CD56 expression could be associated with monocytic differentiation in acute myeloid leukemia with t(8;21)

We analyzed the immunophenotypic characteristics of 11 patients with t(8;21) acute myeloid leukemia (AML) and correlated the expression of CD56 with the myelomonocytic differentiation of the blast cells. All the CD56⁺ blast cells showed monocytic differentiation with co-expression of CD34⁺ CD15⁺ HLA-DR⁺ whereas the CD56⁻ cases showed myeloid maturation without expression of CD15 in the leukemic cells. All the CD56 cases showed an aberrant phenotype at diagnosis.

The study of normal antigen expression pattern for each antigen in relation to myeloid maturation enables us to determine the origin of the pluripotent cell responsible for the leukemic clone. It has been reported that myeloid cells lose CD34 before acquiring CD15 whereas monocytic precursors gain CD15 and then lose CD34.[1,2] The presence of CD56 and the co-expression of CD34 and CD15 in blast cells are two features in AML with a monocytic differentiation.[3,4] We describe the complete immunophenotype of 11 cases of t(8;21) AML with emphasis on the maturation pathway of the neoplastic cells.

BM samples taken at diagnosis were analyzed by flow cytometry using appropriate triple staining combinations. The technique and data acquisition were described previously.[5] Samples corresponding after induction and intensification therapy of patients in CR were analyzed using the aberrant antigenic combinations according to previously reported methodology.[6]

FAB subtype, karyotype, immunophenotype, clinical data and outcome of these patients are summarized in Table 1. CD56 was expressed in 6 out of the 11 cases (55%). All the blast cells which were CD56 negative showed a loss of CD34 before the acquisition of the CD15 antigen, whereas all the cases with CD56 expression acquired CD15 antigen before losing the CD34 (Figure 1). There was only one exception, a CD56⁺ patient with very immature blasts without differentiation. CD56⁺ blast cells showed monocytic differentiation and the CD56⁻ cells showed myeloid differentiation. None of the CD56⁺ cases expressed mature monocytic antigens such as CD14 or CD36.

We analyzed the presence of aberrant phenotypes at diagnosis. Only 1 out of 5 CD56⁻ patients showed an aberrant phenotype. In contrast, asynchronous antigen expression (CD34⁺CD56⁺ and CD15⁺CD117⁺) was detected in all the CD56⁺ cases. We investigated the presence of residual leukemic cells with these antigen combinations in 4 patients in morphologic complete remission. In 2 out of 2 CD56⁻ patients we were unable to detect residual leukemic cells because of the lack of aberrant phenotype. After induction therapy we detected residual aberrant cells in 2 out of 2 CD56⁺ patients. Interestingly, in both cases the abnormal residual cells showed co-expression of CD117⁺ CD15+ in number >2×10⁻³ but lacked CD34/CD56 expression. In both patients the aberrant cells disappeared with the intensification therapy and the patients remaned in CR.

In our study, all the cases with CD56 expression showed a monocytic differentiation pathway with CD34⁺CD15⁺ blast cells. In contrast all the CD56⁻ cases displayed a maturation commit-

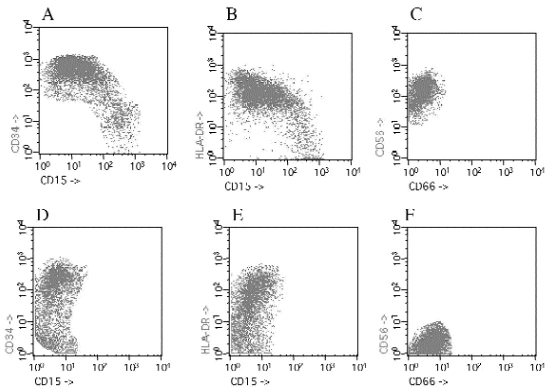

Figure 1. A,B,C: blast cells in a t(8;21) AML patient show differentiation along the monocytic pathway. CD56 is positive in these cells. D,E,F: blast cells in a t(8;21) AML patient show myeloid differentiation. Blast cells are CD56 negative.

Table 1. Biological and clinical data of t(8;21) AML patients.

				Immunophenotype							*Clinical outcome*		
Case	*Age (years)*	*FAB*	*Karyotype*	*AML1/ETO*	*CD15*	*CD33*	*CD33*	*CD117*	*CD56*	*CD19*	*Induction outcome*	*Intensification therapy*	*Outcome*
1	43	M2	46,XY, t(8;21)(q22;q22)	+	-	-	-	+	-	·	CR	HDAC	Relapse
2	41	M2	46,XX, t(8;21)(q22;q22)	+	-	+	+	-	-	+	NA	NA	NA
3	5	M4	46,XX, t(8;21)(q22;q22)	+	-	+	+	+	-	-	CR	AlloSCT	Alive
4	11	M4	45,X,-Y, t(8;21) (q22;q22)	+	+	+	+	+	+	-	CR	AutoSCT	Alive
5	45	M2	46,XX, t(8;21)(q22;q22)	+	+	+	+	+	+	·	CR	HDAC	Alive
6	40	M2	46,XX/45,X,-X, t(8;21)(q22;q22)	+	+	+	+	+	+	-	CR	HDAC	Alive
7	NA	M2	46,XX, t(8;21)(q22;q22)	+	+	+	+	+	+	+	NA	NA	NA
8	35	M2	NA	+	-	+	+	+	-	+	CR	HDAC	Alive
9	30	M2	46,XY, t(8;21)(q22;q22)	+	+	+	+	+	+	+	CR	In treatment	Alive
10	50	M2	46,XX, t(8;21)(q22;q22)	+	-	+	+	+	-	-	CR	In treatment	Alive
11	55	M2	46,XX, t(8;21)(q22;q22)	+	·	+	+	+	+	-	CR	In treatment	Alive

Immunophenotype: all the cases were CD34⁺, HLA-DR⁺, CD13⁺, CD45⁺,CD7⁻,CD66⁻, CD14⁻, CD36⁻, CD64⁻, MPO cyt⁺, CD79a cyt⁻, CD3 cyt⁻ Tdt cyt⁻. NA: not available; HDAC: high-dose cytarabine; AlloSTC: allogeneic stem cell transplantation; AutoSCT: autologous stem cell transplantation.

ment towards the neutrophilic lineage. Our hypothesis is that the CD56+ subpopulation in these patients corresponds to an immature and not always predominant monocytic clone. Interestingly, we found that all the CD56+ patients displayed asynchronous antigen expression. These phenotypic aberrations, especially the co-expression of CD15 and CD117 could facilitate the study of minimal residual disease in CD56+ patients with t(8;21).[7]

In conclusion, CD56 expression is a common feature in t(8;21) AML and could be related to monocytic commitment of the neoplastic cells. Nevertheless, these findings should be confirmed with larger studies. Array studies performed on both types of t(8;21) AML could confirm this hypothesis.

Luz Muñoz, Josep F. Nomdedéu, Salut Brunet, Neus Villamor, Mar Tormo,° Jordi Sierra*

*Hematology Division, Hospital de la Santa Creu i Sant Pau, Barcelona; *Hospital Clínic, Barcelona; °Hospital Clinico Universitario, Valencia, Spain*

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Correspondence: Josep F. Nomdedéu, Laboratori d´Hematologia, Hospital de la Santa Creu i Sant Pau, Avda Sant Antoni M. Claret, 167, 08025 Barcelona, Spain. Phone: international +34-93-2919000-ext. 2359 – Fax: international +34-93-2919192

E-mail: jnomdedeu@hsp.santpau.es

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