Journal on Oncology

www.journalononcology.org

Short Commentary

Open Access, Volume 2

Is CD22 Positive Acute Myeloid Leukemia, a Distinct Myeloid Disease Entity?

Kazunori Nakase*; Hiroshi Miwa; Hiroshi Shiku

Department of Personalized Cancer Immunotherapy, Mie University Graduate School of Medicine, Edobashi 2-174, Tsu, Japan.

Abstract

Although the expression of Lymphoid Associated Antigen (LAA) is related to the pathological status of patients with Acute Myeloid Leukemia (AML), there has been no information regarding a B-lymphoid antigen CD22 in AML so far. In our recent analyses, CD22 positive AML cells showed unusual cellular properties, as evidenced by common expression of leukemia stem cell antigen, interleukin-2 receptor α-chain (CD25) and the presence of various LAAs and immune gene rearrangements. Clinically, patients with CD22 positive AML showed a higher leukocyte count in the peripheral blood than those with the other subtypes of AML. They responded poorly to standard chemotherapy for AML and had an unfavorable outcome. CD22 positive AML might constitute a distinct myeloid disease entity with unique cellular and clinical characteristics. Its recognition seems to be important for the development of therapeutic approaches to this disease.

Keywords: CD22; CD25; Leukemia stem cell; Acute myeloid leukemia.

Introduction

AML is a biologically and clinically heterogenous hematological malignancy. However, until recently similar therapeutic regimens have been administered for patients with AML. Therefore, the management of these patients remains far from resolved, and the survival rate at 5 years does not exceed 40% [1]. At present, newer treatment strategies are developing due to the progress in the understanding of the pathophysiology of AML [1,2]. A close relationship between the expression of lymphoid associated antigen (LAA) such as CD2 [3], CD4 [4], CD7 [5], CD19 [6], and CD56 [7] and the certain AML subtypes has been described by many previous reports. Detailed investigation into AML expressing LAAs might provide us clues that lead to develop newer therapeutic approaches. Although CD22 antigen is well known typical B-lymphoid marker [8], not much attention has been paid to its expression in AML. Therefore, there is a dearth of knowledge about the pathologic significance of CD22 expression in AML.

CD22 expression in AML

We recently published a report on its expression in AML [9]. In this report, we first described the clinicopathological features of CD22 positive AML. CD22 was detected in 10 of the 404 (2.5%) adult patients with previously untreated de-novo AML (6 M1, 3 M4, and 1 M5 patients), being in line with most reports demonstrating its rare expression.

Manuscript Information: *Received: May 21, 2022; Accepted: Jun 09, 2022; Published: Jun 17, 2022*

Correspondance: *Kazunori Nakase, Department of Personalized Cancer Immunotherapy, Mie University Graduate School of Medicine, Edobashi 2-174, Tsu, Japan. Tel: +81-59-231-5187, Fax: +81-59-231-5276; Email: k2nakase@med.mie-u.ac.jp*

Citation: *Nakase K, Miwa H, Shiku H. Is CD22 Positive Acute Myeloid Leukemia, a Distinct Myeloid Disease Entity?. J Oncology. 2022; 2(1): 1029.*

As for cellular features, these cases were characterized by the expression of various LAAs such as CD2, CD4, CD5, CD7, CD10, CD19, CD20, CD21, CD56, TdT, and/or immune-genotypes, immunoglobulin heavy chain and T-cell receptor γ chain gene rearrangements. In addition, CD34 and HLA-DR were exhibited in all cases. Cytogenetically, some cases showed del (5), -7 or t (9;22) chromosomal abnormality. These results suggest that the CD22 positive AML cells originate from the common lymphoid and myeloid progenitors or more immature cells with a flexible pattern of lineage phenotype and genotype.

The most interesting finding in the report was that interleukin-2 receptor α-chain (CD25) was commonly expressed in this leukemia.

We previously reported on the relationship between the presence of CD25 and the other cell surface markers in AML and found that CD25 showed the closest correlation with CD22 among different LAAs [10]. However, at that time we did not evaluate the detailed features of CD22 positive AML. This time, our analyses showed that CD25 was positive in 7, negative in one, and not examined in 2 out of the 10 CD22 positive AML cases. One CD25 unexamined case had t(9;22) and CD25 might be expressed in this case because CD25 has been noted as a predictor of the presence of t(9;22) [11]. The other 2 cases displayed CD7 as well as HLA-DR, and CD25 expression is reported to be easily inducible on both CD7 and HLA-DR positive AML cells [12]. In addition, CD25 expression fluctuates in the leukemia-initiating cell population of CD25 positive AML cells [13]. Therefore, we think that all the 10 CD22 positive AML cases possess a high potentiality of CD25 expression. However, it is unclear why the expression of CD22 and CD25 so closely combine with each other. This issue warrants further investigation.

Gene expression profile of CD25 positive AML cells is involved in leukemia stem cell (LSC) gene signatures, and CD25 is recognized as a surrogate marker for LSC [14]. Further, CD123, which is also well known LSC marker [15], was highly expressed in 4 cases examined, supporting that CD22 positive AML cells represent a population of LSCs.

Sato et al. [16] described that CD13, CD22 and CD25 were simultaneously expressed in basophil related AML, and they were peroxidase-negative AML (M0) and secondary AML (11 of 64 AML patients, 17.2%). However, basophilic features were not observed in leukemic cells from any patient with our CD22 positive AML. Neither AML-M0 nor secondary AML was included in our cases. Furthermore, CD2 and CD19, which were frequently detected in our cases, were not observed in any of their cases, suggesting that our CD22 positive AML cases appeared different AML from those mentioned in the study by Sato et al.

