CD79b expression in B-cell chronic lymphocytic leukemia

We report on the expression of the immunoglobulin-associated membrane protein B29 (recognized by CD79b) in 71 cases of immunologically typical (CD5⁺ CD23⁺) B-cell chronic lymphocytic leukemia using CB3-1 clone. Only 8 cases (11.2%) displayed the CD79b antigen. The expression of CD79b was also found to be related to atypical morphology and strong immunoglobulin density.

Sir,

CD79b monoclonal antibody (B29) identifies a Bcell restricted molecule that is part of the mb1/B29 disulphide-linked heterodimer which is non-covalently associated with membrane IgM and IgG to constitute the B-cell antigen receptor complex.¹ Both B29 and mb1 are restricted to B-lymphocytes, first appearing on the surface at the pre-B-cell stage and remaining through all stages of B-cell differentiation prior to plasma cells.² Starting from the observations first reported by Matutes *et al.*,^{3,4} CD79b is now largely used as one of the most useful markers to discriminate different entities belonging to the broad spectrum of B-cell chronic lymphoproliferative disorders (CLDs).⁵ In fact, the Royal Marsden British Group has recently proposed to substitute, in their initial immunological scoring system based on 5 markers CD22, CD23, FMC7 and (CD5, surface immunoglobulin density), CD79b for CD22 because of its ability to increase diagnostic accuracy (from 91.8% to 96.8%).6 Indeed, using SN8 clone in a large cohort of chronic lymphocytic leukemia (CLL) patients these authors found that only 5% of cases expressed CD79b, whereas a greater number of positive cases was usually detected in other CLDs. However, several other investigators7-10 who have selectively analyzed the CD79b expression in CLL have reported quite conflicting results (Table 1).

We describe here our experience in this field. Peripheral blood samples from 71 immunologically typical (CD5+CD23+) B-CLL untreated patients were analyzed by means of flow cytometry (FACSort, Bec-

Table 1. CD79b expression in CLL (published reports).

Investigators	MoAbs used	No. of CLL evaluated	% of CD79b⁺ cases	Clinico-biological features of CD79b+ CLL
Zomas	SN8	330	5	Correlation with atypical morphology and with strong expression of surface Ig and/or CD22
Molica	SN8	69	15.9	No peculiar clinical features. Correlation with strong surface Ig and CD20 density and FMC7 expression
Alfarano	SN8*	40	25	Not reported (molecular study)
Garcia vela	CB3-1	40	7.5°	Correlation with advanced clinical stage (B and C Binet); all cases with atypical morphology were CD79b+; correlation with strong expression of SmIg
Thompson	CB3-1	22	27	Only the correlation with level of Smlg reported

*In 10 cases CB3-1 was tested along with SN8; no differences between the two monoclonal antibodies were detected; °42.5% of cases were CD79b-negative, 50% with low expression and 7.5% with normal expression (evaluated as MESF compared to normal controls).

Table 2. Clinico-biological features of B-CLL patients according to the expression of CD79b molecules.

Features	CD79b e Negative	р	
Morphology Typical Atypical	59 4	4 4	<0.01°
Clinical stage (Binet) A B C	53 8 2	7 1 0	ns°
Peripheral blood lymphocytosis (/µL)	22,809±7,154	18,512±8,340	ns#
Pattern of bone marro infiltration* Nodular Interstitial Diffuse	w 12 9 18	1 2 5	ns°
Surface immunoglobu Low High	lin density 62 1	2 6	< 0.04°
FMC7 expression Positive Negative	43 20	4 4	ns°
CD20 ABC values	9,702±10,134	14,774±14,278	ns#
CD22 ABC values	6,670±6,555	5,710±3,409	ns#

Data are expressed as number of cases displaying (+) or not (-) CD79b molecule with the exception of peripheral blood lymphocytosis, CD20 and CD22 ABC values, reported as mean ± standard deviations. *evaluated only in 47 cases; °Chi-square test; #Mann-Whitney test.

ton Dickinson, San José, CA, USA) (BDIS) with a panel of fluorescein (FITC) and phycoerythrin (PE) directly-conjugated monoclonal antibodies including CD19 (Leu-12), CD20 (Leu-16), CD22 (Leu-14), CD23 (Leu-20), CD5 (Leu-1), κ/λ light chains, all purchased from BDIS, and FMC7 (Dako, Glostrup, Denmark) and CD79b (CB3-1, Immunotech, Marseille, France). In addition, QuantiBRITE technology (BDIS) was used to determine the number of molecules/per cell, evaluated as antibody binding capacity (ABC) for CD20 and CD22 antigens.

Eight cases (11.2%) were found to be CD79b-pos-

itive (\geq 30% of reactive cells). As shown in Table 2, in the CD79b-positive group we observed more frequently both atypical morphology (*p*<0.01) and strong surface immunoglobulin density (*p*<0.04). On the other hand, no difference was found with respect to clinical stage, absolute peripheral blood lymphocytosis, pattern of bone marrow infiltration, FMC7 expression, or CD20/CD22 ABC values.

