

Editor in Chief, *World Journal of Clinical Cases*
Lian-Sheng Ma, Founder and Chief Executive Officer
Jin-Lei Wang, Science Editor, Editorial Office

June 17, 2019

Dear Editors and Reviewers,

Thank you and the reviewers for a thorough review of our manuscript entitled **“Methotrexate-related lymphoproliferative disorders in the liver: Case presentation and mini-review” (No 46403)** by Mizusawa T and myself for publication as a case report in *World Journal of Clinical Cases*. **The provided ID for this invited case report is (00188507).**

The positive comments and suggestions from the reviewers are greatly appreciated. In preparing for revision, we have carefully studied reviewers' comments and incorporated many of their suggestions into the revised manuscript. For your convenience, we have highlighted the changes made in blue. We hope this revised manuscript is now acceptable for publication in *World Journal of Clinical Cases*.

We declare that this work is original, the manuscript is not under consideration by other journals, and the material has not been previously published. All authors approved the contents submitted. We look forward to hearing from you at your earliest convenience.

Thank you for your consideration.
Sincerely yours,

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Dear Editors and Reviewers:

Thank you very much for your thoughtful comments and suggestions. In preparing the revision, we have carefully studied your comments and incorporated many of your suggestions into the revised manuscript. The following are our point-by-point responses to your comments/concerns. For your convenience, we have highlighted the changes made in blue.

Editor

Please revise the manuscript according to the review report and my comments. And answer all of the reviewers' comments carefully. Please add those two statements: Informed consent statement: CARE Checklist (2016) statement: The structured abstract should be at least 250 words. The abstract subsections will include background, case summary, and conclusion. Under the heading of Case Presentation, the following seven aspects must be presented in this order:

Response: We appreciate for a thorough review of our manuscript. We have prepared all files and modified the abstract and draft according to the suggestions and added the statements. Thank you again for your time and effort on our paper.

Reviewer #1

The authors report on a very rare case of methotrexate-related lymphoproliferative disorder, which is a severe adverse event of immunosuppression in the treatment of rheumatoid arthritis. Methotrexate-related lymphoproliferative disorder has rarely caused tumors in the liver. The authors summarize previously reported cases. The authors should improve the manuscript emphasizing the mechanisms of carcinogenesis and the immunologic interactions in the setting of a lymphoproliferative disorder indicating also the difference with a PTLD.

Response: We appreciate for a thorough review of our manuscript and are grateful for the positive comment. We have added the description and revised the references according to the suggestion (page 11, line one from the bottom and new reference #20).

Reviewer #2

This is an interesting and useful case report that will certainly add to the published literature. Never the less it is just a case report and is too long in it's current form. The introduction and case report are acceptable but the discussion is too long and should be reduced by a third. Figs 1,2,3 are superfluous because Fig 5 tells the whole story. Tables 3 & 4 are repeating what is already in the text and should be removed.

Response: We appreciate for a thorough review of our manuscript. We have modified and significantly deleted the discussion and deleted figures 1, 2, and 3. According to this modification, the number of the figure was changed.

Reviewer #3

Well manuscript written.

Response: We appreciate for a thorough review of our manuscript and are grateful for the positive comment.

Reviewer #4

This manuscript offers a case report with discussion and review of the literature. The list of authors is too long for this kind of publication. The whole article is a bit lengthy and should become more concise. Figure legend 1: "white arrows"/"white arrowheads" in A and "black arrows"/"black arrowheads" in B – there is just one white arrow/one white arrowhead in figure 1A, and one black arrow/one black arrowhead in figure 1B. Figure legend 2: "white arrows"; "black arrows" – there is just one white

arrow in figure 2A and one black arrow in figure 2B. Figure legend 3A: "white arrows" – there is only one white arrow. Figure legend 3B: Please provide an improved description (+ mentioning of the arrowhead). Figure legend 5: The arrows should be mentioned in the caption. Table 1: APTT "30.4 second" -> 30.4 seconds. The abbreviations ChE and SCC are explained, but not used. Table 4: "kupffer's phase" -> Kupffer phase. In spite of editing, there are linguistic and stylistic problems (perhaps changes were made after the editing process or the authors did not take up all the suggestions); e.g., Page 7, last two lines: "The number of patients diagnosed with MTX-LPD has been increasing since its first report in 199[2]." – This sentence is incomplete. Page 8, line 4: "Generally, the average age of patients is 67 (34-87) years old" -> Generally, the average age of patients is 67 (34-87) years. Page 8, line 5: "and occurs in twice as many women as men" -> did you intend to write "and the disease occurs in twice as many women as men"? Page 9, second paragraph, line 6: "This ratio is similar to the seen in all cases of MTX-LPD." - This sentence is grammatically unclear. Page 10, first line: "progression on the disorder in the liver" -> progression of the disorder in the liver.

Response: We appreciate for a thorough review of our manuscript. We have significantly reduced the length of the manuscript and deleted the figures 1, 2, and 3. We have corrected the tables and modified the description regarding the points suggested by the reviewer (page 9, line 1 from the top; page 9, line 6 from the top; page 10, line 3 from the bottom; page 11 line 1 from the top). Thank you again for the effort reviewing our manuscript.