

Dear Reviewers,

We would like to express our sincere thanks to your constructive and helpful comments on our paper (90926). Based on the comments, we have made extensive modification on the original manuscript. Here, we attached the revised manuscript in which major changes were highlighted in yellow so that they may be easily identified. And the point-by-point responds to the comments are as following:

Replies to Reviewer #1:

• Did you aspirate blood before injection of Lauromacrogol to be sure that you were inside a vessel? • What is the pulsed wave Doppler pattern of the injected vessel in the first case? • How did you calculate the amount of the injected Lauromacrogol needed to obliterate the hemangioma? You have injected about 27ml! • Why doing occult blood in stools in the presence of overt bleeding per rectum?! • You have injected Lauromacrogol into a vessel with arterial blood flow in the second case? • History of Osler Weber Rendu and Blue rubber bleb nevus syndromes should be asked for and mentioned in manuscript. • The classification of rectal hemangioma into localized and diffuse types, and capillary and cavernous types and their relation to the previously mentioned syndromes should be mentioned in the discussion section.

Answer: Thank you very much for your valuable comments and suggestions to improve our manuscript! The comments and suggestions are replied point-by-point below.

1. Did you aspirate blood before injection of Lauromacrogol to be sure that you were inside a vessel?

Answer: Thanks very much for the comments! We can accurately inject lauromacrogol into the dilated vessels in cavernous hemangioma under the EUS guidanc. There is no need to withdraw blood to determine the location, and the blood withdrawal of the injection needle can not be clearly seen in the ultrasound mode.

Under the EUS guidance, the needle is accurately inserted into the cavernous hemangioma for the injection of lauromacrogol.

2. What is the pulsed wave Doppler pattern of the injected vessel in the first case?

Answer: Thank you for this valuable suggestion! Color Doppler US showed that the blood flow signal disappeared after lauromacrogol injection and we added **Figure 4B** in the article.

3. How did you calculate the amount of the injected Lauromacrogol needed to obliterate the hemangioma? You have injected about 27ml!

Answer: We apologize for the confusion! Accurate calculation of the preoperative dose is difficult because lauromacrogol is diluted with the blood flow.

The filling of lauromacrogol inside the hemangioma can be observed in real time during the endoscopic ultrasound scan. During the operation, the injection can be stopped when the lesion is full of high echo of lauromacrogol. If the lesions are still residual, supplementary injection of sclerosing agent can be performed again.

4. Why doing occult blood in stools in the presence of overt bleeding per rectum?

Answer: We apologize for the confusion! We accept reviewer's suggestion and have re-written sentences in the revised version.

5. You have injected Lauromacrogol into a vessel with arterial blood flow in the second case?

Answer: Thank you very much for your valuable comments! We apologized for the mistake and corrected it in the revised version for we did not detect any arterial blood signal in the spectrum in the second case.

6. History of Osler Weber Rendu and Blue rubber bleb nevus syndromes should be asked for and mentioned in manuscript.

Answer: Thank you very much for this valuable suggestion! We modified this sentence based on your advice.

The patient had no history of systemic syndromes such as Osler Weber Rendu and Blue rubber bleb nevus syndromes.

7. The classification of rectal hemangioma into localized and diffuse types, and capillary and cavernous types and their relation to the previously mentioned syndromes should be mentioned in the discussion section.

Answer: That is a nice proposal and we have added the classification and related content in DISCUSSION in the revised manuscript.

Colorectal hemangioma is an exceedingly rare congenital benign vascular disorder. The primary pathological subtypes encompass cavernous, capillary, and mixed forms, with cavernous hemangioma being the most prevalent. Cavernous hemangiomas can be further classified as localized or diffuse types, characterized by enlarged blood-filled spaces lined with abnormally thin vessel wall. Additionally, certain systemic syndromes such as Osler Weber Rendu and Blue rubber bleb nevus syndromes may present histologically as telangiectatic, mixed or cavernous hemangiomas in the intestinal vasculature, of which colorectal hemangioma represents only a partial manifestation.

Replies to Reviewer #2:

Answer: Thank you very much for your valuable comments and suggestions to improve our manuscript! The comments and suggestions are replied point-by-point below.

