BCL2 gene aberration as an IPI-independent marker for poor outcome in non-germinal-centre diffuse large B cell lymphoma

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AIM: Diffuse large B cell lymphoma (DLBCL) is the most common lymphoid malignancy in the western hemisphere, and is characterised by a highly variable outcome that impedes individual risk assessment. Lacking reliable biomarkers, the international prognostic index (IPI) has been the most reliable factor to predict survival and stratify patients for therapy. The aim of this study was to investigate the frequency and potential prognostic role of BCL2 aberrations on the chromosomal level and the protein level in a large DLBCL collective. METHODS: Fluorescence in situ hybridisation (FISH) with commercially available dual-colour break-apart probes and immunohistochemistry were used to assess BCL2 gene abnormalities and bcl2 protein expression on validated tissue microarrays containing 224 well-characterised cases of primary DLBCL. RESULTS: FISH analysis of BCL2 revealed a break in 40/215 cases (19%) and a gain in 66/171 (39%) cases. Only BCL2 gains correlated with bcl2 protein expression (p = 0.001). Presence of any BCL2 gene abnormality, particularly gains, correlated independently of the IPI with a significantly worse prognosis in DLBCL of non-germinal centre (non-GC) phenotype as opposed to DLBCL of non-GC type without this genetic alteration (p = 0.003). DLBCL of germinal centre phenotype did not show this association. CONCLUSIONS: Cases of DLBCL of the non-GC type with BCL2 gene aberration are accompanied by a significantly worse prognosis as opposed to cases without such gene abnormalities. It may be helpful to asses BCL2 gene abnormalities by FISH in addition to assessing established parameters for individual risk estimation in DLBCL.
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