

Dear Editor,

Thank you for your kind letter of “Macrophage activation syndrome as a complication of dermatomyositis: a case report” on April 1, 2020. We revised the manuscript in accordance with the reviewers' comments, and carefully proof-read the manuscript to minimize typographical, grammatical, and bibliographical errors.

Here below is our description on revision according to the reviewers' comments.

Part A (Reviewer 1)

1. The reviewer's comment: Some epidemiological specifications about both DM and MAS should be provided in the introduction

The authors' Answer: We have supplemented epidemiological specifications about both DM and MAS in the introduction.

2. The review's comment: Therefore, I would recommend the authors to organize the case presentation in two sections: pre-MAS (chief complaints, initial diagnostic work-up) and MAS episode (including the therapy and follow-up) description, which will be consistent with Table 1. This way the authors can avoid confusion with the temporal expressions used in the case description.

The authors' Answer: Actually, I agree with this suggestion. Because at the beginning I organized my article like this. I have modified the case presentation in two sections: pre-MAS (chief complaints, initial diagnostic work-up) and MAS episode (including the therapy and follow-up) description.

3. The review's comment: Table 1: I would suggest including also the plasmatic sodium and cholesterol. In particular, the plasmatic sodium (and hyponatremia) is another important parameter in systemic inflammatory syndromes. It's important to clarify the time elapsed from these two time points. Moreover, once the authors

provide information about the natremia, also this point could be addressed in the discussion, considering the correlation between hyponatremia and plasma C-reactive protein values.

The authors' Answer: I have added plasmatic sodium and cholesterol in Table 1. The cholesterol level was extremely increased from 3.00 mmol/L to 8.48 mmol/L. Though hyponatremia is a common clinical manifestation of MAS, the plasmatic sodium before MAS was 137(mmol/L) and in MAS happened was 143(mmol/L) in our patient. There was no significant difference in two sections in our patient. I have added related comments in the 3rd and 5th paragraph in the discussion section.

4. The review's comment: This case confirms that, as well as in JDM, MAS in DM patients seems to arise often at the onset of the rheumatic diseases and even before a clear diagnosis, which makes its diagnosis quite challenging. The short-term changes of hemoglobin, platelet, fibrinogen, ESR and PCR are a very important aspect to be emphasized, in order to timely diagnose and act this life-threatening complication, as discussed by some authors (in order to discuss this point, refer to: Autoimmun Rev. 2014 Nov;13(11):1142-8. doi: 10.1016/j.autrev.2014.05.009. Epub 2014 May 29. Review).

The authors' Answer: I agree with this suggestion. I have added relevant discussion on the diagnosis of DM and MAS, and emphasize the short-term changes of laboratory parameters in the 4th paragraph of the discussion section.

5. The review's comment: Indeed, the sentence “However, when MAS occurred in our patient, the above parameters were nearly normal (Table 1)” is not unusual in the MAS setting, but should appropriately valorized, according to the comments and reference above

The authors' Answer: I have deleted this sentence, rewritten the entire paragraph at the same time, and added some related literature discussions to prove that the trigger of MAS in our patients was the onset and flare of dermatomyositis. MAS may have many triggers such as active infection (EB virus, for example: Autoimmun Rev. 2014 Nov; 13(11):1142-8. doi: 10.1016/j.autrev.2014.05.009. Epub 2014 May 29. Review), disease flare, and tumor. The MAS in our patient was associated with the progressive deterioration of dermatomyositis instead of active infection. I think the trigger is important because it may explain why MAS occurs.

6. The review's comment: Conclusion: it's better to emphasize that, even though rare, MAS can complicate DM. The sentence "High serum ferritin levels may be useful for predicting the risk of macrophage activation syndrome in patients with dermatomyositis" should be removed, because it is not an aspect of novelty. Actually, the authors should stress the timing of MAS at the DM onset and the value of the short-term laboratory changes, as discussed above.

The authors' Answer: I agree and have modified it.

Part B (Reviewer 2)

1. The reviewer's comment: I think this case is a rare case of dermatomyositis complicated by macrophage activation syndrome (MAS). The patient had typical symptoms and signs of dermatomyositis and MAS. This case is reportable.

The authors' Answer: I have modified it.

Many grammatical or typographical errors have been revised.

All the lines and pages indicated above are in the revised manuscript.

Thank you and all the reviewers for the kind advice.

Sincerely yours,

Ding-xian Zhu