Session V: Prognostic, Predictive and Response Markers in WM

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Prognostic relevance of 6q deletion in Waldenström's Macroglobulinemia.
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The deletion of the long arm of chromosome 6 (del (6q)) is the most common cytogenetic abnormality in Waldenström's macroglobulinemia (WM), but its prognostic significance is unclear. We therefore investigated 77 patients with WM by interphase fluorescence *in situ* hybridization (FISH) using 6q21 and 6q25 probes, and correlated the 6q status of the clonal lymphoplasmacytic cells with the patients' clinical features and survival. There were 43 males and 34 females with median age of 63 years (range, 34-89). Overall, FISH detected hemizygous 6q deletions in 32 (41.6%) of the 77 WM cases. The 6q21 locus was deleted in 26 (33.8%) of 77 cases, and 6q25 in 25 (33.8%) of 74 cases. Both 6q21 and 6q25 were deleted in 19 (59.4%) of 32 deleted cases. Patients with 6q deletions had higher C-reactive protein levels than non-deleted patients (p= 0.02). There was no correlation between del (6q) and other biological factors such as age, gender, hemoglobin, platelet count, viscosity, beta-2 microglobulin, albumin, IgM level and degree of bone marrow lymphoplasmacytic infiltration. The median follow-up was 57.5 months with median overall survival of 163 months and a 10-year survival rate of 63%. Twenty-eight (93%) of 30 patients with 6q deletion received treatment, while 32 (80%) of the 40 patients without the deletion were treated (p=0.17). There was no significant difference in time to the initial treatment between deleted and non-deleted groups (median 5.6 months vs. 2.6 months, p=0.46), or overall survivals in patients with and without del (6q) (163 months vs. not reached, p= 0.83). In summary, our study indicates that 6q deletions are frequently detected in WM but do not appear to influence the clinical outcome. The 6q deletion extends beyond 6q21 to involve at least the 6q25 locus. Further studies of a larger series with longer follow-up are indicated to confirm these findings, identify the minimal deleted region on 6q, and search for candidate tumor suppressor gene(s) potentially involved in the pathogenesis of WM.