October 22, 2021

Dear Editors:

We wish to re-submit the attached manuscript, titled “Trans-ileocolic endovascular treatment by a hybrid approach for severe acute portal vein thrombosis with bowel necrosis: Two case reports.” The manuscript number is 69385.

The manuscript has been rechecked, and appropriate changes have been made in accordance with the reviewers’ suggestions. The responses to their comments have been prepared and are attached herewith.

We thank you and the reviewers for your thoughtful suggestions and insights, which have enriched the manuscript and produced a better and more balanced account of the research. We hope that the revised manuscript is now suitable for publication in your journal.

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

Sincerely,

Tatsuo Ueda, MD, PhD
Department of Radiology,
Nippon Medical School
1-1-5 Sendagi, Bunkyo-ku,
Tokyo 113-8603, Japan
Tel.: +81-3-5814-6240
Fax: +81-3-5685-1795
E-mail: s9015@nms.ac.jp

Responses to the Reviewers' Comments

We are grateful to the reviewers for their constructive criticism and valuable suggestions that have helped us considerably improve the quality of our manuscript. We are resubmitting a revised manuscript conforming to all of the reviewers' comments. In particular, we have addressed all the reviewers' comments in a point-by-point manner, and our revisions are indicated in red font in the revised manuscript. We hope that the revised manuscript is now suitable for publication in your journal.

(1) To Reviewer 05467120 (Reviewer 1)

Comments by Reviewer 05467120

Nice approach and management for portal vein thrombosis leading to bowel necrosis. However, I suggest to modify the title to indicate that it was a hybrid approach in the first part of the title, so that the reader won't be mislead.

Response:

Based on the reviewer's suggestion, we have modified the title as follows: "Trans-ileocolic endovascular treatment by a hybrid approach for severe acute portal vein thrombosis with bowel necrosis: Two case reports."

(2) To Reviewer 03413692 (Reviewer 2)

Comments by Reviewer 03413692

The paper is good and well written.

Response:

We are thankful for the time and energy you expended and appreciate your positive comment.

(3) To Reviewer 05405967 (Reviewer 3)

Comments by Reviewer 05405967

Trans-ileocolic endovascular treatment for severe acute portal vein thrombosis with bowel necrosis: Two case reports of hybrid treatment Manuscript Type: CASE REPORT Acute and chronic PVT is a rare condition with multiple etiologies. The grades of severity were described and also the technique used. Comparably little information was given to the etiologies of PVT and the influence of the etiologies on necrotic intestinal tissue. The authors repeatedly used the term "study" but case report might be the adequate description. The discussion might appear to general for the description of two cases. The very specific two case reports focusing on the "severity" of PVT treatment techniques but lacking

additional important information on the differential diagnosis of other ischemic intestinal diseases and how to handle acute portal vein thrombosis of different etiologies.

1. Little information was given to the etiologies of PVT and the influence of the etiologies on necrotic intestinal tissue.

Response:

We appreciate the reviewer's concern regarding this point and have added the following text in the Discussion.

9-The etiologies of PVT (Page 11, Lines 275-279)

"In this case report, acute PVT was diagnosed with gastroenteritis and peritonitis. Thus, infections might have induced the three factors of Virchow's triad including intravascular vessel wall damage, stasis of flow, and the presence of a hypercoagulable state and caused PVT."

-The influence of the etiologies on necrotic intestinal tissue (Pages 11, Lines 285-288)

"In severe PVT such as in these cases, a venous congestion is initially induced owing to various etiologies. A hemorrhagic infarction then occurs, and an arteriovenous obstruction finally leads to bowel necrosis."

2. The authors repeatedly used the term "study" but case report might be the adequate description.

Response:

According to the reviewer's suggestion, we have changed the term "study" to "case report" in this report on Pages 6 Lines 130, Pages 12 Lines 291, and Pages 13 Lines 329.

3. The very specific two case reports focusing on the "severity" of PVT treatment techniques but lacking additional important information on the differential diagnosis of other ischemic intestinal diseases and how to handle acute portal vein thrombosis of different etiologies.

1) lacking additional important information on the differential diagnosis of other ischemic intestinal diseases

Response:

In general, it is difficult to diagnose PVT based on clinical symptoms. In fact, both these two cases were difficult to distinguish from other ischemic intestinal diseases, and the diagnosis was made using contrast-enhanced CT. Therefore, we have added an additional explanation on Page 11, Lines 279-283.

"Though focusing on risk factors, such as thrombophilia and portal hypertension, may be effective for diagnosing PVT, it is difficult to distinguish PVT from enteritis and other ischemic intestinal disease such as arterial thrombosis or non-occlusive mesenteric ischemia based on clinical symptoms without imaging evaluation."

2) how to handle acute portal vein thrombosis of different etiologies

Response:

As per the reviewer's suggestion, we have included explanations on PVT treatments according to different etiologies on Page 12, Lines 298-312 and added different etiologies on Page 11, Lines 276-277 as well.

"Sharma et al. revealed that different treatment was shown according to the etiologies[4]. It is reasonable to monitor conservatively without anticoagulation for reversible risk factors such as pancreatitis or abdominal infections in patients with minimal thrombus in PV. In cases of non-cirrhotic, non-malignant, and symptomatic PVT, anticoagulation is recommended. For asymptomatic PVT, especially with extension to the mesenteric veins, non-reversible risk factors, and hypercoagulable states, anticoagulation is reasonable for preventing or reducing symptoms such as abdominal pain, nausea or vomiting, or ischemic complications, including bowel necrosis and portal hypertension-related symptoms. In patients with PVT accompanied by malignancy, anticoagulation is also recommended in the majority of cases. Thrombolytic can be considered in those with thrombus extension or worsening pain while on anticoagulation and in patients with impending or ongoing bowel necrosis owing to thrombosis. For these, anticoagulation is often recommended."