Clinically, leukocyte counts in the peripheral blood were significantly higher in CD22 positive AML than in the other subtypes of AML. The chemotherapeutic effects in patients who were treated with standard chemotherapy showed that the rate of complete remission was significantly lower in the cases with CD22 positive AML (1/7, 14%) than in those with CD22 negative AML (247/343, 72%). Additionally, the overall survival of patients with CD22 positive AML was significantly shorter than that of patients with CD22 negative AML. The average survival of patients with CD22 positive AML was 207 days. These adverse clinical outcomes seem to strongly reflect the cellular properties of chemotherapy-resistant LSCs.

Conclusion

We think that CD22 positive AML is a rare disease but constitutes a distinct myeloid disease entity with aggressive clinical course. This leukemia cells might belong to a pure LSC population expressing multiple LSC antigens. Thus, CD22 survey should be integrated into current prognosis predicting system in AML as soon as possible to improve further AML prognostication. Recognition of CD22 positive AML is essential for better understanding of the role of CD22 expression in AML and the development of novel treatment strategies for this poor prognostic disease.

References

1. Kantarjian H, Kadia T, DiNardo C, Daver N, Borthakur G, Jabbour E, et al. Acute myeloid leukemia: current progress and future directions. Blood Cancer J. 2021 Feb 22; 11: 41.

2. Nair R, Salinas-Illarena A, Baldauf HM. New strategies to treat AML: novel insights into AML survival pathways and combination therapies. Leukemia. 2021; 35: 299-311.

3. Cross AH, Goorha RM, Nuss R, Behm FG, Murphy SB, Kalwindky DK, et al. Acute myeloid leukemia with T-lymphoid features: a distinct biologic and clinical entity. Blood. 1988; 72: 579-587.

4. Miwa H, Mizutani M, Mahmud N, Yamaguchi M, Takahashi T, et al. Biphasic expression of CD4 in acute myelocytic leukemia (AML) cells: AML of monocyte origin and hematopoietic precursor cell origin. Leukemia. 1998; 12: 44-51.

5. Kita K, Miwa H, Nakase K, Kobayashi T, Shirakawa S, et al. Clinical importance of CD7 expression in acute myelocytic leukemia. Blood. 1993; 81: 2399-2405.

6. Kita K, Nakase K, Miwa H, Masuya M, Nishii K, Morita N,et al. Phenotypical characteristics of acute myelocytic leukemia associated with the t(8;21)(q22; q22) chromosomal abnormality: frequent expression of immature B-cell antigen CD19 together with stem cell antigen CD34. Blood. 1992; 80: 470-477.

7. Raspadori D, Damiani D, Lenoci M, Rondelli D, Testoni N, Nardi G, et al. CD56 antigenic expression in acute myeloid leukemia identifies patients with poor clinical prognosis. Leukemia. 2001; 15: 1161-64.

8. Boue DR, LeBien TW. Expression and structure of CD22 in acute leukemia. Blood 1988; 71: 1480-86.

9. Nakase K, Tanaka I, Tawara I, Shiku H. CD22 expression in acute myeloid leukemia: close correlation with interleukin-2 receptor α-chain (CD25) expression and poor prognosis. Leuk Lymphoma. 2022: 1-3.

9. Nakase K, Kita K, Anazawa H, Hoshino K, Shirakawa S, et al. Induction of interleukin-2 receptor alpha chain expression of immature acute myelocytic leukemia cells. Leuk Res. 1994; 18: 269-74.

10. Nakase K, Kita K, Otsuji A, Anazawa H, Shirakawa S, et al. Interleukin-2 receptor alpha chain on acute myelocytic leukemia cells is involved in cell-to-cell interactions. Leuk Res. 1993; 17: 17-21.

11. Nakase K, Kita K, Kageyama S, Tsuji K, Miyanishi E, Miwa H, et al. Clinical importance of interleukin-2 receptor alpha-chain expression in acute leukemia. Cancer Detect Prev. 1997; 21: 273-9.

12. Chen P, Chu A, Zia H, Koduru P, Collins R, et al. CD25 expression in B lymphoblastic leukemia/lymphoma predicts t(9;22)(q34;q11)/Philadelphia chromosome translocation (Ph) and is associated with residual disease in Ph-negative patients. Am J Clin Pathol. 2016; 146: 632-8.

13. Kageyama Y, Miwa H, Arakawa R, Tawara I, Ohishi K, et al. Expression of CD25 fluctuates in the leukemia-initiating cell population of CD25-positive AML. PLoS One. 2018;13: e0209295.

14. Gonen M, Sun Z, Figueroa ME, Patel JP, Abdel-Wahab O, et al. CD25 expression status improves prognostic risk stratification in AML independent of established biomarkers: ECOG phase 3 trial, E1900. Blood. 2012; 120: 2297-2306.

15. Jordan CT, Upchurch D, Szilvassy SJ, Guzman ML, Howard DS, et al. The interleukin-3 receptor alpha chain is a unique marker for human acute myelogenous leukemia stem cells. Leukemia. 2000; 14: 1777-1784.

16. Sato N, Kishi K, Toba K, Watanabe K, Itoh H, et al. Simultaneous expression of CD13, CD22 and CD25 is related to the expression of FcεR1 in non-lymphoid leukemia. Leuk Res. 2004; 28: 691-698.