The expression of the CD56 antigen is associated with poor prognosis in patients with acute myeloid leukemia

Eduardo Magalhães Rego

Hematology and Oncology Department, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo – FMRP-USP, Ribeirão Preto, SP, Brazil

Submitted: 6/20/2011
Accepted: 6/21/2011

Corresponding author:
Eduardo Magalhães Rego
Divisões de Hematologia e Oncologia, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo – FMRP-USP
Av. Bandeirantes, 3900 – Bairro Monte Alegre
14040-900 – Ribeirão Preto, SP, Brazil
Phone: 55 16 3602-2888
edumrego@hotmail.com

www.rbhh.org or www.scielo.br/rbhh

DOI: 10.5581/1516-8484.20110048

The diversity of clinical, hematological and genetic features among patients with acute myeloid leukemia (AML) has been recognized for many decades. However, during recent years, considerable progress has been made in defining new diagnostic and prognostic markers. Among them, the detection of specific molecules in the leukemic cells has special relevance and is mandatory for the identification of certain subtypes of myeloid neoplasms.[1,2] In this context, flow cytometry-based immunophenotyping has had an immense impact on the diagnosis and management of AML and has become a routine procedure.

In the present issue of this journal, Alegretti et al. reported the analysis of the association between expression of CD56 on myeloblasts and treatment outcome in a cohort of 48 patients with AML treated in a single center in Brazil.[3] CD56 is the neural-cell adhesion molecule (NCAM), which is a well known marker for natural killer (NK) cells, but is also expressed on a subset of normal T cells. Alegretti et al. demonstrated that the expression of CD56 was associated with worse prognosis. The overall survival (OS) of patients who expressed CD56 ($CD56^+$) was significantly shorter compared to patients who did not express the marker (mean 4.0 versus 14.5 months; p-value = 0.03). In addition, $CD56^+$ patients presented a higher death rate during induction, even though the difference was not significant (62.5% versus 27.5%; p-value = 0.097). The results may have been affected by the small number of patients in the $CD56^+$ group (n = 6) but the magnitude of the difference in OS is too striking to be ignored. Their results corroborate the studies by Chang et al.[4] and Baer et al.,[5] but in the latter the association between prognosis and CD56 expression was restricted to patients with t(8;21)/RUNX1-RUNX1T1 whereas in the former the association was between CD56 expression and abnormalities involving 11q23 and extramedullary disease. To further complicate the issue, a recent manuscript by Montesinos et al.[6] reported the prognostic relevance of CD56 in acute promyelocytic leukemia (APL).

They analyzed 651 patients with APL of whom 72 expressed CD56 (11%). $CD56^+$ APL was significantly associated with high white blood cell counts, low albumin levels, the BCR3 isoform and coexpression of the CD2, CD34, CD7, HLA-DR, CD15 and CD117 antigens. For $CD56^+$ APL, the 5-year relapse rate was 22% compared with a 10% relapse rate for $CD56^-$ APL (p-value = 0.006). $CD56^+$ APL also showed a greater risk of extramedullary relapse (p-value < 0.001).

The relationship between the expression of CD56 and treatment outcome has also been analyzed in acute lymphoblastic leukemia (ALL). Ravandi et al.[7] demonstrated a high incidence of infiltration of the central nervous system in adult patients with ALL. Dalmazzo et al.,[8] analyzing T-cell ALL, reported that patients expressing CD56 were older, expressed cytotoxic molecules at a higher frequency and presented shorter OS compared to $CD56^-$ patients.

Taken together the existing published data suggest that the expression of CD56 is associated with worse prognosis in acute leukemias and the manuscript by Alegretti et al., corroborates reports from different countries. Nevertheless, the mechanisms underlying this association are unclear. Moreover, it is not clear whether $CD56^+$ AML patients should receive a more intense treatment than those that do not express CD56. At present, this matter should be considered with caution, but, definitely there is opportunity for future multicentric clinical trials to address this issue.

References

1. Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A, et al. The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. Blood. 2009;114(5): 937-51. Comment in: Blood. 2010;115(3):748-9; author reply 749-50.
2. Matutes E, Pickl WF, Van't Veer M, Morilla R,Swansbury J, Strobl H, et al. Mixed-phenotype acute leukemia: clinical and laboratory features and outcome in 100 patients defined according to the WHO 2008 classification. Blood. 2011;117 (11):3163-71.
3. Alegretti AP, Bittar CM, Bittencourt R, Piccoli AK, Schneider L, Silla LM, et al. The expression of CD56 antigen is associated with poor prognosis in patients with acute myeloid leukemia. Rev Bras Hematol Hemoter. 2011;33(3):202-6.
4. Chang H, Brandwein J, Yi QL, Chun K, Patterson B, Brien B. Extramedullary infiltrates of AML are associated with CD56 expression, 11q23 abnormalities and inferior clinical outcome. Leuk Res. 2004;28(10):1007-11.
5. Baer MR, Stewart CC, Lawrence D, Arthur DC, Byrd JC, Davey FR, et al. Expression of the neural cell adhesion molecule CD56 is associated with short remission duration and survival in acute myeloid leukemia with t(8;21)(q22;q22). Blood. 1997;90(4): 1643-8.
6. Montesinos P, Rayón C, Vellenga E, Brunet S, González J, González M, Holowiecka A, Esteve J, Bergua J, González JD, Rivas C, Tormo M, Rubio V, Bueno J, Manso F, Milone G, de la Serna J, Pérez I, Pérez-Encinas M, Krsnik I, Ribera JM, Escoda L, Lowenberg B, Sanz MA; PETHEMA; HOVON Groups. Clinical significance of CD56 expression in patients with acute promyelocytic leukemia treated with all-trans retinoic acid and anthracycline-based regimens. Blood. 2011;117(6):1799-805.
7. Ravandi F, Cortes J, Estrov Z, Thomas D, Giles FJ, Huh YO, et al. CD56 expression predicts occurrence of CNS disease in acute lymphoblastic leukemia. Leuk Res. 2002;26(7):643-9.
8. Dalmazzo LF, Jacomo RH, Marinato AF, Figueiredo-Pontes LL , RL Cunha, Garcia AB, et al. The presence of CD56/CD16 in T-cell acute lymphoblastic leukaemia correlates with the expression of cytotoxic molecules and is associated with worse response to treatment. Br J Haematol. 2009;144(2):223-9.