

Dear prof. Wang and dear reviewers

Re: Manuscript ID: 71088 and Title: Toxic epidermal necrolysis induced by tocolytics in pregnancy: A case report.

Thank you for your letter and the reviewers' comments concerning our manuscript entitled "Toxic epidermal necrolysis induced by tocolytics in pregnancy: A case report" (ID: 71088). We were pleased to know that our work was rated as potentially acceptable for publication in *World Journal of Clinical Cases*, subject to adequate revision. We really appreciate your efforts in reviewing our manuscript during this unprecedented and challenging time. 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 corrections which we hope meet with approval. Based on the instructions provided in your letter, we uploaded the file of the revised manuscript. The changes to my manuscript and the responses to the reviewer's comments within the document are marked by using the track changes mode. Our responses to the reviewer's comments are presented following.

We would love to thank you for allowing us to resubmit a revised copy of the manuscript and we highly appreciate your time and consideration. We hope that the revised manuscript is accepted for publication in *World Journal of Clinical Cases*.

Yours sincerely,

Wenyu Liu

Reviewer #1:

Specific Comments to Authors: In this article, the authors reported a case who had diabetes mellitus and threatened premature labor during the second trimester and developed TEN after administration of insulin, ritodrine hydrochloride, indomethacin, and dexamethasone. Toxic epidermal necrolysis (TEN) is a rare life-threatening cutaneous drug reaction, which may be a threat to the mother and the fetus during pregnancy. So, the report will be useful to remind doctors to re-evaluate the effectiveness and safety of ritodrine when the tocolytic agents is conducted. Queries and suggestions are listed as follows.

Thank you for your summary. We really appreciate your efforts in reviewing our manuscript. We have revised the manuscript accordingly. Our point-by-point responses are detailed below.

Q1: Although the title is Toxic epidermal necrolysis induced by tocolytics in pregnancy, the role of indomethacin could not be ruled out. In this case, TEN appeared after the combination of indomethacin and ritodrine, and other agents. As the authors described, insulin and corticosteroids were not considered to be the trigger. However, the relationship between TEN and indomethacin cannot be ruled out. Indomethacin has been reported to be a cause of TEN, and TEN usually develops 2–35 d after starting indomethacin. This case developed TEN 15 days after starting indomethacin. Although it is 10 days after withdrawing indomethacin, delayed type hypersensitivity (DTH) triggered by indomethacin could not be ruled out.

We deeply appreciate the reviewer's suggestion and agree with your comment. Actually, we can not completely exclude the influence of indomethacin, which is the biggest limitation of our article. According to the reviewer's comment, we have made changes to the article (Lines 250-255, page 15 and Lines 275-280, page 16).

Q2: Please provide the duration of all treatments in table 1.

Thank you for your suggestion. As suggested by reviewer, we have added the suggested content in table 1.

Q3: Please provide a figure or chart to display the relationship between the application of all treatments and the appearance of skin injury.

Thank you for your precious comments and good advice. We are very sorry for we can't find more pictures about the appearance of skin injury because 4 years has passed and we regret that the case should have been reported earlier.

Q4: As the skin injury cover the whole body. It would be better to provide more pictures of different parts and different stages.

We are very grateful to your generous comments. According to your advice, we have amended the relevant part in manuscript. (Fig.1-Fig.5)

Reviewer #2:

Specific Comments to Authors: A very interesting case report in patients with premature contractions with the use of ritodrine, indomethacin, and dexamethasone drugs with side effects of TEN. A good outcome for the patient and the baby. Good job.

We are very grateful to your comments for the manuscript. According to your advice, we amended the relevant part in manuscript. All of your questions were answered one by one.

Q1: Please explain why the author continues to give ritodrine to the patient when the symptoms of TEN appear. Is this very dangerous for the patient and the fetus?

Thank you for your precious comments and advice. There were rare reports about the rash caused by ritodrine at that time and we didn't have the basis to believe that the patient's rash was caused by ritodrine. In this case, we can not stop the use of ritodrine because of the frequent contraction of the patient. We have amended the relevant part required as explained above (Lines 157-160, page 8; Lines 256-258, pages 15).

Q2: Please describe the limitations of this case report especially on the determination that ritodrine is the main cause of TEN 3. Reference numbers 5 and 7 are the same reference

Thank you for underlining this deficiency. According to your advice, we have added the corresponding content in my manuscript (Lines 274-280, page 16) and made changes to the references.

Reviewer #3:

Specific Comments to Authors: I would like to congratulate the authors on completing the paper, and on sharing their experience with practitioners around the world. The authors have made an attempt to share an anecdote of ritodrine, a commonly used tocolytic leading to toxic epidermal necrosis. The authors have done an appreciable job of explaining the necessary details in terms of the development, diagnosis and treatment of TEN. The discussion section is succinct and the authors have justified their actions well. Much of my comments (attached as a word file) revolve around the language used.

We appreciate the reviewer's positive evaluation of our work and we thank the reviewer for the time and effort that the reviewer have put into reviewing the previous version of the manuscript. We apologize for the language problems in the original manuscript and inconvenience they caused in your reading. Following the reviewer's suggestion, we have revised our manuscript and language presentation was improved with assistance from a native English speaker with appropriate research background. We hope it can meet the journal's standard.

Our deepest gratitude goes to you for your careful work and thoughtful suggestions that have helped improve this paper substantially. We have revised the manuscript accordingly, and our point-by-point responses are presented above. We appreciate the reviewer's positive evaluation of our work and agree with the comments regarding the limitations of our study. Your careful review has helped to make our study clearer and more comprehensive. We wish good health to you, your family, and community.

We look forward to hearing from you regarding our submission. We would be glad to respond to any further questions and comments that you may have.