Paraproteins in CLL Are Frequently the Product of Another Clone.

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Abstract

Paraproteins are found in 5–10% of CLL patients using conventional techniques and in a higher number using more sensitive techniques. The significance of this finding is uncertain although it has been suggested to be associated with a worse prognosis. When a paraprotein occurs with CLL it is usually considered to be a product of the leukemic clone. However there is an increased incidence of both B cell clonal expansions and monoclonal immunoglobulins (Igs) in the elderly suggesting an alternative source may exist.

We examined the clinicopathological features of 34

cases of paraproteins who had an immunophenotype consistent with CLL (CD5+ B cells and CD23+ if tested). These were untreated patients who had an elevation of one or more immunoglobulins (Igs) on routine screening and subsequently had immunofixation (IF) to determine the presence of a paraprotein.

In a database of chronic lymphoproliferative disorders 1380 patients had Ig quantitation and 168 were found to have an elevation in one or more Igs. Cases were excluded from this group if the disease was found to be T cell, CD5- or CD23-. This left 116 CLL patients with elevated Igs, of which 53 had IF. A polyclonal increase was detected in 19 and paraproteins in 34 (14 IgG, 16 IgM, 1 IgA and 3 oligoclonal). The level of paraprotein ranged from 0.2–4.4 g/dl for IgG, 0.2–2.4 g/dl for IgM and was 0.4 g/dl for IgA. Bence Jones Protein was associated with both IgG and IgM paraproteins when tested (2 patients in each group). Suppression of other Igs was observed in 12 patients (35%) with paraproteins and only one patient (5%) with a polyclonal increase.

When compared to patients with a polyclonal increase in Igs, the patients with paraproteins had more advanced disease and higher bone marrow lymphocytosis, β2-microglobulin and LDH ($p<0.05$). The immunophenotype in approximately half of the cases in both groups was atypical for CLL with features including CD22+, CD79b+, FMC7+ and moderate to strong expression of surface Ig. Cytogenetic abnormalities were present in 8 of 34 cases with paraproteins but were not detected in the polyclonal group. The most frequent abnormality was trisomy 12 found in 4 cases. The survival of the 2 groups was not statistically different with a median

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The origin of paraproteins is usually considered to be the CLL clone with CLL cells capable of secreting IgM as well as producing IgG and IgA paraproteins by isotype switching. In this cohort 5/14 patients with an IgG paraprotein had a different light chain expressed on the CLL clone. In addition 3/16 patients with IgM paraproteins had biclonal IgMs and in one case the 2 Igs had different light chains suggesting that at least one was not a product of the CLL clone. In conclusion, paraproteins in CLL are frequently not the product of the CLL clone but may reflect an associated age-related restriction in B cell repertoire and existence of other clonal expansions. Further studies are needed to determine if CLL emerges from one of these clones or develops independently.
