

Dear Editor,

We thank you for giving us an opportunity to revise our manuscript (ID: 94351) entitled **“Long-term survival of patients with hepatocellular carcinoma with hepatic, pulmonary, peritoneal and rare colon metastasis: case report”**. We appreciate the editor and reviewers very much for their comments and suggestions on this paper. All of these comments and suggestions are valuable and helpful for revising and improving our manuscript.

Our team has been committed to gastrointestinal tract cancers-related research over the years. Fortunately, we have received a number of national project funding and have published several articles in related fields. We have studied the comments and suggestions of the reviewers carefully. We invest a lot of effort and time into polishing the manuscript. We make the following revision in response to their comments point-by-point. We believe this article will be very useful to anyone interested in this field. We hope that the revised manuscript will be accepted for publication in *World Journal of Gastrointestinal Surgery*.

Once again, thank you very much for your letter. We are looking forward to hearing from you soon.

With kind regards,

Yours sincerely,

On behalf of my co-authors

Chao-Wu Chen

Dear Reviewers,

Thank you very much for your careful review. We sincerely appreciate your comments, which are helpful and instructive for improving the quality of our manuscript. We include here with a point-by-point detailed revision made in response to your suggestions. We think the revised manuscript is much better. We hope our modification will meet your expectation and you can accept our paper. Thank you so much.

### **Replies to Reviewer 1:**

1. An interesting article focusing on an unusual pattern of natural history of hepatocellular carcinoma with digestive tract metastatic involvement and long survival. The case is well presented, however along the entire text the language should be deeply revised before the article could be considered for publication.

**Response:** Thanks so much for your valuable suggestions. We try our best to proofread our manuscript for grammar, syntax, and punctuation, *etc.*. Also, we have asked a native English speaker to go over the manuscript in depth for errors. The revised details can be found by highlighting in the yellow text. Please check.

### **Replies to Reviewer 2:**

1. The author mentioned in the history that the patient had tumor rupture and hemorrhage, which may increase the risk of metastatic implantation in the abdominal intestine, although the surgical irrigation procedure was done after that. And this cause may be different from the normal intestinal metastases due to hepatocellular carcinoma. In addition, The postoperative pathological biopsy confirmed a moderately differentiated HCC. Can we suppose that this patient might have a better prognosis relative to normal blood metastases to the intestinal tract with worse differentiation? It is suggested the authors would be able to add relevant contents to

the discussion.

**Response:** Thank you for kind suggestion. As you mentioned, the patient underwent abdominal and pelvic exploration and irrigation for liver cancer with rupture and hemorrhage. It is worth considering whether the rare colon metastasis is through normal intestinal metastasis or abdominal implantation. We do not rule out the risk of intraperitoneal implantation, but we still consider the possibility of metastasis through the normal intestinal pathway to be greater. First, the patient had liver, lung, and peritoneum metastases successively, and then intestinal metastasis occurred 2 years later. If colonic metastasis of HCC is dominated by peritoneal implantation, it may occur almost simultaneously with abdominal metastasis. Besides, it is considered that colonic metastasis grows in the intestinal cavity, rather than infiltrating and growing into the intestinal cavity through imaging and colonoscopy examination. In addition, The postoperative pathological biopsy of this patient confirmed a moderately differentiated HCC. As you consider, the pathology contributes to the relatively good prognosis of HCC. However, we reported a patient with a high-risk recurrence of ruptured and hemorrhagic HCC with multiple extrahepatic metastases at a late stage. The clinical efficacy and prognosis of such cases are generally poor. According to National Cancer Institute's SEER database, the average five-year survival rate of HCC patients in the US is 19.6% but can be as low as 2.5% for advanced metastatic disease. We were surprised to find that the survival time of this patient could be prolonged after comprehensive treatment, which brought great encouragement and confidence to our clinical treatment. Therefore, although this patient is a moderately differentiated HCC, an 8 year effective survival period can still be assessed as long-term survival rate. Combining with domestic and foreign literature reports, we believe that this case does belong to long-term survival. As you suggested, we have added relevant contents to the discussion in the revised manuscript. Please check. Thank you very much!