

Cover Letter

Date: Mar 5th, 2021

Dear Editor,

Please find our revised manuscript entitled “Myocarditis Related to Immune Checkpoint Inhibitors Treatment: Two Cases reports and literature review” (Manuscript ID: APM-20-2620), which we would like to submit for further review to *Annals of palliative medicine*.

Thank you very much for your attention and kindly response to our research and the corresponding manuscript. We do thank editors and reviewers for their work, suggestions and comments on our manuscript very much. After learning the associate editor’s and reviewers’ comments, we have checked the raised questions carefully. We have responded to the comments of reviewers one by one and revised the manuscript carefully. And our replies to the comments one by one are attached in the page 2 to page 4 of this cover letter. We confirm this manuscript has not been submitted to any other journal for publication. We believe that the manuscript meets the high standard of *APM* and are looking forward to your positive response. Thank you very much for your attention and consideration.

Kind Regards. Best wishes!

All of authors of this manuscript

Manuscript number: APM-20-2620

**Manuscript title: “Myocarditis Related to Immune Checkpoint Inhibitors
Treatment: Two Cases reports and literature review”**

Authors: Yukai Chen et al.

First of all, we would like to thank all reviewers and editors for the excellent comments that are important to improve this paper. The comments are reviewed carefully and a response to each individual comment is provided in the following. We hope this paper will be accepted after this revision.

Reviewer Comments:

Comment 1

Provide references for following

- line 39 - " ICIs associated myocarditis accounting for less than 1% of immune-related adverse events, but was correlated with a mortality of over 40%. "
- line 127 – ‘It is reported that ICIs combination therapy is associated with an almost two-fold higher incidence and mortality of myocarditis.’
- Line 150- where authors mentioned mode and dose of steroids.

Reply 1

These three references were revised and cited at the corresponding places.

Changes in the text

- Line 39 – the sentence is now at line 34-36. We revised it and added reference.
- Line 127 – the sentence is now at line 142-144. We revised it and added reference.
- Line 150- the sentences are now at line 176-183. We revised it and added reference.

Comment 2

Provide normal values in bracket wherever labs are reported. For instance, line 59-60, line 83-84, line 94-96

Reply 2

We have added it as you suggested.

Changes in the text

We added some data line 54-64, line 91-95, line 106-110.

Comment 3

Providing images of PET-MRI would make the case report more educational and interesting to readers.

Reply 3

This is a good point, thank you! Images would make the case report more educational and interesting.

Changes in the text

We have added this part to the Figure 1.

Comment 4

For case 1, please provide final outcome. Did the patient follow up?

Reply 4

The patient got severe abdominal infection but was not affordable to high-grade antibiotics. He gave up all treatment and spent his last moment at home.

Changes in the text

We have added this part to the line 79-80.

Comment 5

Authors mentioned plasmapheresis and intravenous immunoglobulin should be considered. I would recommend providing literature data to support these recommendations.

Reply 5

Thank you for your kind suggestions. The use of plasmapheresis and intravenous immunoglobulin is indeed controversial. We have consulted some literature data and made corresponding modifications.

Changes in the text

We have modified our text as advised in line 189-193.

Editorial Comments:

Comment 1

The article already followed a Checklist for reporting standards. Please place “Y” in the “Submission Checklist”.

Reply 1

Thank you for your suggestion.

Changes in the text

A filled "Submission Checklist" has been submitted to the editorial department in the revised edition.

Comment 2

“Data Sharing Statement” is not required for this paper.

Reply 2

Thank you for your suggestion. We have deleted this part.

Changes in the text

We have deleted this part.

Comment 3

Conflict of Interest (COI) Form must be provided, as suggested by ICMJE: (<http://www.icmje.org/conflicts-of-interest/>). Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. COI form download link:

https://cdn.amegroups.com/static/public/coi_disclosure.docx.

Reply 3

Thank you for your suggestion. We have added this part as an attachment.

Changes in the text

We have added this part an additional file.

Comment 4

Please indicate if any of the authors serves as a current Editorial Team member (such as Editors-in-Chief, Editorial Board Member, Section Editor) for this journal.

Reply 4

Thank you for your reminder. No authors serves as a current Editorial Team member for this journal.

Comment 5

Please confirm that all figures/tables/videos in this manuscript are original; if not, permission is needed from the copyright holder for the reproduction.

Reply 5

We make sure all figures/tables/videos in this manuscript are original.

Comment 6

We are using the "Submission Checklist for Authors" to double-check your manuscript, place "Y" on blank space if you confirm your manuscript has followed the requirement. Place "N/A" if not applicable. If further explanation is needed on a certain item, you can copy the Item and write explanations down below. A filled "Submission Checklist for Authors" should be submitted to the editorial office, along with other required documents.

Reply 6

A filled "Submission Checklist for Authors" has been submitted to the editorial department an additional file.