Immune thrombocytopenia in patients with chronic lymphocytic leukemia is associated with stereotyped B-cell receptors

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Abstract

Purpose: To assess biologic features related to the development of immune thrombocytopenia (ITP) in patients with chronic lymphocytic leukemia (CLL).

Experimental design: We retrospectively analyzed 463 patients with CLL with available immunoglobulin heavy-chain variable (IGHV) gene status and B-cell receptor (BCR) configuration [heavy-chain complementary-determining region 3 (HCDR3)], of whom thirty-six developed ITP, according to previously defined criteria. Most of them had available cytogenetic analysis.

Results: We observed a significant association between ITP occurrence and IGHV unmutated gene status (P < 0.0001), unfavorable cytogenetic lesions (P = 0.005), and stereotyped HCDR3 (P = 0.006). The more frequent stereotyped HCDR3 subsets were #1 (IGHV1-5-7/IGHD6-19/IGHJ4; 16 of 16 unmutated) and #7 (IGHV1-69 or IGHV3-30/IGHD3-3/IGHJ6; 13 of 13 unmutated), both being significantly more represented among patients developing ITP (P = 0.003 and P = 0.001, respectively). Moreover, restricting the analysis to unmutated patients, subset #7 confirmed its independent significant association with the occurrence of ITP (P = 0.013). Both unmutated IGHV mutational status, del(11)(q23) and stereotyped BCR were significantly associated with shorter time to ITP development (P < 0.0001, P = 0.02, and P = 0.005, respectively) than other patients.

Conclusion: Our data suggest that patients with CLL and peculiar BCR conformations are at higher risk of developing secondary ITP and that stereotyped BCR may be involved in the pathogenesis of this complication.

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