BCL-6 EXPRESSION BUT NOT CASPASE-3 EXPRESSION CORRELATES WITH SURVIVAL IN UNSELECTED PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA

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Background: Cleaved caspase-3 based apoptotic counts have been described as a prognostic factor in anaplastic large cell lymphoma and Hodgkin's disease, while evidence of activated B-cell phenotype (ABC) or germinal center differentiation (GC) have been described as a prognostic factor in diffuse large B-cell lymphoma. In this study we investigated the impact on prognosis of cleaved caspase-3 expression and markers of ABC and GC differentiation in diffuse large B-cell lymphoma and correlated cleaved caspase-3 expression with markers of ABC and GC differentiation.

Design: A tissue array of 96 diffuse large B-cell lymphomas from unselected patients (median age 67) was utilized. Immunohistochemical stainings were performed for BCL-2, BCL-6, IRF-4, CD10, CD138, and cleaved (activated) caspase-3. Multiple models of immunohistochemical classification of diffuse large cell lymphoma into GC type and ABC type and compared to cleaved caspase-3 expression. Correlations with prognosis as measured by overall disease specific survival (median follow up 80 months) were performed.

Results: Of all the immunohistochemical stainings analyzed only detection of BCL-6 in neoplastic cells correlated with a better prognosis. None of the various models of immunohistochemical classification into ABC and GC types used, resulted in prognostic stratification of the 96 patients. There was a trend for a higher apoptotic rate to associate with a shorter survival. However, both BCL-2 positive lymphomas and ABC lymphomas showed lowest apoptotic counts, while GC lymphomas and BCL-6 positive lymphoma showed highest apoptotic counts.

Conclusions: The data suggest that of the immunohistochemical staining and subclassification models evaluated, only detection of BCL-6 is sufficiently strong a factor to result in prognostic stratification of unselected patients with diffuse large cell lymphoma. They further suggest that prognostic correlations of diffuse large cell lymphoma should be closely controlled for clinical or patient related factors and therapy. Similarly, Caspase 3 expression, is insufficiently strong a factor to result in prognostic stratification of unselected patients with diffuse large B-cell lymphoma. Bcl-6 positive GC lymphomas, however, retain the high rates of apoptosis of non-neoplastic GC centroblasts, while low spontaneous apoptosis in ABC lymphomas may be related to their frequent expression of BCL-2.