Dear Editor, Dear reviewers:

Thank you for your letter dated June 8. We were pleased to know that our work was rated as basically meet the publishing requirements of the World Journal of Clinical Cases, subject to adequate revision. We thank the reviewers for the time and effort that they have put into reviewing the previous version of the manuscript. Their suggestions have enabled us to re-examine and improve our work. Based on the instructions provided in your letter, we uploaded the file of the revised manuscript. Appended to this letter is our point-by-point response to the comments raised by the reviewers. We would like also to thank you for allowing us to resubmit a revised copy of the manuscript.

Reviewer #1:

Question 1:

However, I can’t help feeling the doubt for their pathological diagnosis within the provided information. Typical figures of sarcomatoid carcinoma is poorly differentiated carcinoma with spindle-shaped cells and commonly pleomorphic (including giant cells) morphology showing co-expression of CK and vimentin; as they described in discussion section. However, in Fig 1A, provided HE image seems to simply “poorly differentiated adenocarcinoma

with desmoplastic reaction" and highlighted figures of tumor cell by PCK-IHC showed no spindle-shaped or pleomorphic morphology.

Answer1:

Thank you very much for the professional opinions of the reviewer. The picture we selected before is certainly not very typical and does not well show the pathological features of sarcomatoid carcinoma. To this end, we re-screened the images and selected the more representative ones (Figure 1). In some reports, Vimentin has a high rate of co- expression of PCK in sarcomatoid carcinoma. However, according to the World Health Organization Classification of Tumours of the Digestive System[1], gallbladder sarcomatoid carcinoma is kind of poorly differentiated carcinoma with spindle-shaped cells and commonly pleomorphic morphology. The expression of cytokeratin in the spindle cells can distinguish this tumor from sarcoma, which is also the most important indicator for the diagnosis of sarcomatoid carcinoma. For these cases collected in this paper, we can determine the pathological diagnosis of sarcomatoid carcinoma through information on the HE staining 、PCK and other indicators of IHC. Due to the impact of the current COVID-19 outbreak, many of the work that requires multi-sectoral collaboration has been affected, and we are very sorry that it is

difficult to supplement vimentin information in the short period of time.

Question 2:

In addition, IHC figures of Fig. 1c (desmin) and Fig 1d (p63) makes no sense for pathological diagnosis of sarcomatoid carcinoma. Further, expression of p63 and squamous cell carcinoma components (documented in “Pathological diagnosis” section) indicated possibility of adenosquamous cell carcinoma.

Answer2:

Once again, we would like to thank the reviewers for raising these specific and professional questions from a pathological point of view. Desmin and other indicators such as a-SMA, CD34, and even syn, Cga (Table 4) are not intended to prove the diagnosis of sarcomatoid carcinoma, but to exclude other pathological types. Sarcomatoid carcinoma has a variety of forms and usually needs to be differentiated from other tumor types. We list these indicators in order to further justify the diagnosis of sarcomatoid carcinoma.

Question 3:

Expression of p63 and squamous cell carcinoma components indicated possibility of adenosquamous cell carcinoma.

Answer 3:

Thanks for reviewer’s suggestion .Gallbladder sarcomatoid carcinoma

consists of variable proportions of spindle, giant and polygonal cells, and other kinds of tumor, like adenocarcinoma or adenosquamous carcinoma, are usually found in some of these tumours after extensive sampling. Of the 7 cases we collected, there were 2 cases with mixed adenosquamous carcinoma .The expression of p63 was found in these cases.

Question 4:

The diagnosis of well-differentiated cases is doubtful because sarcomatoid carcinoma generally considered as poorly differentiated carcinoma"

Answer4:

Thank the reviewer for this question. The description of well-differentiation is indeed inaccurate, because sarcomatoid carcinoma is supposed to be poorly differentiated. Well differentiation is a mixed well-differentiated adenocarcinoma component. We also thought that the previous description was inaccurate, so we deleted the description of the differentiation level of the case.

Question 5:

In discussion, first paragraph, the version of WHO classification and citation in reference should be added.

Answer5:

Thanks for reviewer’s suggestion. We've referenced the fourth edition of the WHO classification and have added it to the reference.

Reviewer #2:

Question:

Only minor revision is required for example ca19-9 instead of ca-199 etc. and minor language polishing in discussion section. Also conclusion should be more revised in order to present more precise in presenting basic characteristics of the disease.

Answer：

Thank you very much for the reviewer's detailed comments. We have replaced ca-199 with CA19-9. We have made appropriate deletions to the discussion part of the article, and the conclusion part has also made some changes.

We hope that the revised manuscript is accepted for publication in the World Journal of Clinical Cases.

Sincerely, Qing Qin,Ming Liu,Xin Wang