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Hiten RH Patel
Editor-in-Chief
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Dear Editor,

Manuscript No: 54312
Angioimmunoblastic T-cell lymphoma accompanied by pure red cell aplasia: a case report

We would like to express our sincere thanks to you and the reviewers for the thorough review of our manuscript and for the opportunity to submit a revised and improved version. We have carefully reviewed the comments and revised the manuscript No: 54312 on the basis of the reviewers' comments. Our point-by-point responses to the reviewers' comments are listed below this letter. Changes to the manuscript are shown in red font.

We hope that you find the current version of the manuscript suitable for publication. We will certainly be willing to make additional changes should they be required. Thank you for your consideration. We look forward to the publication of our manuscript in the *World Journal of Clinical Oncology*.

Sincerely,

Teiko Kawahigashi

Reviewer 1

1) in the laboratory examination section, MCV was 92.7fL (line 34), while the anemia was named microcytic (line 33).

Response: Thank you for the feedback. We apologize for the confusion caused by this error. "Normocytic normochromic anemia" is correct. We have revised the sentence (line 116).

2) in the Discussion section, a positive direct Coombs test in the patient is noted (line 53), but not mentioned in the laboratory examination section;

Response: Thank you for the suggestion. We have included the other results of the laboratory examination, and they are shown in Table 1.

3) some sentences and even paragraphs are duplicated: for example, lines 100-105 and 129-133;

Response: Thank you for the comment. We have revised the sentences (lines 120-126 and 160-166) in conformance with your feedback.

4) according to the authors, only 8 cases of the AITL and PRCA combination are described in the literature. It is necessary to compile a table with the characteristics of the described cases and this case, to enrich the Discussion section;

Response: Thank you for the valuable feedback. I have included a table that summarizes the previous case reports (Table 2).

5) considering the hemoglobin abrupt decrease during hospitalization, requirement of "almost every day" transfusion, and positive direct Coombs test, an autoimmune hemolytic anemia complicating the AITL course should be excluded. It is necessary to provide data in the laboratory examination section on the level of lactate dehydrogenase;

Response: Thank you for the insightful feedback. The level of lactate dehydrogenase is shown in Table 1. An autoimmune hemolytic anemia (AIHA) should be considered in this case, as you have pointed out. However, we did not consider AIHA in the differential diagnosis based on the clinical findings: first, there was no evidence of hemolysis, such as jaundice, splenomegaly, elevated levels of indirect bilirubin, or decreased levels of haptoglobin. Second, findings on the peripheral blood smear were not consistent with those of AIHA. There was no evidence of hemolysis or microspherocytosis. Third, the other clinical findings were not consistent with those of AIHA. For example, the patient

had a very low absolute reticulocyte count and near-complete absence of erythroblasts from an otherwise normal marrow. We have included this explanation on lines 192-201.

6) given the presence of palpable purpura, it is necessary to provide data on the complement C3 and C4 component, gamma-globulins level, and cryoglobulinemia;

Response: Thank you for this feedback. We have added additional details of the results of the laboratory examination in Table 1.

7) it is necessary to describe in more detail the histological picture of the lymph node; micrographs are also desirable;

Response: Thank you for the feedback. We have added additional details of the histological findings. Unfortunately, it is difficult to obtain the images of the histological study because I have retired from the hospital.

8) was the immunohistochemical study performed using antibodies to CXCL13 (the marker most specific for the immunohistochemical characterization of AITL), PD1 (CD279), BCL6, and ICOS? Although the minimum criteria for assessing the TFH-cell phenotype have not been established, it is desirable to test two (and preferably three) TFH-cell markers besides CD4. Immunohistochemical micrographs would also beautify the article;

Response: Thank you for these suggestions. The immunohistochemical studies of this patient did not show common markers for AITL (CXCL13, PD-1, Bcl-6, and CD10), with the exception of CD10. Therefore, we diagnosed AITL based on its characteristic pathological findings: namely, high endothelial cell venules and follicular dendritic cells. We have mentioned this on lines 154-159 of the revised manuscript.

9) PRCA was established based on the criteria (used not only in Japan). However, the article does not contain any data on the conduct of appropriate virologic studies in the bone marrow. First, data are needed on the presence of parvovirus B19 in erythroid progenitors. Patients with AITL exhibit an immunodeficiency secondary to the neoplastic process, which can theoretically lead to persistence of parvovirus B19 and result in PRCA. In addition, data are desired on the presence of EBV, CMV and HIV in the patient;

Response: Thank you for the feedback. I have included additional details of the results of laboratory examination. These details have been included in Table 1. The diagnostic criteria of PRCA have also changed to that of UpToDate. We have mentioned this on lines 160-166 of the revised manuscript.

10) there is a clear error in the treatment section (line 111). The CHOP course was conducted not "three times a week", but once every three weeks. It would be interesting to discuss the choice of therapy in the Discussion. Why was the patient not prescribed cyclosporine A in this situation?

Response: Thank you for the feedback. I have revised the sentence stating "three times a week" (line 132). We did not prescribe cyclosporine A for the treatment of PRCA because we thought that the PRCA was associated with AITL. In such cases, as previously reported, the PRCA is improved by the treatment of AITL. Moreover, most of the cases that we have shown in Table 2 achieved remission of PRCA only with chemotherapy. Therefore, we did not prescribe cyclosporine A in this patient. This explanation has been included on lines 201-208.

Reviewer 2

1. It is advisable to add a photomicrograph of the lymph node biopsy findings.

   Response: Thank you for this suggestion. However, it is difficult to obtain the images of the histological study because I have retired from the hospital.

2. Were any imaging techniques employed for examination of lymph nodes?

   Response: Thank you for the comment. We conducted contrast-enhanced computed tomographic scanning of the abdomen and pelvis.

3. Please mention the follow-up status of the patient, if available

   Response: Thank you for the suggestion. We apologize, but we have no current update on the present follow-up status of this patient.

4. Discuss the management protocol of patients with AITL alone as well aas those with AITL and PRCA?

   Response: Thank you for the feedback. Most previous reports have suggested that PRCA associated with AITL is improved by the treatment of AITL, which is chemotherapy. However, it has not been elucidated whether chemotherapy, the treatment for only AITL, is sufficient for the management of the complication of PRCA because of the limited number of cases that have been identified. This aspect needs further research, and we have mentioned it on lines 201-208.