abstract/Conclusion: "This a rare case with high invasiveness, rapid growth, easy recurrence, and metastasis in a short duration. Imaging and laboratory tests are could easily miss or misdiagnose the cancer; the final diagnosis relies on pathology", etc.

Response: We polished the article again. And the sentences have been revised and highlighted in blue in the text.(lines 27-30)

Re-reviewer:

1.The figures and the tables are not displayed correctly in the revised manuscript transmitted to me.

Response: The figures and the tables have been re-added.(lines 253-283)

2. Title, Key words: "cholangiolocellular" -> cholangiocellular (consistent with abstract and text).

Response: The word have been consistent.

3.Author contributions: "Qiong Huang provide pathological pictures; Di Ke manage the patient" -> Qiong Huang provided pathological pictures; Di Ke managed the patient.

Response: The sentences have been revised and highlighted in blue in the text.(lines 294-295)

4.Abstract/Background, last sentence: "The present stud described the fifth patient" -> The present study describes the fifth patient.

Response: The sentences have been revised and highlighted in blue in the text.(10-11)

5.Abstract/Conclusion, first sentence: "This is a rare case that is highly aggressive, rapidly grow, and metastasizes in a short period of time" -> This is a rare case that is highly aggressive, grows rapidly, and metastasizes in a short period of time.

Response: The sentences have been revised and highlighted in blue in the text.(lines 27-28)

6.Core Tip: "However, the combination of hepatocellular carcinoma, cholangiocarcinoma, and neuroendocrine carcinoma exhibiting three differentiation pathways are extremely rare" -> However, the combination of hepatocellular carcinoma, cholangiocarcinoma, and neuroendocrine carcinoma exhibiting three differentiation pathways is extremely rare.

Response: The sentences have been revised and highlighted in blue in the text.(lines 31-34)

7.History of present illness: "The patient' s symptoms started 30 days" -> The patient' s symptoms started 30 days before.

Response: The sentences have been revised and highlighted in blue in the text.(line 60)

8. Laboratory examinations: Please check the units ("Hepatitis B virus DNA normal range < 3.0 × 10<sup>1</sup> IU/mL?").

Response: The unit have been revised and highlighted in blue in the text.(Hepatitis B virus (HBV) DNA 2.327×10<sup>2</sup> (normal range <1000) IU/mL)(line 78)

9. Imaging examinations: "MRI with gadoxetate disodium (Eovist®) revealed a significant enhancement than the CT scan" -> MRI with gadoxetate disodium (Eovist®) revealed a more significant enhancement than the CT scan; "Apparent diffusion coefficient(ADC) images" -> apparent diffusion coefficient(ADC) images.

Response: The sentences have been revised and highlighted in blue in the text.(lines 86-87)

10. Treatment: "In order to control tumor growth, the patient was treated with TACE,to embolize the blood vessels supplying the tumor,including oxaliplatin (150 mg), fluorouracil (4 g), and leucovorin (0.9 g)" - please check the dosages.

Response: The dosage have been revised and highlighted in blue in the text.(lines 124-125)

11.Discussion, last paragraph: "The more the NEC component, the worse the prognosis and high the probability of recurrence and metastasis" -> The larger the NEC component, the worse the prognosis and the higher the probability of recurrence and metastasis.

Response: The sentences have been revised and highlighted in blue in the text.(lines 217-219)

12.Conclusion: "First, clinical examination was suggested HCC or other malignant tumors" -> First, clinical examination suggested HCC or other malignant tumors; "NEC. co-occurrence" -> NEC co-occurrence.

Response: The sentences have been revised and highlighted in blue in the text.(lines 231-246)

13.Informed consent statement: "None,The..." -> None, the...

Response: The sentences have been revised and highlighted in blue in the text.(line 285)

14.Figure legend 1E: "...at the arterial phase than the normal liver" -> in the arterial phase (-> omit "than the normal liver").

Response: The sentences have been revised and highlighted in blue in the text.(line 259)

15.Figure legend 3: "Fig 3. The white arrow points to the lesion. A: 2021.10.8 CT of the abdomen showing a new mass of approximately 53mm×25 mm in size in the right lobe of the liver; B and C: MRI of the patient' s abdomen on the same day. D and E: CT images of the abdomen on November 24, 2021, showing an enlarged and increased intrahepatic lesion compared to the previous scan" -> Figure 3. The white arrows point to the lesions. A: CT of October 8, 2021, showing a new mass of approximately 53mm×25 mm in the right lobe of the liver; B and C: MRI of the same day. D and E: CT of November 24, 2021, showing an enlarged and increased intrahepatic lesion.

Response: The sentences have been revised and highlighted in blue in the text.(lines 268-271)

16.Table 1: "Three differentiated types of liver tumors have been reported (hepatocellular, cholangiocytic, and neuroendocrine)" -> Reports on liver tumors with triple (hepatocellular, cholangiocellular and neuroendocrine) differentiation.

Response: The sentences have been revised and highlighted in blue in the text.(line 278)

17.The fact that there are linguistic and stylistic problems in spite of professional editing could be due to changes made after the editing process (or maybe the authors did not take up all the suggestions).

Response: We polished the article again.

