WJCC Manuscript 85733 Author's responses to reviewers and editorial office

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Manuscript Number: 85733

Manuscript Type: CASE REPORT

Manuscript Title: Synchronous adenocarcinoma and mantle cell lymphoma of the colorectum: A case report

Authors: Kim-Van Vu, Nguyen-Van Trong, Nguyen-Thi Khuyen, Do Huyen Nga, Hoang Anh, Nguyen Tien Trung, Pham Trung Thong and Nguyen Minh Duc

Dear Jin-Lei Wang and editorial office:

Please find attached revised version of our manuscript (No. 85733), entitled "Synchronous adenocarcinoma and mantle cell lymphoma of the colorectum: A case report", which we resubmit again for publication as a case report in *World Journal of Clinical Cases*.

We thank you and the reviewers for your insightful comments and patience to help us improving the quality of our work. Accordingly, we have carefully checked and revised this manuscript again, and added some discussion and references. And our point-by-point responses to each of the reviewers' comments are presented below.

We hope that our manuscript is now acceptable for publication in the journal. On behalf of the co-authors, I am looking forward to your favorable decision. Thank you very much for your kind consideration.

Sincerely,

Trong Van Nguyen

Corresponding Authors:

Trong Van Nguyen M.D.,

Department of Oncology, Hanoi Medical University, 1 Ton That Tung Trung Tu Ward Dong Da District Ha Noi City 100000, Vietnam

Email: vantrong.hmu@gmail.com

Responses to Reviewers

Responses to Reviewer #1:

The revisions made to the manuscript according to the suggestions of Reviewer #1 are written in green ink.

Specific comments:

1. It is great to defense on your work with a scientific way. However, I see that some notes you try to defense but in a wrong way (for example, the introduction should be rewritten into 2 paragraphs according to CARE Checklist 2016). Please take care of these.

Response:

Thank you for your helpful advice. According to the CARE Checklist 2016, the introduction consists of 1 to 2 paragraphs introducing the current standard and the general contribution of this case. We have revised it into two paragraphs as per your suggestion.

2. The authors are missing some of the raising points such as the writing the full-term of the abbreviations (PET/CT) in the abstract.

Response:

Thank you for your helpful comment. We have added it to the abstract section.

3. I'd like to draw your attention to the following: Yes, I found a file titled [85733-Answering-Reviewers-revision.docx] that answers the reviewers' directives for the research team in the paper, but the other file titled [85733_Auto_Edited.docx] doesn't explain what was done. I hope the author(s) would highlight the paper's revisions in "yellow color" or "add comments" on the Word file [82948_Auto_Edited.docx] to make follow-up easier to follow up on actually added edits. I hope that the authors should take these issues seriously in the second revision round. Warm greeting.

Response:

Thank you very much for your comment. There may have been some mistake in the file submission process, we have sent the files: Response to the reviewers, manuscript with comments and marked revisions, and final manuscript with removed text highlighting and font color. In this final submission, we will pay attention to this issue. Thank you.

Responses to Reviewer #2:

Specific comments:

I think the manuscript has already been properly revised accordingly. I think the manu will be accepted in wjcc.

Response:

Thank you very much for your encouragement. We have tried very hard to have a complete manuscript, and hope that it will be accepted and published in the journal.

Responses to Reviewer #3:

The revisions made to the manuscript according to the suggestions of Reviewer #1 are written in red ink.

Specific comments:

1. Please add a new table summarizing the characteristics of the cases of colorectal cancer with MCL that have been reported to date in Pubmed

Response:

Thank you for your insightful and helpful advice. In the second paragraph of the discussion section, we have added a table summarizing the characteristics of cases of colorectal cancer with MCL that have been previously reported in Pubmed.

2. Please add the data on tumor markers (CEA, CA19-9, s-IL2-R) in the test results. This is important as it may be a predictor of future recurrence.

Response:

Thanks for your suggestion. However, this patient did not have markers performed before treatment. It's unfortunate that this was overlooked.

3. Did you examine a small bowel endoscopy or small bowel contrast scan? Please add endoscopic images or contrast x-p pictures

Response:

Thank you for your comment. The patient had a previous colonoscopy, but the scope only examined from the cecum colon back and did not survey the terminal ileum. I have provided a MRI image (Figure 1.C), in which an abnormal mass in the right iliac fossa is shown, thought to be an ileal mass.

4. The main lesion of the ileal MCL is a large tumor (4 x 6 cm), why was it not detected preoperatively? please add to your discussion a reflection on the need for s-IL2-R, small bowel endoscopy and small bowel contrast studies. Preoperative screenings are important because of the recent increase of the number of gastrointestinal malignant lymphomas in Asia.'

