Editor in Chief, ***World Journal of Clinical Cases***
Jin-Lei Wang, Company Editor-in-Chief

June 27, 2021

Dear Editors and Reviewers,

Thank you and reviewers for a thorough review of our manuscript entitled "**Rapid Progression of Mucinous Colorectal Carcinoma with Immunosuppressive Condition: Rare Case Report and Review of Literature**" (Manuscript No.: 67082) by Yohei Koseki and myself. The thoughtful comments from the reviewers are greatly appreciated. In preparing for revision, we have carefully studied reviewers' comments and incorporated many of their suggestions into the revised manuscript. For your convenience, we have marked our changes in blue in the revised manuscript. We hope this revised manuscript is now acceptable for publication in ***World Journal of Clinical Cases***. **The provided ID for this invited case report is (00188507).**

We declare that this work is original, the manuscript is not under consideration by other journals, and the material has not been previously published. All authors contributed significantly on this study and approved the contents submitted.

Thank you for your time and effort in reviewing our work. We look forward to hearing from you at your earliest convenience.

Sincerely,
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Dear Editor and Reviewers,

Thank you for a thorough review of our work and your thoughtful comments and suggestions are greatly appreciated. In preparing the revision, we have carefully studied your comments and incorporated your suggestions into the revised manuscript. The following are our point-to-point responses to your comments/concerns. For your convenience, we have typed the changes in the manuscript in blue.

Editors

1 Scientific quality: The manuscript is case report of ascending colon mucinous adenocarcinoma progression in immunosuppressive status. The topic is within the scope of the WJCC. (1) Classification: Grade B;C, (2) Summary of the Peer-Review Report: The case is well written with sufficient discussion, however there are several points must be addressed to be accepted. Clarify standard usage of medical terms. List normal lab reference values. Clarify why CK7, CK20 and CDX2/SATB2 were not used to confirm this colonic primary. Discussion should be expanded referencing published cases and rapid tumor progression after immunosuppressant therapy. This paper requires further language polishing. (3) Format: There are 3 Tables and 4 Figures; (4) References: A total of 28 references are cited, including 3 reference published in the last 3 years; (5) Self-cited references: There is no self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B;B. A certificate was issued by Enago. 3 Academic norms and rules: The authors provided the Signed Informed Consent Form(s) or Document(s), Non-Native Speakers of English Editing Certificate; CARE Checklist–2016.No academic misconduct was found in the Google/Bing search. 4 Supplementary comments: This is an invited manuscript. The topic has not previously been published in the WJCC. 5 Issues raised: (1) Core-tip audio is missing. (2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (3) Conflict-of-Interest Disclosure Form, Copyright License Agreement are missing. (4) Please update manuscript format per journal guideline. (5) Please expand the reference list, including up to date literature. 6 Re-Review: Not required. 7 ***Recommendation: Conditional acceptance.***

Response: We appreciate you and reviewers for recognizing the significance of our work and suggestive comments. We have modified the Case presentation and Discussion section according to your suggestions.

Reviewer #1

The authors reviewed one case of ascending colon mucinous adenocarcinoma progression in immunosuppressive status.

Response: We are grateful to this reviewer for recognizing the significance of our work and suggestive comments.

1. Title: Would suggest to change to: Progression of COLONIC Mucinous Adenoarcinoma with Immunosuppressive Condition: Rare Case Report and Review of Literature.

Response: We appreciate the reviewer for the thorough review. We have modified the title and running title (page 1, line 4 and 6 from the top).

2. Please also change in the main text and abstract from Mucinous colorectal carcinoma to colorectal mucinous adenocarcinoma. Mucinous carcinoma is one subtype of adenocarcinoma. Also ehen the authors mention the current case report, please use colonic mucinous adenocarcinoma. For example: "Here we report a rare case of ascending mucinous colorectal adenocarcinoma" should be "Here we report a rare case of ascending colon mucinous adenocarcinoma". Since this carcinoma was located in ascending colon, please do not use "colorectal". Colorectal can be a general term to describe the carcinomas in colon and rectum.

Response: We appreciate the reviewer for the thorough review. We have modified the descriptions (page 4, line 3, 5, 8, 11, 16 from the top; page 5, line 7 from the top; page 6, line 2, 6, 9; page 10, line 4, 8, 12, 14, 16 from the top and line 3 from the bottom; page 11, line 3 from the top) according to the reviewer's suggestion.

3. For the tumor stage stage T4aN2aM1b. I think this is a clinical stage (cT4aN2aM1b), right? Is it AJCC 8th edition for the staging? can you explain why it is N2a? where are 4-6 lymph nodes are positive (N2a:Four to six regional lymph nodes are positive). Why is M1b? Based on your description, the liver is the only involved organ. If only liver is involved, it should be M1a (M1a: Metastasis to one site or organ is identified without peritoneal metastasis; M1b: Metastasis to two or more sites or organs is identified without peritoneal metastasis; pM1c: Metastasis to the peritoneal surface is identified alone or with other site or organ metastases).

