

September 20, 2019

Mr. Lian-Sheng Ma

Founder and Chief Executive Officer

World Journal of Clinical Cases

Re: Revised Decision on Manuscript NO: 49697

Dear Mr. Lian-Sheng Ma:

I, along with my coauthors, would like to ask you to consider this revised version of our manuscript, Manuscript NO. 49697 entitled " Pure Squamous Cell Carcinoma of the Gallbladder Locally Invading the Liver and Cavity: A case report and review of literature" for publication in World Journal of Clinical Cases.

We previously submitted this manuscript to your journal and were invited to resubmit the manuscript after addressing the reviewers comments. Those comments are valuable and very helpful for revising and improving our paper. We are very cherishing the opportunity that you offered. After reading the comments and suggestions carefully, we revise the manuscript and point-by-point responses to the reviewers' and editors' comments. We tried our best to improve the manuscript and made some changes in the manuscript. In the manuscript, the revised sections and sentences are presented in red in the text for easy identification.

We are grateful to the reviewers, who provided many insightful comments on our work. We hope that our revised manuscript meets their expectations. Please let us know if you have any questions.

We also appreciate for you and your colleagues warm work, and we are looking forward to this revision will be able to get your approval. Once again, thank you very much for the comments and suggestions.

As previously noted, this manuscript has not been published or presented elsewhere, in part or in entirety, and is not under consideration by another journal. All authors have approved this revised manuscript and agree with submission to your esteemed journal.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

Shan Jin

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Correspondece To: Lijuan Pang

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Responses to the reviewers' comments:

The authors indicate in the introduction the importance of clinicopathological and biological characteristic of these type of tumors and their aggressiveness. However, they insist in their biological characteristics. Would it be possible to indicate: 1) What do they refer to with biological characteristics? 2) Would it be possible to describe some biological characteristics in the introduction?

Response: Thank you for your important comments.

Squamous differentiation is rather uncommon in the gallbladder. Our study reveals that pure squamous cell carcinomas, which we defined as invasive carcinomas composed entirely of squamous differentiation, are constituted only 1% of the cases. A large majority of SCCs are invasive carcinoma entity, often invading the entire gallbladder wall. **It had been speculated that adenosquamous carcinomas/squamous cell carcinomas are more aggressive than ordinary gallbladder adenocarcinomas. It has been testified that the squamous component of gallbladder carcinomas proliferates at a higher rate than the glandular component. However, despite their high proliferation rate, these tumors appeared to less frequently present with lymph node metastasis than gallbladder adenocarcinomas. Their aggressive biological behavior has been attributed to their potential for direct extension and early invasion into the liver and neighboring organs, such as the stomach, duodenum and transverse colon. Generally, SCC is usually aggressive, with infiltration into the liver, and rarely metastasize to lymph nodes. The clinicopathological and biological features of SCC remain to be fully elucidated, owing to its uncommon occurrence.**

We have revised the text accordingly in the Introduction section. **(page 5, line: 9---16).**

Responses to the editors' comments:

1. Please provide and upload the approved grant application form(s).

Response: We appreciate your important comments. We have provided and upload the approved grant application forms.

2. Please re-upload the surgical consent form after the official seal of the hospital or department.

Response: Thank you for your important comments. We have re-uploaded the surgical consent form after the official seal of the hospital.

3. Please provide the author's office landline number.

Response: We apologize for this mistake, we will provide the author's office landline number in manuscript. (page 2, Telephone: +86-0993-2850955).

4. Please provide the image documents without arrows and "A", "B", "C", "D".

Response: We appreciate your important comments. We will replace the images documents without arrows and "A", "B", "C", "D" . (page 15-19, Figure: 1, 3, 4, 6).

5. This image of abdominal ultrasonography is not clear. Please provide the original image document.

Response: Thank you for your important comments, we have provided the original image document.(page 18, Figure: 5).