Response:

Thank you for your comment. The patient presented with cyclical abdominal pain, a characteristic manifestation of Koenig's syndrome, indicative an incomplete small bowel obstruction. The MRI showed a 6cm mass in the ileum. However, these findings were not

enough to confirm a definitive diagnosis. Therefore, surgery was performed to treat the rectal cancer and concurrently diagnose the small bowel mass.

5. You should mention "multiple lymphomatous polyposis (MLP)", which refers to the multiple small MCL polyps (2-5 mm) around colorectal cancer and in the small intestine. MLP is a disease of the small intestine, the colon, and the large intestine. Please add the extent of MCL involvement in small intestine and colon.

Response:

Thanks for your helpful comments. According to your advice, we have revised the content.

6. The staging of gastrointestinal malignant lymphoma is the Lugano classification. Please revise it.

Response:

Thanks for your helpful comments. According to your advice, we have revised the content.

7. Are there any causative factor or factors behind the coexistence of colorectal cancer and MCL? Please add your own thoughts on this important question

Response:

Thank you for your comment. In some previous reports, lymphoma appeared one to three years after treatment for adenocarcinoma, but there was no significant association. The coexistence of these tumors may be fortuitous rather than showing a specific association. I have made this conclusion in the discussion section.

8. Translocation results can be shown by FISH, please add figures if possible

Response:

Thank you for your suggestion. However, this patient did not undergo FISH to evaluate translocation. It’s unfortunate that this was overlooked

9. MCL has a good response to treatment but is prone to recurrence and has a poor prognosis. MCL can be relapsed in the near future in the reported case, I think, because MLP lesions except main tumors has not been resected by surgion, and remained now. Further, you did not confirm whether MLP were cured and disappered with chemotherapy yet. If MCL relapse in both small and large intestine in the near future, what is the best treatment strategies for 2nd line therapy? Monoclonal antibody, bispecific antibody, anti-PD-L! antibody, Lenaridomide, BTKi, BCL2 inhibitor, epigenetic regulator, PI3K-inhibitor, PI3K/mTOR inhibitor, CAR-T cell therapy have recently shown high efficacy in malignant lymphomas, especially nodal

lymphomas. Please briefly mention these future treatment options to your discussion section at the last paragraph.

Response:

Thank you for your helpful comments. MCL has a good response to treatment, but it is prone to recurrence and has a poor prognosis. In our case, after undergoing an induction treatment phase with the RDHAP/RCHOP regimen, the patient underwent a PET/CT scan for re-evaluation. The results showed a complete response with no hypermetabolic lesions present throughout the body, as mentioned in our paper. We appreciate your suggestion regarding second-line treatment options for the patient. As per your suggestion, we have included future treatment options at the end of the discussion section.

Responses to Reviewer #4:

The revisions made to the manuscript according to the suggestions of Reviewer #2 are written and highlighted in yellow

Specific comments:

1. The title should be changed owing to that MCL was found in the ileum. Please take care of this point throughout the whole manuscript to remove the confusion to the readers.

Response:

Thank you for your suggestion. In our case, the MCL lesion appeared as multiple lymphomatous polyposis in both the resected colon and ileum segments, not just in the ileum. Figure 3A shows that the colon segment has two different lesions, both adenocarcinoma tumors (white arrow) and lymphoma tumors (black arrow). Thank you for your suggestion regarding the issue of changing the title of the paper. After reviewing, we have decided that the title of this paper is: “Synchronous rectal adenocarcinoma and intestinal mantle cell lymphoma: A case report”.

2. The running title is long, therefore, I suggest the following "synchronous colorectal adenocarcinoma and ileal MCL”.

Response:

Thank you for your comment. We have taken your suggestion into consideration and have decided to use the title proposed in the first comment. As per your helpful feedback, the running title would be "Synchronous rectal adenocarcinoma and intestinal MCL".

3. Abstract a. Page 2, line 9: It is better to replace the word "man" with "gentleman". Please do the same throughout the whole manuscript. b. Page 2, line 17: Please write these abbreviations "PET/CT". c. The conclusion should be rewritten depending on your case summary. Please remove this sentence " Our patient presented with abdominal pain due to a

large polyp in the small intestine, confirmed as MCL by histology." Because it is related to the case summary.

Response:

Thank you for your helpful suggestions. a. We usually use the word “man” in our papers, so we may keep this view. b. We do not understand your question, the phrase was already abbreviated as “PET/CT” previously. Please let us know if there is anything else that needs to be edited. c. Thank you for your helpful suggestions, we have revised the paper according to your suggestion.

