

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Multiple Synchronous Anorectal Melanoma with Different Color: A Case Report and Review of Literature" (ID: 45706). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewers' comments are as flowing:

Responds to the editor' s comments:

1. Response to comment 1, the figures have been uploaded separately as tiff files, 300 dpi.
2. Response to comment 2, running title has been added.
3. Response to comment 3, author contribution has been added.
4. Response to comment 4, statement of Conflict-of-interest and CARE Checklist (2016) has been added.
5. Response to comment 5, the author' s office number has been added in substitution for the former mobile phone number.

6. Response to comment 6, section of case presentation has been revised according to the required style, following seven subtitles.

7. Response to comment 7, reference has been edited according to requirement.

Responds to the reviewer' s comments:

Reviewer #1:

1. Response to comment: This is not really a review of literature. Modified the title to Multiple Synchronous Anorectal Melanoma with Different Colors: A Case Report

Response: The title has been modified according to reviewer' s advice.

2. Response to comment: "AM is defined as an extremely..." : AM is rare however it is not DEFINED as an extremely rare malignant. Rare is not a definition!

Response: It is really true as Reviewer suggested that rare is not a definition. The 'defined as' has been deleted.

3. Response to comment: Case presentation: - admitted to our institution: correct to "admitted in our institution"

Response:

We have made correction according to the Reviewer' s comment.

4. Response to comment: She had previously received a colonoscopy:
correct to "she previously underwent a colonoscopy"

Response:

We have made correction according to the Reviewer' s comment.

5. Response to comment: Digital rectal exam should be performed before the colonoscopy and not after as describe in the case presentation. Please clarify.

Response: Actually we performed digital rectal exam before we performed colonoscopy after admission. We described result of colonoscopy before result of digital rectal exam because the patient had underwent colonoscopy in community hospital suggesting diagnosis of anorectal melamona.

6. Response to comment: You need to give more details about the lesion in the case presentation, such as size, characteristics...

Response: Detail including size and characteristics of lesions has been added into case presentation.

7. Response to comment: Figure 2: In the pictures include just A and B as label and not 2A and 2B. - Figure 1 and 2: the label for figure 2 is in the place of the label of figure 1. Please correct. - Figure labels: both of the masses invaded: please correct to both masses...

Response: We have made correction according to the Reviewer' s comment.

8. Response to comment: Include final diagnosis section as a paragraph in the case presentation.

Response: We have made correction according to the Reviewer' s comment.

9. Response to comment: Additionally, included the histopathologic image to improve the quality of your paper.

Response: We have made correction according to the Reviewer' s comment.

10. Response to comment: Include treatment section as a paragraph in the case presentation section.

Response: We have made correction according to the Reviewer' s comment.

11. Response to comment: Figure 3: include arrows to show the two mucosal melanocytic zones.

Response: Arrows has been included in fig 3.

12. Response to comment: "Abdominoperineal resection with negative resection margin was performed eventually." : Sentence needs English revision.

Response: We have made correction according to the Reviewer' s comment. Sentence was revised to 'Abdominoperineal resection was performed eventually. Intraoperative frozen pathological report suggested negative resection margin.'

13. Response to comment: Table 1: include label m=months or write months besides of m.

Response: We have made correction of Table 1 according to the Reviewer' s comment.

14. Response to comment: Include outcome and follow-up section as a paragraph in the case presentation section.

Response: We have made correction according to the Reviewer' s comment.

15. Response to comment: Please ask a native English with experience in medical terms to correct this section: Postoperative recovery was uneventful, so the patient was discharged two weeks after surgery. Upon completion of Nivolumab treatment, the patient had 24 months of disease-free follow-up. However, due to economic burden, the patient stopped Nivolumab for a few months and was diagnosed lung metastasis 3 months ago.

Response: We have made correction according to the Reviewer' s comment.

16. Response to comment: Discussion - Needs to improve. You have to correlate your case with the literature and not just discuss the disease.

Response: Considering the Reviewer' s suggestion, A Paragraph correlating this case has been added into the discussion.

17. Response to comment: The first sentence is the same as introduction. Please remove it.

Response: We have made correction of the first sentence in the discussion according to the Reviewer' s comment.

18. Response to comment: "About 25% of AM appears to be amelanotic, which explains to the poor prognosis of this disease.^{4, 5}

Late and incorrect diagnoses are common due to atypical symptoms and low incidence.¹⁰ Misdiagnosis occurs in more than half of the patients, mistaken for hemorrhoids, polyps or rectal cancer.¹¹ But interestingly, misdiagnosis has no significant negative effect on survival time as reported by Zhang.¹² : Please clarify this contradiction.

Response: We have made correction of logistic problem in this paragraph. What we mean to express is that AM is too malignant that early diagnosis do not bring advantage in survival time.

19. Response to comment: Ballo¹³; mean survival: 27m vs 10m, Das¹⁴ :

This is not a correct way to cite an author. Correct to Ballo et al

Response: We have made correction according to the Reviewer' s comment.

20. Response to comment: Amelanotic melanoma type in AM was reported to have a worse prognosis than melanotic type in some studies.^{3, 6, 7} The reason for this phenomenon remains uncertain, but some authors believe this is either because amelanotic melanoma is more difficult to diagnose, or it is possibly more invasive in nature.¹⁴ : Again there is a contradiction between this sentence and the other sentence above.

Response: We have made logistic correction in this sentence according to the Reviewer' s comment. 'Amelanotic melanoma is more difficult to diagnose, or it is possibly more invasive' are just hypothesis of some researchers without accurate evidence and large cohort of patients.

21. Response to comment: line 112: Aditionally – correct to Additionally

Response: We have made correction according to the Reviewer' s comment.

22. Response to comment: The discussion section is a section to discuss your case and not just the literature. Please try to correlate your case with the literature.

Response: A Paragraph correlating this case has been added into the discussion.

23. Response to comment: Conclusion: - Your conclusion is too long.

This should not a summary of your paper. Try to be more clear.

Response: Conclusion has been correlated according to reviewer' s comments.

24. Response to comment: Conclusion: Consent - "Written informed consent was obtained from the patient and her relatives." : is this traditional in your country? In most countries just a consent from the patient is enough.

Response: It is tradition in our country for gaining written informed consent from the patient and direct relative.

25. Response to comment: References - Most references are before 2013. Just two reference after 2014. Please include recent references. Additionally, this is a case report and 31 references is too much for this manuscript. Include maximum of 10 to 20 references.

Response: References have been revised and updated.

Special thanks to you for your good comments.

Reviewer #2:

1. Response to comment: There is typological error on the 54th line of manuscript (it is written CA-199, it should be CA 19-9).

Response: We have made correction according to the Reviewer's comment.

Special thanks to you for your good comments.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.