Journal Editorial Office

Dear Editor,

We would like to resubmit the revised manuscript entitled “MutL homolog 1 germline mutation c.(453+1_454-1)_(545+1_546-1)del identified in lynch syndrome: A case report” for consideration by the ***World Journal of Clinical Cases***.

We would like to thank the reviewers for thoroughly reviewing our manuscript and making many thoughtful comments. We were very pleased to see that the reviewers recognized the novelty and potential significance of our work. We have revised the manuscript to address the reviewers’ comments. The manuscript has been edited by a professional language company. Thank you for your consideration of our manuscript.

Yours sincerely,

Yan Jia, MD, Chief Doctor, Professor,
Department of Gynecology, The Second Hospital of Jilin University, 218 Ziqiang Road, Changchun, Jilin Province, China;
Phone: +86 13844884509;
Fax: 86043188796747;
E-mail addresses: jiayan@jlu.edu.cn;

**Comment**:

Reviewer #1:

Comments

1. According to the authors, deletion of MLH1 exon 6 (c.(453+1 454-1) (545+1 546-1)del) infrequently caused LS in Chinese. However, the Discussion made no mention of previously reported cases with the same MLH1 genetic variant. The authors should compare the clinicopathological characteristics of this case to those of previously reported ones.

**Response**: Thank you for your very constructive comments. We have reviewed several articles, supplemented the data with MLH1 exon deletion in the discussion section, and compared the clinicopathological characteristics of this case to those of previously reported ones.

2. The final pathological diagnosis should be made using the most recent WHO classification. Due to the fact that there are several histological subtypes of endometrial cancer, the term "endometrial cancer" alone is insufficient.

**Response**: Thank you for your very constructive comments. We have modified the final pathological diagnosis according to your opinion.

3. The results of the IHC staining appear to be somewhat peculiar. "Immunohistochemical (IHC) staining results of pathological findings showed MLH1 (-), PMS2 (-), MSH6 (partial lesions +), and MSH2 (partial lesions weak +)," the authors wrote. If the tumor had MLH1 gene mutations, both MLH1 and PMS2 should be lost in the majority of such cases. However, both MSH6 and MSH2 expression appeared to be abnormal. The authors should provide a rationale for this occurrence. Additionally, readers should be able to recognize intact MMR protein expression in internal control cells via microphotographs of IHC. The present form of microphotographs seems to be inappropriate.

**Response:** Thank you for your very constructive comments. Our language expression in the first submitted manuscript was not accurate enough. In fact, our IHC results suggest *MLH1* (-), *PMS2* (-), *MSH2* (+), *MSH6* (+), and the IHC results are similar to a previous study[1]. Now, we have revised the manuscript according to your suggestion. Besides, we have modified

Figure 2 so that the reader can identify the intact MMR protein expression in internal control cells.

4. Some typographical errors are present.

**Response**: Thank you for your very constructive comments. A professional language company has edited the manuscript.

Reviewer #2:

1. Please, de-crypt all used abbreviations upon the first use (including genes) and add the abbreviation list.

**Response**: Thank you for your very constructive comments. We have revised the manuscript according to your opinion.

2. Please, explain briefly the function of the MLH1 gene. Where described mutation is located? How does it affect proteins' function?

**Response**: Thank you for your very constructive comments. In the first paragraph of the introduction, we added the function of the *MLH1* gene, the mutation site, and the effect of *MLH1* gene deletion on the protein.

3. Please, consider the title correction. The mutation induces or causes LS?

**Response**: Thank you for your very constructive comments. We have revised the title according to your opinion.

4. Please, provide a more detailed explanation of used gene detection steps (methods, bioinformatic tools, equipment).

**Response**: Thank you for your very constructive comments. We have revised the manuscript according to your opinion.

## References

1 Jia S, Zhang M, Sun Y, Yan H, Zhao F, Li Z, Ji J. A Chinese family affected by lynch syndrome caused by MLH1 mutation. *BMC Med Genet* 2018; **19**(1): 106 [PMID: 29929473 PMCID: PMC6014015 DOI: 10.1186/s12881-018-0605-x]