Response to Reviewer's Comments

Reviewer(s)' Comments to Author:
There is lack of evidence to support the development of X. Why choose N as sample size? The author should add baseline analysis of different type of SRBC to adjust the differences.

Reviewer #1:

Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision
Specific Comments to Authors: Dear author's I was pleased to review your article. You describe a rare case.

1. Please explain the novelty of the case presented.

Reply: Thank you for reviewing our manuscript. It should be noted that the present case is not the first case of relapsed T/myeloid mixed-phenotype acute leukemia (MPAL) successfully treated with venetoclax and a hypomethylating agent (HMA), as highlighted in the concluding paragraph of the DISCUSSION. However, we believe it is essential to present this case report, as treatment guidelines for MPAL are lacking in NCCCN or ELN guidelines. Importantly, the concept of combining venetoclax and HMA as a bridging treatment prior to hematopoietic stem cell transplantation should be explored and compared with other treatment strategies.

2.It will be interesting to a add a pucture with the pathological exam.

Reply: Thank you for this suggestion. In accordance with this suggestion, an image of the underlying pathology, accompanied by an explanation, has been included.

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Laboratory examinations

Neutropenia (1.12 × 10^3/mm^3), anemia (4.0 g/dL), and thrombocytopenia (12 × 10^3/mm^3) were detected in peripheral blood. Figure 2 describes the findings of the bone marrow examination. Flow cytometry showed the expression of cMPO+, CD 13+, CD33+, CD64+, CD117+, CD34+, and high cytoplasmic CD3. Chromosomal karyotyping revealed a 48, XY, add(11)(q23), add(12)(p13).-20,-22,+4mar karyotype. Fluorescence *in situ* hybridization revealed KMT2A positivity.~

Figure 2. Bone marrow (BM) aspiration and biopsy. Medium-to-large-sized leukemic blasts can be observed in (A) BM aspiration smear (Wright-Giemsa stain, 400×) and (B) biopsy section (hematoxylin and eosin stain, 100×) at the initial diagnosis of MPAL. In leukemic blasts, immunohistochemical staining of (C) CD34 (100×), (D) CD3 (100×), and (E) myeloperoxidase (100×) appear positive and show similar distribution.

Abbreviations: MPAL, mixed-phenotype acute leukemia

3. Please highlight the role of transplantation in this pathology.

Reply: Thank you for this suggestion, which further highlights the value of our manuscript. In the revised manuscript, we focused our conclusions on 'pre-transplantation bridging treatment'.

DISCUSSION

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However, overall survival (OS) rates between ALL and AML induction regimens did not differ (3-year OS, 48±6.9% vs 47±5.0%, respectively) according to a multivariate analysis of detailed clinical data, including the type of therapy, MPAL subgroup, and patient age.

Hematopoietic stem cell transplantation has been shown to substantially increase the 5-year survival rate in patients with MPAL[7], and bridging therapy should ideally be associated with less toxicity and complications. A combined regimen (a hybrid of ALL and AML therapy) was shown to significantly reduce the survival of patients (3-year OS, 23% 8.6%, p = 0.001), probably due to increased toxicity[4].

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CONCLUSIONS

Herein, we present a patient with MPAL who experienced serious

complications with standard chemotherapy. Subsequently, the patient received combination therapy with venetoclax and HMA and underwent hematopoietic stem cell transplantation. Therefore, it is necessary to establish whether combination therapy with venetoclax and HMA could be beneficial as bridging therapy pre-transplantation. Accordingly, future investigations should compare the potential of venetoclax and HMA with traditional chemotherapy in patients who can eventually undergo transplantation.

Reviewer #2:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors:
(1) The overall structure of the manuscript is complete and contains a title, abstract, keywords, core tip, introduction, case presentation and results, discussion, acknowledgments, and references.
(2) The scientific question is to emphasize the beneficial effect of the administration of venetoclax along with a hypomethylating drug (HMA) in patients with T/myeloid mixed-phenotype acute leukemia (MPAL).

This is presented in the introduction section, along with the relevant background, rationale, aim, significant findings, and potential significance of the given case. Therefore, this section is suitable to attract readers' attention.
(3) The methods and techniques adopted in the paper are presented in the Methods section. Besides, the manuscript provides adequate details of methods to allow a reader to repeat the research.
(4) The data source is reliable and indicated by the information presented in the case presentation section.

However, pathological diagnostic findings (such as blood smears and/or bone marrow biopsies) should be submitted as microscopic figures.
(5) The conclusion of the case presentation is presented.

This section should be ameliorated to inform the readers briefly about the

contributions of the data to the field.

Besides, the future research directions should be given in detail.

(7) The manuscript cites all critical, relevant, and timely references.

(8) There is no indication of academic misconduct in the study.

(9) The manuscript contributes to understanding the pathogenesis of the disease and treatment.

(11) The manuscript describes an important direction of research

(12) The title of the manuscript does not contain grammatical errors.

(13) The manuscript falls within the scope of WJCC

(14) The language of the paper needs to reach the standard of publishing, and minor revisions are required. Peer-reviewer's Conclusion: The manuscript falls within the scope of WJCC. The experiences and lessons presented in the manuscript improve the readers' practice.

The content of the manuscript has value for publication.

However, necessitate revisions according to the comments listed above.

1. Pathological diagnostic findings (such as blood smears and/or bone marrow biopsies) should be submitted as microscopic figures.

Reply: Thank you for highlighting this critical omission. Accordingly, an image of the underlying pathology, along with an explanation, has been included in the revised manuscript.

CASE PRESENTATION

Laboratory examinations

Neutropenia (1.12 × 10^3/mm^3), anemia (4.0 g/dL), and thrombocytopenia (12 × 10^3/mm^3) were detected in peripheral blood. Figure 2 describes the findings of the bone marrow examination. Flow cytometry showed the expression of cMPO+, CD 13+, CD33+, CD64+, CD117+, CD34+, and high cytoplasmic CD3. Chromosomal karyotyping revealed a 48, XY, add(11)(q23), add(12)(p13).-20,-22,+4mar karyotype. Fluorescence *in situ* hybridization revealed KMT2A positivity.~

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of (C) CD34 (100×), (D) CD3 (100×), and (E) myeloperoxidase (100×) appear positive and show similar distribution.

Abbreviations: MPAL, mixed-phenotype acute leukemia

2.This section should be ameliorated to inform the readers briefly about the contributions of the data to the field.& Besides, the future research directions should be given in detail.

Reply: Thank you for this suggestion, which further highlights the value of our manuscript. In accordance with this suggestion, our conclusions highlight the potential of 'pre-transplantation bridging treatment'.

CONCLUSIONS

Herein, we present a patient with MPAL who experienced serious complications with standard chemotherapy. Subsequently, the patient received combination therapy with venetoclax and HMA and underwent hematopoietic stem cell transplantation. Therefore, it is necessary to establish whether combination therapy with venetoclax and HMA could be beneficial as bridging therapy pre-transplantation. Accordingly, future investigations should compare the potential of venetoclax and HMA with traditional chemotherapy in patients who can eventually undergo transplantation.

3. The language of the paper needs to reach the standard of publishing, and minor revisions are required.

Reply: To polish the language, we entrusted the manuscript to a professional English language editing company in Korea.