

May 2023

Dear Professors Monjur Ahmed and Florin Burada,

We appreciate the Editor and the Reviewers for the opportunity to revise our work entitled **“MUTYH-associated polyposis: is it time to change upper gastrointestinal surveillance? A single-center case series and a literature overview”** (Manuscript NO.: 83802, Case Report) for consideration for publication in *World Journal of Gastrointestinal Oncology*.

We believe that the helpful comments of the Reviewers have contributed in making our paper clearer and stronger. In addition, you can find below an exhaustive point-by-point reply to all the critical aspects underlined by the reviewers' comments.

We remain fully available for any further and we thank you in advance for the kind availability.

Our best regards,

Dr Lupe Sanchez-Mete  
On behalf of all authors.

**Reviewer #1:**

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Thank you for inviting me to review this article. The authors identified 2 (6%) cases of small-bowel adenocarcinoma with no prior history of duodenal polyps in a single-center MAP follow-up. Further combined with previous literature, suggested that a more perfect evaluation system and monitoring mode may be needed for small-bowel cancer in MAP patients, but a larger study is needed to verify it. A total of 38 MAP patients were followed up in the single center, each of whom had a clear gene variant.

**Authors' response:**

*Thank you very much for your interest and appreciation in our manuscript.*

I would like to know if there is a genotypic-phenotypic correlation in this series of patients.

**Authors' response:**

*Thank you for this remark. We did not perform a genotype-phenotype correlation, because it was not the aim of the study. However, we observed that the most reported pathogenic variant, c.452A>G;p.Tyr151Cys (NM\_001048174.2), known to be associated with a more aggressive disease, was detected in both patients with small bowel cancer. This observation has been inserted in Table 2 and in the revised manuscript (see line 155-157). Proper reference was added.*

**Reviewer #2:**

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Generally, this manuscript, reporting on two patients with small bowel adenocarcinoma in MUTYH-associated Polyposis (without previous duodenal polyposis) fits the scope of the journal. There are rare reports regarding this situation. The manuscript is written

in an elegant manner, easily to be followed. The scientific content in Introduction is based on the recent literature and emphasizes correctly the importance of the topic. Discussion paragraph is nicely approached.

**Authors' response:**

*Many thanks for your interest in our study and for your kind words.*

I have listed some comments for consideration, below:

1. Please insert the strength and limitations of your research.

**Authors' response:**

*Thank you for this suggestion. Strength and limitations of the study have been added in the revised manuscript (see lines 191-195).*

2. Please insert (in Discussion) the literature review in a table, with all necessary data.

**Authors' response:**

*Thank you for this suggestion. Table 3 has been added in the revised manuscript.*

3. Both endoscopic images should have better resolution and more details in the Figure legend.

**Authors' response:**

*Thank you for this suggestion. In the revised manuscript we provided endoscopic images with better resolution (see figure 1, A1 and A2 panels).*

4. Please provide also the histopathological images for both cancers with details and a generous figure legend.

**Authors' response:**

*Thank you for this suggestion. Histopathological images with details and figure legends were provided and added to the manuscript (see figure 1, B and C panels).*

5. Table 1: for NCCN, the Figure legend mentions reference [25]. However, in the Table, for NCCN, it is mentioned "NCCN (v.1.2022)", which has reference [7]. Please revise.

**Authors' response:**

*Thank you for this report. We corrected this typo in the revised manuscript.*

6. Table 2 should contain more data.

**Authors' response:**

*Thank you for this suggestion. Additional data were properly added to Table 2*

7. Please revise the format of the manuscript, including references, in order to respect the requirements of the journal.

**Authors' response:**

*Thank you, this has been done.*

8. Reference 7 – please write the web address for MUTYH-associated polyposis, not the general address of the site.

**Authors' response:**

*Web address for reference 7 was added:*

*NCCN Guidelines version 2.2022. [https://www.nccn.org/guidelines/category\\_1](https://www.nccn.org/guidelines/category_1). Accessed on 10/10/2022*

9. References 8 and 9 are identical. Please remove one of them and adjust in the whole text.

**Authors' response:**

*The duplicate was removed and the references renumbered*

10. Please insert Authors' ORCID Numbers.

**Authors' response:**

*Please find below the Authors' ORCID numbers:*

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