AID protein expression in chronic lymphocytic leukemia/small lymphocytic lymphoma is associated with poor prognosis and complex genetic alterations

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Author(s) Leuenberger, Mona; Frigerio, Simona; Wild, Peter J.; Noetzli, Franziska; Korol, Dimitri; Zimmermann, Dieter R.; Gengler, Carole; Probst-Hensch, Nicole M.; Moch, Holger; Tinguely, Marianne
Author(s) at UniBasel Probst Hensch, Nicole ;
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The biological behavior of chronic lymphocytic leukemia and small lymphocytic lymphoma is unpredictable. Nonetheless, non-mutated IgV(H) gene rearrangement, ATM (11q22-23) and p53 (17p13) deletion are recognized as unfavorable prognosticators in chronic lymphocytic leukemia. The mRNA expression of activation-induced cytidine deaminase (AID), an enzyme indispensable for somatic hypermutation processes, was claimed to be predictive of non-mutated chronic lymphocytic leukemia cells in blood. Here, we evaluated AID protein expression compared with known molecular and immunohistochemical prognostic indicators in 71 chronic lymphocytic leukemia/small lymphocytic lymphoma patients using a tissue microarray approach. We found AID heterogeneously expressed in tumor cells as shown by colocalization analysis for CD5 and CD23. Ki-67 positive paraimmunoblasts of the proliferation centers displayed the highest expression. This observation is reflected by a significant association of AID positivity with a high proliferation rate (P=0.012). ATM deletion was detected in 10% (6/63) of patients and p53 deletion in 19% (13/67) of patients. Moreover, both ATM (P=0.002) and p53 deletion (P=0.004) were significantly associated with AID. IgV(H) gene mutation was seen in 45% (27/60) of patients. Twenty-five percent (17/69) of patients with AID-positive chronic lymphocytic leukemia/small lymphocytic lymphoma displayed a shorter survival than AID-negative chronic lymphocytic leukemia/small lymphocytic lymphoma patients (61 vs 130 months, P=0.001). Although there was a trend, we could not show an association with the IgV(H) gene mutation status. Taken together, our study shows that AID expression is an indicator of an unfavorable prognosis in chronic lymphocytic leukemia/small lymphocytic lymphoma patients, although it is not a surrogate marker for the IgV(H) status. Furthermore, the microenvironment of proliferation centers seems to influence AID regulation and might be an initiating factor in its transformation

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