Response: We appreciate the reviewer for the thorough review. We have corrected and added the descriptions (page 8, line 10 from the top; page 9, line 12 from the top).

4. This patient is young (39 yrs) and the tumor morphology is mucinous. A possibility of MMR deficiency by immunohistochemical stain or MSI test by PCR is a must for the cancer management and rule out the possibility of Lynch Syndrome, although this patient had no family history of cancer. Please do at least IHC for MLH1, PMS2, MSH2 and MSH6 stains to show the MMR/MSI status for this case. Patients with MSI-high CRCs including mucinous adenocarcinoma often have better prognosis. Please discuss this too.

Response: We agree with the reviewer and added the description in Discussion (page 11, line 10 from the top).

5. Although CT study did not reveal colon cancer before the PSL treatment, the possibility of missing the colon cancer initially cannot be completely excluded. The authors should discuss that too.

Response: We agree with the reviewer and added the description in Discussion (page 11, line 3 from the bottom).

6. The authors used "with lymphatic and liver metastases". You meant lymph node metastasis? lymphatic and lymph node metastasis are 2 different concepts.

Response: We agree with the reviewer and added the description in Case presentation and Discussion (page 4, line 6 from the bottom; page 5, line 5 from the bottom; page 9, line 10 from the top).

7. Pathologic diagnosis: The authors used Muc2 and MUC5AC to diagnose this colonic mucinous adenocarcinoma. Muc2 is intestinal marker but Muc5AC is a gastric mucin-type marker. Why Muc5AC is positive. Why commonly used markers such as CK7, CK20 and CDX2/SATB2 were not used to confirm this colonic primary? Would suggest to run these markers to confirm is is colonic primary? Especially the biopsy picture (Figs 3a and 3b) did not show any precursor lesion and the tumor cells/mucin looks like underneath the surface mucosa.

Response: We agree with the reviewer and added the Figure 2c to show that the tumor was from epithelial mucosa and description of the tumor in Case presentation (page 8, line 1, 4, 5, 6, and 9 from the bottom; page 9, line 1 and 5 from the top), Discussion (page 11, line 1 from the top), added references #17, #18 and modified the Figures. 3a and b and legends for Figure 2 and 3.

8. Tables 1 and 2. Please also list the normal reference range of the lab data.

Response: We agree with the reviewer and added the normal reference range in the Table 1 and 2.

9. The current case is mucinous adenocarcinoma. How about other reported cases in table 3, how many of them were mucinous adenocarcinoma?

Response: We agree with the reviewer. We have confirmed the reports shown in Table 3, however, unfortunately no minute description regarding the histological classification were presented. To further expand the discussion, we have added the description and references in Discussion and modified the Table 3 (page 12, line 8 from the bottom; new references #31, #32; revised Table 3). Thank you again for your thorough review of our manuscript and the insightful suggestions.

Reviewer #2

In this manuscript, Dr. Kamimura presents the case of a young woman with mucinous colorectal carcinoma showing significantly rapid progression within four months of immunosuppressant therapy for Henoch–Schönlein purpura. The report is straightforward and provides us a relatively sufficient discussion. The following comments are offered.

Response: We are grateful to this reviewer for recognizing the significance of our work and suggestive comments.

1. The diagnosis is based on various dimensions including colonoscopy examination and histological analysis, both are the most convinced criteria, but a concern comes to the following events after treatment that we could monitor tumor progression directly by performing a colonoscopy in addition to the outcomes of the laboratory and imaging examinations, according to which we could offer a more suitable cure plan and prevent tumor recurrence.

Response: We agree with the reviewer and added the description in Case presentation and Discussion (page 10, line 4 from the top; page 11, line 10 from the top).

2. The report provides experiences and instructions while addressing patients with rapid tumor progression after immunosuppressant therapy, and we should discuss more about the complicated relationship between long-term use of immunosuppressants, glucocorticoid therapy and colorectal cancer, besides that, the methods to obtain favorable treatment and the effects of primary disease should be investigated more.

Response: We agree with the reviewer. To further expand the discussion, we have added the description and references in Discussion and modified the Table 3 (page 10, line 4 from the top; page 11, line 10 from the top; page 12, line 8 from the bottom; new references #31, #32; revised Table 3).

3. Several references should be updated and it would be more obviously while presenting standard values in tables.

Response: We agree with the reviewer and added the references (new references #17, #18, #31, #32;

revised Table 3) and tables have been updated with the standard values. Thank you again for your thorough review of our manuscript and the insightful suggestions.

Thank you again for your time and effort in reviewing our paper.

Sincerely yours,

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