

June, 26th, 2021

Dear Lian-Sheng Ma

Science Editor, Company Editor-in-Chief

World Journal of Clinical Cases

Manuscript NO.: 64803

Title:

We are thankful for the conditional acceptance of our case report and for the opportunity to make the revisions to meet the requirements for final acceptance and publication. We thank you and the reviewers for your thoughtful suggestions and insights. We have carefully revised the manuscript in line the guidelines provided to us.

All language issues have been resolved and a native-English speaker has edited the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability to meet the journal's publishing requirements. We trust you will find that the revised manuscript meets the requirements of the journal for acceptance and publication.

We assure you this manuscript has not been published or presented elsewhere in part or in its entirety and is not under consideration by another journal. The patient provided informed consent for us to collect and share his clinical information for the purposes of publication. We have read and understood your journal's policies, and we believe that neither the manuscript nor the study violates any of these. There are no conflicts of interest to declare.

Again, thank you for this opportunity to resubmit our manuscript. I look forward to hearing from you.

Sincerely,

Dr Pingping Xiao, Associate Chief Physician

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Point-by-point response

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: 1. Title should include treatment option not just a case report. 2. Please write full forms in abstract 3. There is discrepancy in rise in hemoglobin, in abstract it is 110, while in core tip it is 100. 4. In abstract should include treatment with erythropoietin. 5. In treatment section, it is not clear whether erythropoietin is stopped or continued. 6. In treatment section, authors have mentioned that HGB increased after 3 months, but in abstract it is 2 months. 7. It is reported that $\gamma\delta$ variant is very similar $\alpha\beta$ (J Hematop. 2008 Sep; 1(2): 139–143). Then, what is the novelty in treating patients with cyclophosphamide with case mentioned in manuscript. 8. Please discuss in detail about the use of prednisolone and methotrexate can increase in hemoglobin in these patients in discussion section. 9. Methotrexate can cause bone marrow suppression; it cannot increase hemoglobin. Please discuss how it could increase hemoglobin levels. 10. How cyclophosphamide could have increased hemoglobin in the patient. Describe it mechanistically. 11. As mentioned in ref 10, that CTX has highest response. Then what is the novel finding from this case. 12. Conclusion should be related to case reports. It should highlight the results from case report. 13. In manuscript, missing space between words, 14. Figure 2 should be provided with 1000 X magnification, as used in figure 1.

1. Title should include treatment option not just a case report.

The title was revised on the recommendation of the reviewer.

2. Please write full forms in abstract .

I have revised.

3. There is discrepancy in rise in hemoglobin, in abstract it is 110, while in core tip it is 100.

The hemoglobin in abstract is 100, and I have revised.

4. In abstract should include treatment with erythropoietin.

I have revised and added the erythropoietin in the treatment.

5. In treatment section, it is not clear whether erythropoietin is stopped or continued. Because of the hemoglobin was not improvement, So the erythropoietin is discontinued.

6. In treatment section, authors have mentioned that HGB increased after 3 months, but in abstract it is 2 months.

HGB increased after 3 months is corrected, I have revised.

7. It is reported that $\gamma\delta$ variant is very similar $\alpha\beta$ (J Hematop. 2008 Sep; 1(2): 139–143). Then, what is the novelty in treating patients with cyclophosphamide with case mentioned in manuscript. Similar to $\alpha\beta$ T-LGL leukemia where over 95% of cases express CD57, the vast majority of $\gamma\delta$ cases express CD57 (J Hematop. 2008 Sep; 1(2): 139–143). our case the $\gamma\delta$ T-LGL were not express CD57, so it is atypical, The novelty is that cyclophosphamide in treating patients which is CD57-negative $\gamma\delta$ T-LGL combined with PRCA, the HGB was significantly improved.

8. Please discuss in detail about the use of prednisolone and methotrexate can increase in hemoglobin in these patients in discussion section.

