

Dear Editor,

World Journal of Gastroenterology Oncology

Manuscript NO:80653

Title: *Local recurrence after successful endoscopic submucosal dissection for rectal mucinous mucosal (Tis) adenocarcinoma: A case report and a molecular analysis*

Thank you very much for giving us a chance to revise our manuscript. We revised and resubmit the paper for publication in *World Journal of Gastroenterology Oncology*.

We attached a point-by-point response. We believe this manuscript is relevant to the scope of your journal and will be interest to its readership.

We look forward to learning your decision in due course.

Sincerely yours,

Hiroki Tanabe

Point-by-point

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: It is a good paper, with an important theme. The language is good and details are convincing. I have nevertheless a major perplexity with regard to this paper: a case report cannot have 16 (sixteen) authors ! Maybe I have counted wrong; otherwise please clarify the role of each author (what contribution) to the editorial office.

Comment to reviewer #1:

Thank you for your suggestion.

As suggested, we performed pathological and genetic analyses of cases from two institutions for this rare case presentation. Since many researchers and clinicians

contributed to this research, we will add an “Author contributions” section, as follows.

Author contributions

YMu designed this case report and performed the whole study. HT helped write this manuscript. YO and YMi performed the genetic analyses. YS, YK, TK, ES, and KT were involved in the patient’s diagnosis and endoscopic treatment. KA and NU organized the patient’s treatment in the hospital. KM and SK processed the experimental data and performed the analysis. SY performed the histological analysis. MF and TO supervised this research. (Page 2)

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Thanks for sharing such an interesting case, but I have one question: The authors mentioned that the pathological result was mucinous adenocarcinoma with signet-ring cell carcinoma after the first rectal ESD procedure, and "Mucinous adenocarcinomas with signet-ring cell carcinomas are distinctively different from adenocarcinoma in their tumor biology and

aggressive phenotype[5]". When the follow-up colonoscopy revealed possible recurrence, Why was EUS not performed for preoperative evaluation, such as the presence or absence of submucosal invasion? If EUS was performed as in most conditions, the Mile's operation might have been directly advised instead of the unnecessary second ESD procedure.

Comment to reviewer #2:

The usefulness of EUS for conducting a depth analysis before endoscopic resection has been reported, and we sometimes perform ultrasound using a 12-MHz miniprobe before ESD. EUS can detect a mucinous lake under the fibrotic ESD scar. As the reviewer notes, however, EUS was not performed. In the present case. There is no evidence supporting a depth evaluation for a recurrent lesions at present. We have now mentioned this point in the revised manuscript, as follows.

One limitation associated with the present study warrants mention. The patient ultimately underwent Mile's operation after undergoing ESD twice through the clinical course. Endoscopic ultrasound (EUS) is useful for evaluating the depth of submucosal invasive lesions in the rectal tumors before endoscopic resection [25].

The second ESD procedure might have been avoided if a more accurate pretreatment diagnosis concerning the depth of the local recurrence had been available. (Page 13)

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which

all components are movable and editable), organize them into a single PowerPoint file.

Response:

As suggested, we revised figure legends in our manuscript.