

[6/5/2021]

Lian-Sheng Ma
Editor-in-Chief
World Journal of Gastroenterology

Dear prof. Lian-Sheng Ma and dear reviewers:

Re: Manuscript ID: 66416 and Title: Hepatic perivascular epithelioid cell tumor: clinicopathological analysis of 26 cases with emphasis on disease management and prognosis

Thank you for your letter and the reviewer's professional and enlightening comments concerning our manuscript entitled "Hepatic perivascular epithelioid cell tumor: clinicopathological analysis of 26 cases with emphasis on disease management and prognosis" (ID: 66416). Your professional attitude and pertinent comments have given us great encouragement. 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. Revised portion are marked **in red** in the paper. The responds to the reviewer's comments and the main corrections in the paper are as flowing:

1. Responds to the reviewer's comments:

Reviewer #1:

1.1 Comment 1: What is the surgical method of "hepatic lobe enlargement resection"? Does it mean that the operator has a large surgical margin? In this article, surgical methods were classified by two surgical procedures, simple resection and enlargement resection groups. However, it is concerned that these comparison are not correct, because enlargement liver resection might be simply needed in those each cases. Simple resection was needed the patients with small size tumor. Therefore, I think that Table 4 is not needed.

Response: ① In this study, "partial lobectomy" (including the tumor) and "hepatic extensive resection of the tumor" (beyond the tumor margin >2cm), which were collectively referred to as "hepatic lobe enlargement resection", and were distinguished from "hepatic tumor simple resection". Compared with simple tumor resection, the surgical incision is larger and varies according to the location and size of the tumor. ② In this study, the majority of patients with tumor diameter greater than 5cm chose extensive liver lobe resection, while a few patients still chose simple tumor resection. At the same time, the majority of patients with tumor diameter less than 5cm chose simple tumor resection. However, due to tumor location, growth mode, relationship between tumor and surrounding tissues, combined with other tumors and clinical manifestations, some cases still chose extended liver lobe resection. This situation provides the possibility to compare the two surgical methods in this study. ③ Due to the small number of rare cases of this disease, it is impossible to be classified and screened in detail before inclusion for comparison, which leads to certain deviation in the statistical study results in this study. Therefore, I agree to delete Table 4 and have modified the corresponding part of the article.

- 1.2 Comment 2: In adjuvant chemotherapy, who received the mTOR inhibitor sirolimus? What were the pathological findings of tumor in patients with mTOR therapy? Please tell us the criteria of using mTOR in your institute.

Response: ①In this study, only 2 patients received mTOR inhibitors: Case No. 8, male /47 years old, with a 6.5cm tumor in the right lobe of the liver, and Case No. 11, female /56 years old, with an 8.0cm tumor in the right lobe of the liver. ②The pathological findings of tumor in patients with mTOR therapy is not significantly different from that of other patients, but the combination of history and clinical presentation usually does not support surgical treatment. After treatment, the tumor will gradually shrink in size.③In our study, the criteria used for mTOR were : PEComa with tumor diameter >5cm requiring therapeutic intervention but not suitable for surgical resection; For patients with TCS1/2 gene mutation; For patients with previous use of similar drugs with therapeutic effect, the recommended dose is 10mg once a day.

- 1.3 Comment 3: As the authors state, hepatic PEComa is difficult to distinguish from malignant disease and to diagnose preoperatively. According to the article and previously reported, malignant potential seemed to be very low only in hepatic PEComa compared to the other primary tumor. This is a concern because if diagnosis is obtained by biopsy, surgical intervention may not be needed. If patients who have diagnosis by biopsy with hepatic PEComa do not have any symptoms, do you do the surgical resection? Minor Please describe the approval number of the ethics committees of hospital partaking in this study.

Response: If biopsy can confirm the diagnosis of hepatic PEComa and have not any clinical symptoms, I will choose conservative treatment and regular follow-up first. If drug intervention or surgical treatment is needed in the later stage, I will proceed to the next treatment plan. Then, this study was approved by the Ethics Committee of The First Affiliated Hospital of Bengbu Medical College (No. 2020057).

2. Responds to the editor's comments:

- 2.1 Comment 1: The title its too long, and it should be no more than 18 words

Response: The title of the passage is made up of 17 words.

- 2.2 Comment 2: The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: The corresponding forms have been uploaded in this revision .

- 2.3 Comment 3: The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all

graphs or arrows or text portions can be reprocessed by the editor.

Response: The corresponding original files have been uploaded in this modification as required.

We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in World Journal of Gastroenterology. Thanks again to the reviewer for his/her evaluation comments and your hard work for the publication of our paper. Looking forward to your reply.

Sincerely,

Zhenzhong Feng

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