WHAT DOES ATYPICAL CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) REALLY MEANS? MORPHOLOGY VS IMMUNOPHENOTYPE

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BACKGROUND

Atypical CLL is defined according to the well established French-American-British (FAB) morphological criteria of peripheral blood lymphocytes. Despite no criteria have been proposed to differentiate typical and atypical CLL from an immunophenotypic point of view, the definition of immunological atypical CLL, defined as deviance from the typical immunophenotypic profile (i.e., high expression of CD20 and/or CD22 and/or SmIg, CD79b and/or FMC7 expression), is frequently used.

METHODS

A cohort of 72 patients (mean age 68 yrs; range 48-89 yrs; 46 [61%] males), with CLL diagnosed at our Institution was reviewed aiming at evaluating whether a correlation between the morphological diagnosis of atypical CLL and immunophenotypic definition of atypical CLL, defined, has a clinical and biological relevance

Stored May-Grunwald Giemsa peripheral blood smears from 72 patients with CLL diagnosed at our Institution, according to iwCLL criteria, were independently reviewed by two of us (G.D and G.P.) . Medical records of these patients collected at diagnosis were also evaluated. Only patients with a complete immunophenotypic profile (CD5/CD19/CD23/CD20/CD22/FMC7/CD79b/CD43 /CD200,kappa and lambda) and a follow-up longer than 12 months were included in the study.

Patients were classified as having typical or atypical CLL according to FAB morphological criteria and according to the deviation from the typical immunophenotypic profile: deviation from the typical immunophenotypic (CD5+, CD23+, CD20+ and CD22+ at low expression, negativity for CD79b and FMC7, weak expression of surface immunoglobulin light chains) for at least two antigens.

RESULTS

Twenty-eight pts were found discordant for both morphology and immunophenotype and 48 concordant. No differences were found according to Binet clinical stage, WBC and lymphocyte count, hemoglobin levels and platelet count, IgVH (mutated or unmutated) status, FISH abnormalities according to Dohner classification, LDH and beta2-microglobulin serum concentrations. Time to-first-treatment and overall survival were also not different. Data are summarized in Table 1.

CONCLUSIONS

We failed to demonstrate the morphological or immunophenotypic atypical features of CLL as a category risk in CLL and the prevalence of morphology or immunophenotype. Probably this is due to the small series of patients. Further evaluation are currently undergoing to try to better define the significance of "atypical" and the role of immunophenotype or morphology, or both, to identify patients with a better or worse prognosis.

Table 1

	All patients (n=76)	Discordant (n=28)	Concordant (n=48)	p
Age, median (range)	68 (48-89)	68 (52-89)	67 (48-88)	NS
Males, number (%)	46 (61%)	17 (61%)	29 (60%)	NS
Binet Stage, number (%)				NS
A	38 (52%)	11 (42%)	27 (58%)	
B	30 (41%)	13 (50%)	17 (36%)	
C	5 (7%)	2 (8%)	3 (6%)	
Bulky disease (Yes/no) (no; %)				
WBC count, x109/L, median (range)	17.9 (9.3-140.3)	15.3 (9.4-93)	19 (9.3-140.3)	NS
Lymphocyte count, x109/L, median (range)	13 (5-112.6)	10.3 (5-86.6)	14.1 (5.1-112.6)	NS
Hemoglobin, g/dL, median (range)	13.9 (9.6-16.6)	13.2 (9.6-16.6)	14 (9.9-16.4)	NS
Platelet count, x10^9/L, median (range)	174.5 (33-462)	174 (86-265)	175 (33-462)	NS
IGHV unmutated, number (%)	20 (35%)	8 (44%)	12 (31%)	NS
FISH abnormalities, number (%)				NS
Negative	15 (25%)	4 (20%)	11 (27%)	
Del13q14	31 (51%)	10 (50%)	21 (51%)	
Trisomy 12	11 (18%)	5 (25%)	6 (15%)	
Del11q	2 (3%)	0	2 (5%)	
Del17p	2 (3%)	1 (5%)	1 (2%)	
LDH, IU/dL, median (range)	187 (126-530)	192 (134-404)	184 (126-530)	NS
Beta2-microglobulin, mg/L, median (range)	2.3 (1.4-5.6)	2.3 (1.6-5.3)	2.3 (1.4-5.6)	NS

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