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Biologic characterization of adult MYC-translocation positive mature B-cell lymphomas other than molecular Burkitt lymphoma.

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Abstract

Chromosomal translocations affecting the MYC oncogene are the biologic hallmark of Burkitt lymphomas but also occur in a subset of other mature B-cell lymphomas. If accompanied by a chromosomal break targeting the BCL2 and/or BCL6 oncogene these MYC translocation positive (MYC+) lymphomas are called double-hit lymphomas, otherwise the term single-hit lymphomas is applied. In order to characterize the biologic features of these MYC+ lymphomas other than Burkitt lymphoma we explored, after exclusion of molecular Burkitt lymphoma as defined by gene expression profiling, the molecular, pathological and clinical aspects of 80 MYC-translocation positive lymphomas (31 single-hit, 46 double-hit & 3 MYC+-lymphomas with unknown BCL6 status). Comparison of single-hit and double-hit lymphomas revealed no difference in MYC partner (IG/non-IG), genomic complexity, MYC expression or gene expression profile. Double-hit lymphomas showed more frequent GCB-like gene expression profile and higher IGH and MYC mutation frequencies. Gene expression profiling revealed 130 differentially expressed genes between BCL6+/MYC+ and BCL2+/MYC+ double-hit lymphomas. BCL2+/MYC+ double-hit lymphomas showed a more frequent GCB-like gene expression profile. Analysis of all lymphomas according to MYC partner (IG/non-IG) revealed no substantial differences. In this series of lymphomas, in which immunochemotherapy was administered in only a minority of cases, single-hit and double-hit lymphomas had a similar poor outcome in contrast with molecular Burkitt lymphoma and lymphomas without MYC break. Our data suggest that, after excluding molecular Burkitt lymphoma and pediatric cases, MYC+ lymphomas are biologically quite homogenous with single-hit and double-hit lymphomas as well as IG-MYC and non-IG-MYC+ lymphomas sharing various molecular characteristics.

KEYWORDS: Burkitt, DLBCL, Double hit, FISH, MYC

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