

Abstract: P628

Title: RICHTER SYNDROME DIFFUSE LARGE B-CELL LYMPHOMA TYPE: PHENOTYPIC CHARACTERIZATION AND COMPARATIVE ANALYSIS WITH THE ORIGINAL CLL AND WITH DE NOVO DIFFUSE LARGE B-CELL LYMPHOMAS

Abstract Type: Poster Presentation

Topic: Chronic lymphocytic leukemia and related disorders - Biology & translational research

Background:

The immunophenotypic profile of Richter Syndrome diffuse large B-cell lymphoma type (DLBCL-RS) has scarcely been studied, even less compared to the original chronic lymphocytic leukemia (CLL). Besides, suspecting a transformation from a prior non-diagnosed CLL in newly DLBCL may be crucial due to prognostic and therapeutic implications.

Aims:

To characterize DLBCL-RS phenotype and to compare it with the prior CLL population and with de novo (not transformed) DLBCL.

Methods:

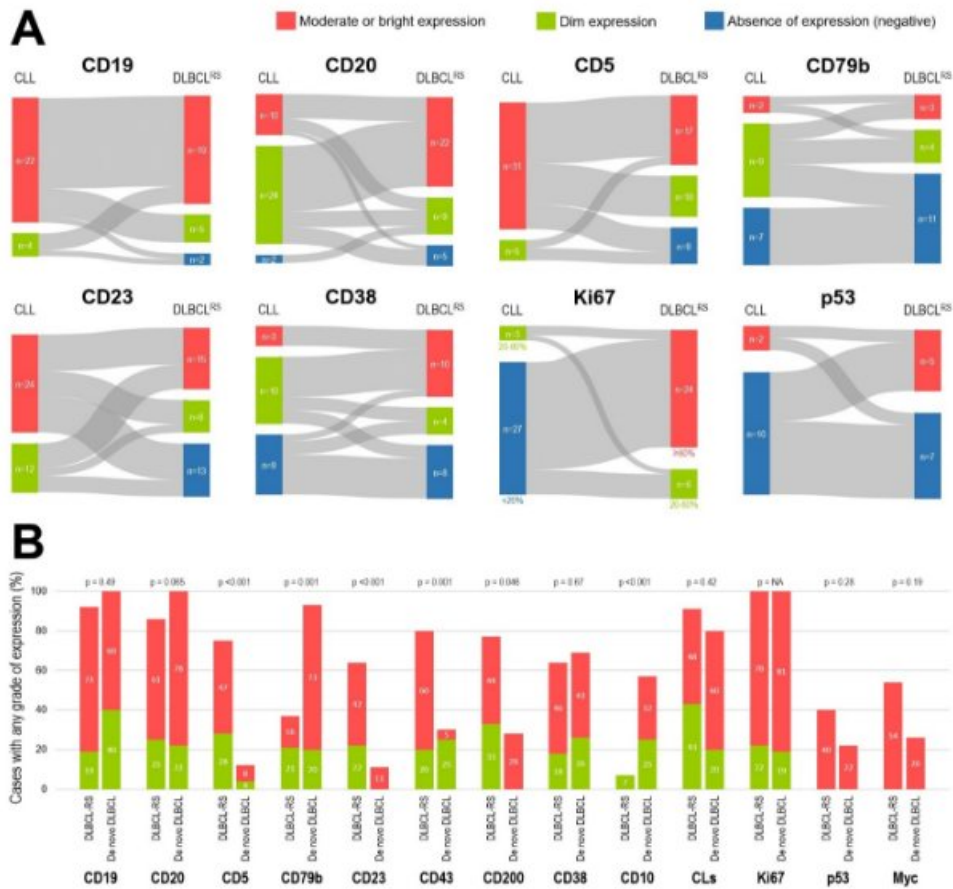
Retrospective multicenter study of patients histologically diagnosed with DLBCL-RS (N=36). Multiparametric flow cytometry (FCM) and/or immunohistochemistry (IHC) were used to characterize the phenotypic profile of DLBCL-RS, classifying marker expression as bright or moderate, low (dim), or absent. Marker-selection was made according to EuroFlow, ERIC, ESCCA, WHO, and ICC recommendations. CLL and DLBCL-RS phenotypes were compared in available tissues. The prognostic impact of each marker on overall survival (OS) was also studied (Kaplan Meier and log-rank). For comparison with de novo DLBCL, a unicentric independent cohort of not transformed DLBCL cases with available FCM and IHC information from bone marrow samples was used (N=28).

Results:

Median age at DLBCL-RS diagnosis was 73 years (33-89) and 50% were males. Five cases were concomitantly diagnosed with CLL and DLBCL-RS; the median time to transformation in the remaining 31/36 was 50 months (5-299), and their median prior CLL lines was 1 (0-4). Clonal relationship was demonstrated in 13/14 cases with available information. Thirty cases received treatment for the DLBCL-RS and the median OS of the global cohort was 6.5 months. **Figure 1A** shows the most relevant phenotypic comparisons between CLL and DLBCL-RS. A substantial variability was found for most markers. CD19, CD20, CD5, CD79b, and CD200 tended to decrease their pattern of expression in the DLBCL-RS phase (17 patients had received rituximab in the CLL). On contrary, CD38 and Ki67 were constant in increasing their expression. Other markers such as CD23 and CD43 showed a higher variability. Two cases were CD10 dim at transformation, while it remained negative in the other 27/29 with available data. The light-chain expression tended to increase after transformation, and two cases presented a switch of the restricted light-chain (one from κ to λ and the other from λ to κ) when compared with the CLL. PD-1 was overexpressed in 46% of DLBCL-RS cases with available data (6/13). CD43 was the only marker related to prognosis, with longer OS for CD43 negative cases compared with dim/positive ones (median OS 26 vs 6 months, $p=0.013$). Compared with an independent cohort of de novo DLBCL cases (**Figure 1B**), patients with DLBCL-RS presented a higher rate of CD5 (75% vs 12%, $p<0.001$), CD23 (64% vs 11%, $p<0.001$), CD43 (80% vs 30%, $p=0.001$), CD200 (77% vs 28%, $p=0.046$), p53 (40% vs 22%, $p=0.28$), and myc (54% vs 26%, $p=0.19$) expression, while CD79b (37% vs 93%, $p=0.001$) and CD10 (7% vs 57%, $p<0.001$) were most commonly expressed in de novo DLBCL.

Summary/Conclusion:

Here is presented one of the largest series focused on the phenotypic comparison between CLL and DLBCL-RS, and between DLBCL-RS and de novo DLBCL. Richter transformation is a dynamic process which results in phenotypic changes whose determination may be a potential tool for predicting the development of an aggressive B-cell lymphoma from CLL. Substantial phenotypic differences were found between DLBCL-RS and de novo DLBCL, which may be useful to suspect a transformation from an undiagnosed prior CLL.



Keywords: Chronic lymphocytic leukemia, Diffuse large B cell lymphoma, Transformation, Immunophenotype