I have revised in discussion section.

9. Methotrexate can cause bone marrow suppression; it cannot increase hemoglobin. Please discuss how it could increase hemoglobin levels.

Methotrexate as an immunosuppressant, oral tablets once a week, in many immune diseases play a role, large dose or intravenous use can cause bone marrow suppression. Methotrexate has anti-inflammatory as well as antiproliferative effects and may mediate its actions, at least in part, through induction of apoptosis of activated T-cells.

Osuji N, et al. T-cell large granular lymphocyte leukemia: A report on the treatment of 29 patients and a review of the literature. Cancer 2006; 107(3):570-578 [PMID:16795070 doi:10.1002/cncr.22032].

Genestier L, et al. Immunosuppressive properties of methotrexate: apoptosis and clonal deletion of activated peripheral T cells. J Clin Invest 1998; 102(2):322-328 [PMID:9664073 doi:10.1172/JCI2676]

10. How cyclophosphamide could have increased hemoglobin in the patient. Describe it mechanistically.

I have describe the mechanism in discussion.

11. As mentioned in ref 10, that CTX has highest response. Then what is the novel finding from this case.

In our case ,after treatment with CsA 、 MTX 、 Pred 、 EPO , the level of HGB was not improved , after treatment with CTX alone ,the level of HGB was significantly improved in 3 months, especially its a CD57-negative $\gamma\delta$ T-LGL combined with PRCA.

12. Conclusion should be related to case reports. It should highlight the results from case report. I have revised the conclusion under the recommendation.

13. In manuscript, missing space between words, 14. Figure 2 should be provided with 1000 X magnification, as used in figure 1.

The figure 2 is provided with 1000 \times magnification.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This case report is important to understand about the treatment of rare $\gamma\delta$ T-LGLL with pure red cell aplasia (PRCA). I am interested to know which gene/s are likely involved for this disease. There are few reports suggested that STAT3, STAT5b, AIRE genes when mutated, then directly linked with $\gamma\delta$ T-LGLL with pure red cell aplasia (PRCA) disease. So, if possible, research team can identify the molecular mechanism of the disease by whole genome sequencing.

There are few reports suggested that STAT3, STAT5b, AIRE genes when mutated, then directly linked with $\gamma\delta$ T-LGLL with pure red cell aplasia (PRCA) disease. So, if possible, research team can identify the molecular mechanism of the disease by whole genome sequencing.

We have suggest the patient to detect STAT3, STAT5b, AIRE genes, she refused the further detection.

Science editor: 1 Scientific quality: The manuscript describes a Case Report of atypical $\gamma\delta$ T cell large granular lymphocytic leukemia with pure red cell aplasia. The topic is within the scope of the WJCC. (1) Classification: Grade C, Grade C; (2) Summary of the Peer-Review Report: This

case report is important to understand about the treatment of rare $\gamma\delta$ T-LGLL with pure red cell aplasia. The questions raised by the reviewers should be answered; (3) Format: There are 4 figures; (4) References: A total of 10 references are cited, including 3 references published in the last 3 years; (5) Self-cited references: There are 0 self-cited references; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B, Grade B. A language editing certificate issued by Editage was provided. 3 Academic norms and rules: The authors provided the Signed Informed Consent Form(s) and CARE Checklist-2016. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by Xiamen Medical and Health Guidance Project (No. 3502Z20199137), Fujian Medical and Health Training Project for young and middle-aged backbone talents (No.2020GGB068), and Educational and scientific research program for young and middle-aged teachers of Fujian Province (No.JAT190838). The topic has not previously been published in the WJCC. 5 Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); And (2) the authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. 6 Re-Review: Required. 7 Recommendation: Conditional acceptance.

(1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

The required funding documentation has been uploaded. (File name: 64803-Approved Grant Application Form.pdf)

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Images and figures have been provided in PowerPoint as requested. (File name: 64803-Figures.ppt)

