

Dear Dr. Zhang:

Thank you very much for the decision letter and advice on our manuscript entitled “ **Mesenteric phlebosclerosis with amyloidosis in association with the long-term use of medicinal liquor: a case report**”.

We thank the reviewers for their constructive and helpful comments and suggestions. We have revised the manuscript according to their suggestions. All amendments are highlighted in red in the revised manuscript. In addition, point-by-point responses to the comments are listed below this letter.

We hope that the revised manuscript is suitable for publication in your journal.

We look forward to hearing from you soon.

Best wishes,

Yours sincerely,

Qunying Wang

First of all, we would like to express our sincere gratitude to the reviewers for their constructive and helpful comments.

Reply to Reviewer 1

(1) editor will communicate.

Reply: Some sentences have been modified or newly added in the revised manuscript. In addition, point-by-point responses to the comments are listed (All amendments are highlighted in red).

Reply to Reviewer 2

(1) Background: Mesenteric phlebosclerosis has not been described in the text.

Reply: Thank you for your insightful suggestion. Some sentences have been newly added in the revised manuscript (All amendments are highlighted in red).

(2) Please provide Discussion section: i suggest to report (if published) the criteria for diagnosis.

Reply: Thank you for your insightful suggestion. Mesenteric phlebosclerosis (MP) is difficult to diagnose because its etiology and pathophysiology are unclear, and many patients are asymptomatic or present with atypical symptoms. However, there were no criteria for diagnosis of MP so far. The correct diagnosis of MP requires the observation of characteristic imaging features, including multiple calcifications on CT and purple-blue mucosal discoloration on colonoscopy. Histological features of MP include thickening and calcification of the venous walls and marked fibrous deposits in the colonic wall. We have described the above in the text (Discussion section: Line 13-22, Page 8; Line 1-13, Page 9). **Shimizu et al** had the same view that a diagnostic criterion of MP is necessary (Involvement of herbal medicine as a cause of mesenteric phlebosclerosis: results from a large-scale nationwide survey. *J Gastroenterol.* 2017; 52(3):308-14. doi:10.1007/s00535-016-1218-9).

(3) Also report if possible, the composition of this medica liquor

Reply: Thank you for your insightful suggestion. This medical liquor is mainly made from gardenia fruit and containing geniposide, which we have reported in the text (Case presentation section: Line 20, Page 6). Since the composition of this medical

liquor is complex, we have no idea about others. However, we will have the composition analysis in the future.

Reply to Reviewer 3

(1) The authors reported MP with amyloidosis. The reviewer doubts the diagnosis of amyloidosis in this case. Because this Congo red staining might be weak and a false-positive in Fig. 4. The authors should show Congo red stain under polarizer filter showing in green, and classify the type of amyloidosis such as AL, AA. Then, the authors should diagnose amyloidosis carefully.

Reply: Thank you for your insightful suggestion. We made hard work for the biopsy material. Hematoxylin and eosin staining showed obvious thickening and calcification of the vein walls. Masson trichrome staining of the biopsy material revealed dense perivascular and mucosal collagen degeneration. Congo red staining highlighted amyloidosis in the venous walls (Figure 4). The staining was made by our professional colleague. The diagnosis of amyloidosis was considered. In our opinion, MP produces amyloid deposits secondarily. The role of amyloidosis in this context requires further study. We will keep working.

(2) In this case, 1 year after discontinued the Chinese medicinal liquor, the mesenteric vein calcification was disappeared in abdominal CT findings. Please describe the other reports that the mesenteric vein calcification was disappeared after discontinued medicines which might be caused MP.

Reply: Thank you for your insightful suggestion. One year later, the abdominal CT showed that the mesenteric vein calcifications had disappeared in this patient after he discontinued the Chinese medicinal liquor. However, few studies reported this condition. Some patients with calcifications underwent surgery, some patients had no abdominal CT during the follow-up and some patients may still have calcifications because of short-time follow-up. Since the composition of this medical liquor is complex, we are not sure the reason for disappearance of calcifications. More multicenter clinical trials with a large sample size are warranted, and we will continue to work on this subject.