

[Abstract 11]

GENETIC PREDISPOSITION IN WALDENSTROM'S MACROGLOBULINEMIA

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Background: Sporadic reports have documented the existence of familial cases of various B-cell disorders including Waldenstrom's macroglobulinemia (WM) among patients with WM, though the frequency, as well as any differences in clinical, laboratory and cytogenetic features between patients with and without a familial history remains to be defined.

Methods: We examined the medical records and laboratories for 262 sequential patients who presented over a 5-year period with the consensus panel defined diagnosis of WM. Five patients, all family members of another clinic patient were censored to prevent referral bias. Therefore, data for 257 unique patients were analyzed. Conventional G-banding, metaphase-fluorescence in-situ hybridization (M-FISH), and bacterial artificial chromosome (BAC)-FISH analysis to chromosome 6q were performed for 66 of these patients, 18 of whom had a familial history of a B-cell disorder.

Results: Forty-eight of the 257 (18.7%) unique family patients had at least one first degree relative with either WM (n=13; 5.1%), or a related B-cell disorder: non-Hodgkin's lymphoma (n=9; 3.5%); multiple myeloma (n=8; 3.1%); chronic lymphocytic leukemia (n=7; 2.7%); monoclonal gammopathy of unknown significance (n=5; 1.9%); acute lymphocytic leukemia (n=3; 1.2%) and Hodgkin's disease (n=3; 1.2%). Patients with a familial background of WM or any plasma cell disorder (PCD) were diagnosed at a younger age and had greater bone marrow involvement versus patients without a familial history. BM cytogenetic and M-FISH studies for all patients demonstrated numerical losses in >10% of cases for chromosomes 17, 18, 19, 20, 21, 22, X, Y, and 8, 14, 18, 19, 20, 21, 22 and X, respectively, though no differences between familial and non-familial WM patients was found. Deletions in 6q were also found by conventional G-banding studies in 4 non-familial cases, and this was the only recurrent structural abnormality. BAC-FISH analysis for 6q demonstrated deletions in 6q21-22.1 in most patients, irrespective of familial background.

Conclusions: B-cell disorders are common among first degree relatives of patients with WM. Patients with a family history of WM are more likely to present earlier, and with more bone marrow disease involvement. Deletions in 6q21-22.1 are present in most patients with WM, irrespective of familial background. Genomic studies to help delineate genetic predisposition to WM are underway.