Dear Editor:

I wish to submit the revised manuscript titled “Gray zone lymphoma effectively treated with R-CHOP chemotherapy: A case report”.

Answers to Reviewer #1:

Thank you for your very appropriate suggestions. We explained the points as follows, and based on that, we made a major revision of the text and figures.

1. We corrected the sentence “BCLu-DLBCL/cHL was diagnosed based on PD-L1 positivity” to “GZL was diagnosed based on histopathology and immunophenotyping with ancillary PD-L1 positivity” in the Abstract, CONCLUSION.

2. We added the staging results and the follow-up information such as “The lymphoma was stage IV according to the Lugano classification and high-risk according to the International Prognostic Index for aggressive non-Hodgkin lymphoma.” and “She has remained in complete remission for 3 years.” in the Abstract, CASE SUMMARY.

3. We changed “intermediate features of diffuse large B-cell lymphoma” to “features intermediate between diffuse large B-cell lymphoma” in the Core tip and
INTRODUCTION.

4. We changed this text to the following: “The patient was diagnosed based on the characteristic pathological findings, the immunophenotype (CD20+, PAX5+, OCT2+/BOB1 (focal+), CD30+, CD15-), and the strong positive expression of neoplastic programmed cell death protein ligand 1 (PD-L1) in her lymphoma cells.”

5. The features borderline with classical HL in this patient were lack of clonal immunoglobulin in the tumor cells identified by FCM and the low BOB1 expression level in the tumor cells (focal+). These findings are similar to those observed in H-RS cells in cHL but consistent with DLBCL. Regarding PD-L1 expression, Tanaka Y. et al reported that nearly half of gray zone lymphoma cases, and more than 70% of the lymphoma cells, are PD-L1 positive. Sakakibara et al. reviewed the diagnostic utility of PD-L1 (clone SP142) immunohistochemical expression in large cell lymphomas, predominantly cHL and DLBCL. They pointed out that nodal gray zone lymphoma (EBV-negative) cells were positive for PD-L1 (3/3); on the other hand, nodal DLBCL (EBV-negative) and nodal avDLBCL (EBV-negative) cells were negative (0/275 and 0/11, respectively). We used PD-L1 clone SP142 instead of clone 22C3 to replicate the conditions used in previous studies.

Answers to Reviewer #2:

Thank you for your very appropriate suggestions. We have revised the text accordingly as follows.

1. We added the clinical manifestations, susceptible populations and invasive sites of gray zone lymphoma to the DISCUSSION, such as the passages beginning “Regarding the clinical manifestations....” and “GZL can be divided into mediastinal GZL (MGZL) and nonmediastinal GZL (NMGZL) depending on the presence or absence of mediastinal lesions....”.
2. We have added phrases and changed information as follows: “The patient was initially treated with a reduced dose (60% of the scheduled dose) of CHOP chemotherapy to prevent tumor lysis syndrome, and it was initially unclear whether the tumor cells were CD20 positive. Subsequently, five cycles of R-CHOP chemotherapy were administered at standard doses.”

Thank you for your consideration. I look forward to hearing from you.

Sincerely,
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