Progressive humoral immune suppression in indolent B-cell malignancies

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Bacterial infections, particularly of the respiratory tract, are a common cause of morbidity and mortality in B-cell malignancies such as WM, MZL and CLL. Recurrent infections may be due primarily to inhibition of normal B-cell and plasma cell production and function. Individuals with hypogammaglobulinemia have an increased risk of recurrent infections and although intravenous Ig is reported to reduce the risk of infection, it is costly and has variable efficacy. A small proportion of patients at presentation show hypogammaglobulinemia but the majority will show an ineffective response to vaccination.

We have reviewed presentation and longitudinal data on individuals with early stage B-cell disorders including patients with IgM MGUS and asymptomatic WM as well as the pre-malignant condition Monoclonal B-cell Lymphocytosis (MBL) with the aim of identifying better predictors of severe bacterial infection risk. In cases where the neoplastic B-cells represent a small proportion (e.g. <10%) of total circulating B-cells, the outcome is identical to matched controls with respect to overall, disease-free and infection-free survival over a five-year period. This is independent of the abnormal B-cell phenotype. In early stage B-cell malignancies it is possible to detect normal B-cells in the majority of cases at presentation but there is progressive depletion of normal B-cells over time. The depletion is independent of whether the B-cell disorder is stable or progressive. Recurrent infections are common and in individuals without disease progression are a major cause of early mortality. Hypogammaglobulinemia also develops with time but is a relatively late event occuring approximately 2-3 years after normal peripheral B-cells are depleted. Because of the survival duration of normal plasma cells and the long half-life of immunoglobulin it appears that measuring depletion of normal peripheral B-cells could provide a better indicator for risk of infectious morbidity and mortality.