4. Please add the other 2 keywords to be 6 in number as per journal style. Besides each word should be started with a capital letter

Response:

Thank you for the helpful comment. We have added 2 keywords according to your suggestion.

5. The core Tip is short (47 words). Please rewrite it to be more informative.

Response:

Thank you for your comment. We have rewritten it to incorporate your suggestions.

6. Introduction a. You should split this section into two paragraphs; the first paragraph for the descriptive and the other for the challenging part. b. The challenging part is deficient. c. This sentence " To our knowledge, only a few cases have previously been reported in the literature." Needs a reference. d. This case report is presented in line with the SCARE Criteria[4]. This differs from what was written in the "CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016)". Please unify them. e. There is no objective of the study at the end of this section

Response:

Thank you for your helpful advices. Regarding dividing the introduction into smaller sections, our introduction aims to provide readers with a general understanding of MCL and its rarity when it occurs simultaneously with adenocarcinoma. More detailed content is specifically described in the discussion section. Thank you for your suggestion on the citation, we have corrected it in the latest version. We have agreed that this article is written according to the CARE Checklist (2016). We have added objectives to the introduction section.

7. Case presentation a. Chief complaints: please mention just the main complaints. b. History of present illness: more detail is needed. You can use what you wrote in the chief complaints. c. 154 g/L. I think you mean 15.4 g/L. d. Please write the full term of each abbreviation. e. Figure 1C is not mentioned in the text. f. Figures 2 and 3 need the main titles in the figures'

legends. g. Please remove the writing from Figure 2B. h. Our multi-disciplinary tumor boards → Our multi-disciplinary tumor board. i. Follow-up: I think it is deficient, therefore, it needs more detail.

Response:

a. Chief complaints: The patient was admitted to the hospital due to their main complaints of abdominal pain and hematochezia for the past month, which we have described in this section. b. History of present illness: Thank you for your suggestion, we have provided a more detailed description of the patient's illness history in the article. c. The patient's hemoglobin level was 154 g/L, we think you meant 15.4 g/dL. d. We have made the correction according to your suggestion. e. We have mentioned Figure 1C in the Imaging examinations section. f. We have added main titles to Figures 2 and 3 and removed the writing from Figure 2B. Thank you, we have corrected the spelling and added details about follow-up.

8. Discussion: a. This "Lymphadenopathy occurs in 90% of cases and frequently involves extranodal sites such as bone marrow, the spleen, gastrointestinal tract, Waldeyer's ring, and lungs." needs a reference. b. B symptoms: please explain these. c. Please take care that you already use the abbreviation "MCL" for the full term "mantle cell lymphoma". d. The section does not explore the differences between this case and other previously reported cases. It is better to add a table for this aim.

Response:

Thank you for your helpful comments. a. We have added a citation for the sentence "Lymphadenopathy occurs in 90% of cases and frequently involves extranodal sites such as bone marrow, the spleen, gastrointestinal tract, Waldeyer's ring, and lungs." b. We have explained the B symptoms in the discussion section. c. Thank you, we have reviewed and used the abbreviation "MCL" for "Mantle cell lymphoma" in the article. d. That is a great suggestion, similar to the suggestion from Reviewer #1, we have incorporated it and presented it in the discussion section.

9. References a. Only 4 out of 23 references belong to the five years and no reference belongs to the year 2021-2023. Therefore, updating the references is of utmost importance. This link is useful for this purpose https://pubmed.ncbi.nlm.nih.gov/36509538/. b. The references should follow the journal style.

Response:

Thank you for your comment. There has not been much recent literature on the topic, especially on the synchronous of MCL and adenocarcinoma. Therefore, despite our active search, we were only able to obtain the references we have included. Thank you for your suggestion, we have reviewed the link you provided and added it to our article. The references have been edited according to the journal style.

Responses to Editorial office

Specific comments:

1. Please refer to the attached peer reviewer's second review comments for revision.

Response:

Thank you for your suggestion. We have reviewed and revised the manuscript according to the comments of the reviewers.

2. Please add text editable Table 1 at the end of the article.

Response:

Thank you for your comment. We have moved the editable Table 1 to the end of the article.

3. Regarding the figures: Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. -Figures.ppt" on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes. Also, please add "Copyright © The Author(s) 2023" below the image. Figure file names should identify the figure and panel. e.g. "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ..."

Response:

Thank you for your helpful and insightful comment. We have revised the file 85733-Figures.ppt according to your suggestions.

Thank you very much for your comments. This article is the effort of the entire author team over a long period of time. We would like to thank Jin-Lei Wang and the editorial office, as well as the reviewers for their insightful comments and patience in helping us improve the quality of our work. We hope that our manuscript is now acceptable for publication in the journal.