

## Response to Reviewers

[Cover letter]

Dear Mr. Peter Schemmer and Editorial Board Members,

We are grateful for the time and insightful comments you and the reviewers provided on our manuscript. Your feedback has been invaluable in improving our work. We have carefully considered all comments and diligently addressed each point in the revised version. We believe these changes significantly enhance the quality and clarity of our paper and bring it closer to your high standards.

We have provided a point-by-point response below, with modifications highlighted in red in the revised manuscript. Should you have any further constructive feedback, we welcome it with open arms.

Thank you again for your consideration.

Sincerely,

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Response to Reviewer 1:

1. **[Comment]** low-grade mucinous neoplasm is common in appendix and is not a rare tumor. There is nothing particularly special about the present case. The histological and immunohistochemical results of present case were also typical.

→**Response:** While our case initially seemed "rare," we updated the description to "not rare, but still uncommon tumors" due to its actual frequency (line 35). Although the immunohistochemical results in our case aligned with typical findings and did not offer any novel insights, we opted to present them in their entirety to contribute to the development of a comprehensive database (line 358).

2. **[Comment]** The patient had transverse colon adenocarcinoma accompanied with low-grade appendiceal mucinous neoplasm. What was the subtype of the colon adenocarcinoma? Did it contain mucinous adenocarcinoma components? Before diagnosing LAMN, it is necessary to exclude the involvement of colon mucinous adenocarcinoma in the appendix. The authors did not describe and discuss the above question.

→**Response:** The final pathological diagnosis identified the adenocarcinoma subtype as classical (line 156). No components of mucinous adenocarcinoma were observed, and intact expression of MMR proteins was confirmed, indicating a low probability of microsatellite instability-high (MSI-H) status (line 144). Given the significant distance between the adenocarcinoma and the LAMN, and the immunohistochemical evidence indicating distinct tumor origins, we believe the patient is suffering from the rare occurrence of a double tumor.

3. **[Comment]** The immunohistochemical examination is important for pathological diagnosis of LAMN, but immunohistochemistry is not absolutely specific, and we cannot rely entirely on immunohistochemistry. Clinical and imaging manifestations are more important. The author did not specify whether there is a space occupying lesion in the ovaries. If no lesions are found in the ovaries, there is no need to overly consider the ovarian origin.

→**Response:** We have incorporated the reviewer's valuable suggestion and included the requested statement in our case report (line 369).

However, we believe that the innovative applications for diagnosing AMNs are rapidly evolving, and we provided this information not only for the benefit of our patient's diagnosis but also to contribute to the

development of a comprehensive database for future studies (line 343). Regarding the reviewer's comment about the ovarian lesion, we would like to clarify that the patient in our case is a 74-year-old male who does not have ovaries. Nevertheless, we appreciate the reviewer's advice and have included a discussion focusing on potential implications for female patients (line 346).

## Response to Reviewer 2:

**[General Comment]** I read with interest the manuscript by Hao-Cheng Chang and colleagues "Appendiceal mucinous neoplasm: from incidental discovery to in-depth understanding – A case report" submitted to World Journal of Gastroenterology. The authors described a rare case of metachronous cancer - an appendiceal mucinous tumor and transverse colon adenocarcinoma, and provided interesting discussion. This manuscript may bring new to the field and may be interesting to the readers.

**Response:** Thank you very much.

1. **[Comment]** However the "in-depth understanding" stated in the title is far from being reached yet. This may require correction of the title. Moreover, according to what is described, may it be better to reflect the literature review in the title (a case report and literature review)? This could allow higher interest from the readership.

→**Response:** We really appreciate the reviewer's opinion and change our title into "Appendiceal mucinous neoplasm: a Case Report and Literature Review". (Line 4)

2. **[Comment]** Although the concurrent diagnosis (transverse colon adenocarcinoma) is not in the main focus of the case, it would be nice to reflect full histological description.

→**Response:** We add the full histological description of our transverse colon adenocarcinoma and showing the subtype of our adenocarcinoma is classical. (Line 138 )

3. **[Comment]** Introduction: I would suggest that the authors add more detailed information on why this case may be interesting.

→**Response:** We add some descriptions to present a compelling case report highlighting a common misdiagnosis, emphasizing the importance of considering double cancer, and providing valuable diagnostic insights. This report also raises awareness of a rare condition and contributes significantly to medical knowledge, captivating the attention of our readers. (Line 81)

4. **[Comment]** I'd like to advert the attention of the authors that the type of the paper is a description of a case, then, "This study examines..." is not correct.

→**Response:** We have incorporated the reviewer's valuable suggestion and change the description to "This case report describes..." (Line 81)

5. **[Comment]** Please, describe more details on the laboratory abnormalities

with certain values obtained.

→**Response:** Thank you for your feedback. We will incorporate additional details regarding the patient's laboratory results within the 'Laboratory examinations' section."

6. **[Comment]**Figures: Please, mark specific points of interest on the images.

→**Response:** We will remark our images.

7. **[Comment]**Please, disclose all the abbreviations at the footnotes (some of them are not clear).

→**Response:** We will rewrite the abbreviations carefully.

8. **[Comment]**Fig. 5 - please, check, whether correct verb is used in the sentence starting with "Immunohistochemically..." (plural or singular). I hope that my comments help the authors make their manuscript even better.

→**Response:** We have submitted our case report to a professional English editing service for further refinement and polishing to ensure the highest level of accuracy and readability.