1. The figure 1 A-C looks almost identical. Was leakage of contrast medium observed?

Answer: We apologize for the confusion! CT revealed diffuse thickening of the rectum with multiple calcification foci, and the enhanced rectal wall was not obvious in CT arterial phase in the first case. CT findings are nonspecific, making it

difficult to differentiate colorectal cavernous hemangioma from the surrounding soft tissue and to determine the exact extent of the lesions.

2. What do you want to report by Figure 4C and 4D? These figures are difficult to understand.

Answer: We apologize for the confusion! We have added more details in the revised manuscript.

Doppler US showed small internal strips of blood flow (Figure 3C). And contrast-enhanced EUS using SonoVue (a contrast-enhanced ultrasound agent) distinctively revealed a septum-like structure and small internal enhancement in the anechoic areas (Figure 3D).

(NOTE: The Figure 3 and Figure 4 has been adjusted in the revised article)

3. In page 8, last line, the cavernous hemangioma showed the solid echo in EUS?

Answer: Thank you for this valuable suggestion and we are very sorry for our incorrect writing! In the two cases reported in this paper, EUS showed that the cavernous hemangioma originated from the colorectal submucosa and appeared as honeycomb hypoechoic appearance.

EUS can clearly display the intestinal wall hierarchy, determine the location and origin of the tumor, show echo of the lesion, and detect blood flow signals under Doppler US, providing a reliable diagnostic basis for colonic hemangioma.

4. Only general considerations were described in discussion section. It is described that EUS is the best device for diagnosing cavernous hemangioma. Could you please describe the EUS findings in more detail? The actual EUS findings in the two cases also should be discussed.

Answer: Thank you very much for your valuable comments and suggestions to improve our manuscript! We have added more EUS findings in the recent version.

In the two cases reported in this paper, EUS showed that blue-purple lesions originated from the colorectal submucosa and appeared as honeycomb hypoechoic appearance, and Doppler US detected a small amount of blood flow signals. Contrast-enhanced endoscopic ultrasonography (CE-EUS) can enhance the Doppler blood flow signal through injection of ultrasound contrast agent. Clearly showing whether there is abnormal perfusion in the blood flow of the lesion, which is helpful for the diagnosis of the disease and the judgment of blood supply.

5. Could you discuss the adaptation of endoscopic treatment in colorectal cavernous hemangioma patients?

Answer: Thank you very much for this valuable comment! The brief statement of adaptation of endoscopic treatment in colorectal cavernous hemangioma patients was added in the DISCUSSION in revised manuscript.

Under the EUS guidance, the needle is accurately inserted into the cavernous hemangioma for the injection of lauromacrogol. The filling of lauromacrogol inside the hemangioma can be observed in real time during the endoscopic ultrasound scan. During the operation, the injection can be stopped when the lesion is full of high echo of lauromacrogol. It can not only effectively reduce the risk of extravascular injection caused by "blind" injection under the direct vision of ordinary endoscope, but also monitor the changes of the echo in the hemangioma cavity during the injection process, and accurately control the injection amount of lauromacrogol. However, the local lesions may not penetrate completely due to the dilution of lauromacrogol with the blood flow after a single injection of lauromacrogol. Therefore, sequential treatment should be performed as appropriate. In the follow-up review, if the lesions are still residual, supplementary injection of sclerosing agent can be performed again. Compared with other non-surgical conservative treatment methods, EUS-guided injection of lauromacrogol in the treatment of colorectal cavernous hemangioma is more targeted and

thorough, with fewer intraoperative and postoperative complications.

The EUS-guided injection of lauromacrogol for treatment of colorectal cavernous hemangioma is a safe, effective, cost-efficient, and minimally invasive technique, especially in instances where an extensive resection is not feasible or not tolerant for the patients.

We have tried our best to improve the manuscript, and hope that the answers and corrections will meet with approval. Thank you!

Sincerely yours,

Hongtan Chen

Department of Gastroenterology

The First Affiliated Hospital, College of Medicine, Zhejiang University

79 Qingchun Road, Hangzhou 310003, P.R. China

E-mail: chenhongtan@zju.edu.cn