April 13, 2019

Dennis A Bloomfield, FACC, FACP, FRACP, FRCP (Hon), MD, MRCP
Sandro Vento, MD
Editors-in-Chief
World Journal of Clinical Cases

Dear Editors:

According to your recommendation, we wish to transfer our revised manuscript titled "**Endoscopic submucosal dissection as excisional biopsy for anorectal malignant melanoma: A case report and review of literature**" to *World Journal of Clinical Cases*. The manuscript number is 46407 and the original title was "**Endoscopic submucosal dissection for anorectal malignant melanoma: A case report and review of literature**."

Thank you very much for considering our manuscript for publication in your journal. We are very pleased to see the favorable comments from the reviewers. We have revised our manuscript according to the reviewers' comments and hope that it is now suitable for publication. Our point-by-point responses to all the reviewers' comments are attached herewith.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,
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To Reviewer 00070509

This is the first case report of ESD for AMM. AMM is very rare and has an extremely poor prognosis. Accurate pathologic diagnosis of endoscopic biopsy for AMM is difficult. AMM have massive submucosal invasion with both lymphatic and venous invasion-like this case, ESD is not a treatment of choice. However, this case report demonstrated that ESD provide a good enough surgical sample for adequate pathological diagnosis of the early stage AMM. So, ESD could be a diagnostic and treatment method for AMM.

Response: We really appreciate your sincere comments and positive feedback. As you have mentioned, we believe that ESD can be one of the diagnostic and treatment methods for AMM.

To Reviewer 03706560

First, I want to congratulate the authors for this interesting case report. The paper is well written and I have made some comments (review mode - attached). I think it will be better to show a case where ESD really treated the lesion. If this manuscripts is published in WJG, some readers who do not read the full-text can think ESD just works as a diagnostic modality and not as a treatment modality. Please try to clarify this in the abstract.

Response: Thank you very much for your pertinent advice. According to your suggestion, we have made the following major changes.

First, in order to clarify that ESD worked as the method for diagnosis in this particular case, we have revised the title of this case report as shown below.
Original title: "Endoscopic submucosal dissection for anorectal malignant melanoma: A case report and review of literature"
Revised title: "Endoscopic submucosal dissection as excisional biopsy for anorectal malignant melanoma: A case report and review of literature"

Second, we have excluded two co-authors who had made comparatively less contribution to the study.

Lastly, we have clarified that ESD could work not only as a diagnostic modality but also as a treatment modality for AMM in the Abstract (page 3, lines 8-9), Core tip (page 4, lines 14-18), Discussion (page 10, line 19-page 11, line 1 and page 11, line 19-page 12, line 1), and Conclusion (page 12, lines 5-9) sections.

To Reviewer 02542415

Comment 1: Anorectal malignant melanoma is a rare disorder with an extremely poor prognosis and there is currently no consensus on the treatment methods for AMM. Therefore, this manuscript is very meaningful because this paper suggests that ESD may be one way of treating early–stage AMM.

Response: Thank you very much for your kind comments. We believe that this case report will help establish the diagnostic and therapeutic strategy for AMM since it describes the efficacy of ESD as an excisional biopsy for AMM.

Comment 2: The lesion with more than 20 mm and the protruding type is known to be higher in SM invasion, would the ESD be the appropriate method for treatment of lesion?

Response: As you mentioned, before ESD, this lesion was expected to have invaded the submucosal layer as it measured more than 20 mm and was protruded. Besides, the findings of endoscopic ultrasonography and narrow-band imaging with magnifying endoscopy also suggested that this lesion invaded the submucosal layer deeply.

In terms of curability, ESD would be inferior to surgical treatments for lesions that invade the submucosal layer deeply. However, considering that this lesion was located in the lower rectum, we believe that ESD would be a better first choice as an excisional biopsy than other surgical procedures such as abdominoperineal resection that would be highly invasive for this particular case. We have included this information in the Further diagnostic work-up subsection (page 7, lines 7-13).

Comment 3: The findings of EUS and NBI with magnifying endoscopy suggested a deep SM invasion rather than a superficial SM invasion. In this situation, it may not be appropriate to choose ESD as a choice of treatment for the lesion.

Response: Please refer to our response above to your comment number 2.

Comment 4: ESD would be unsuitable for method as an excisional Bx because of difficult procedures and high incidence of complications. What about using a large Jumbo forceps Bx instead of ESD for a safe diagnosis?

Response: As you mentioned, ESD is technically one of the most difficult endoscopic procedures, and it is still associated with a high incidence of complications such as perforation. However, it is relatively easier to perform ESD for lower rectal lesions such as in this particular case than for lesions located in other parts of colon, and perforation does not occur as long as the lesion is located under the level of peritoneal reflection. We have mentioned this information in the Discussion section (page 11, lines 20-23).
Besides, we could not reach the accurate diagnosis of AMM regardless of several sufficiently sized initial biopsy specimens, and the pathological findings of the initial biopsy already suggested the high possibility that this lesion was a malignant tumor. Therefore, we decided to perform ESD not only for diagnosis but also for treatment instead of performing biopsy again using large Jumbo forceps. We have mentioned this information in the Further diagnostic work-up subsection (page 7, lines 2-13).

Comment 5: Why did not you once again perform a biopsy when the initial biopsy did not produce an accurate diagnosis?

Response: Please refer to our response above to your comment number 4.

Comment 6: Was there any non-lifting sign meaning SM invasion during ESD?

Response: Fortunately, no non-lifting sign was observed during ESD. We have added this information to the Treatment section (page 8, lines 13-14).