The relatively discordant data reported in the literature on the expression of CD79b antigen by neoplastic B-cells in CLL could be due to the different antibodies (SN8 or CB3-1 clones) or fluorocromes (PE or FITC) used as well as to the heterogeneous clinical, immunologic and laboratory features of patients evaluated. In this setting, we would like to stress that in our hands the substitution of CD79b for CD22 in the practical approach to the diagnosis of leukemic B-cell CLDs has improved our diagnostic ability from 90% to 92% of cases (data not shown). In other words, 8% of CLDs remained difficult to categorize from our immunologic point of view. Thus, further studies on larger numbers of patients with well-defined immunologic characteristics, and testing for both SN8 and CB3-1 clones (conjugated with several fluorocromes) need to be performed in order to obtain more useful informations on the significance of CD79b expression in B-CLL (and in other CLDs). Whether this information will be useful to classify CLDs better and to refine prognostic assessment remains to be established.

Giovanni D'Arena, Nicola Cascavilla, Pellegrino Musto, Rosario Colella Bisogno, * Giuseppe Pistolese, * Mario Carotenuto

Division of Hematology, IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo and *Immunohematology and Transfusional Service, "S. Giovanni di Dio e Ruggi D'Aragona" Hospital, Salerno, Italy

Key words

CD79b, chronic lymphocytic leukemia, flow cytometry

Correspondence

Giovanni D'Arena, M.D., Division of Hematology, IRCCS "Casa Sollievo della Sofferenza", 71013 San Giovanni Rotondo, Italy. Phone: international +39-0882-410315 – Fax: international +39-0882-410258 – E-mail: ematologia@operapadrepio.it

References

- Vasile S, Coligan JE, Yoshida M, Seon BK. Isolation and chemical characterization of the human B29 and mb-1 proteins of the B-cell antigen receptor complex. Tissue Antigens 1993; 31: 419-27.
- Tissue Antigens 1993; 31: 419-27.
 Clark MR, Campbell KS, Kazlauskas A, et al. The B cell antigen receptor complex: association of Ig-alpha and Ig-beta with distinct cytoplasmic effectors. Science 1992; 258: 123-6.
- Matutes E, Owusu-Ankomah K, Morilla R, et al. The immunological profile of B-cell disorders and proposal of a scoring system for the diagnosis of CLL. Leukemia 1994; 8: 1640-5.
- Zomas AP, Matutes E, Morilla R, Owusu-Ankomah K, Seon BK, Catovsky D. Expression of the immunoglobulin-associated protein B-29 in B cell disorders

with the monoclonal antibody SN8 (CD79b). Leukemia 1996; 10: 1966-70.

- D'Arena G, Keating MJ, Carotenuto M. Chronic lymphoproliferative disorders: an integrated point of view for the differential diagnosis. Leuk Lymphoma 2000; 36:225-37.
- Moreau EJ, Matutes E, A'Hern RP, et al. Improvement of the chronic lymphocytic leukemia scoring system with the monoclonal antibody SN8 (CD79b). Amer J Clin Pathol 1997; 108:378-82.
- Cabezudo E, Carrara P, Morilla R, Matutes E. Quantitative analysis of CD79b, CD5 and Cd19 in mature B-cell lymphoproliferative disorders. Haematologica 1999; 84: 413-8.
- Molica S, Levato D, Dattilo A, Lentini M. Clinico-biological features of B-cell chronic lymphocytic leukemia (CLL) expressing the B29 protein of B-cell receptor (CD79b). Haematologica 1999; 84 (EHA-4 abstract book):162.
- Alfarano A, Indraccolo S, Circosta P, et al. An alternatively spliced form of CD79b gene may account for altered B-cell receptor expression in B-chronic lymphocytic leukemia. Blood 1999; 93:2327-35.
- García Vela JA, Delgado I, Benito L, et al. CD79b expression in B cell chronic lymphocytic leukemia: its implication for minimal residual detection. Leukemia 1999; 13:1501-5.

Non-gastrointestinal malt lymphomas: a study of 10 cases and comparison with 27 patients with gastrointestinal MALT lymphoma

The main clinical and analytic parameters, the response to treatment and survival in patients affected by gastrointestinal (n=27) or extradigestive (n=10) MALT lymphomas diagnosed in a period of 15 years in a single hospital were analyzed. The location, gastrointestinal or not, did not have any influence on either the response to treatment (85% vs 100%), overall survival (71% vs 100%) or diseasefree survival (61% vs 89%) probabilities.

Sir,

Mucosa-associated lymphoid tissue (MALT) lymphomas are a subtype of extranodal lymphomas characterized by local involvement and good response to conservative therapy.¹⁻³ The stomach is the most common location of MALT lymphomas although other mucosal organs or tissues can be involved.^{4,5} There are few studies focused on the influence of the localization of MALT lymphomas on prognosis. We analyzed the response to treatment and survival of a group of 10 patients diagnosed with extradigestive MALT lymphoma in a single hospital, and compared such features with those of 27 patients with gastrointestinal MALT lymphoma diagnosed in the same center and the same period.

From November 1983 to October 1998, 15 patients were diagnosed with extranodal lymphomas arising in non-gastrointestinal MALT sites. In 10, unequivocal criteria of MALT lymphoma were demonstrated. The mean (SD) age was 60±17 years and 7 patients were females. The main clinical and analytic parameters are reported in Table 1. The primary site involved was the parotid gland (6 patients), the conjunctiva (3 cases)