Session II: Genetic Basis and Pathogenesis

of WM and IgM Related Disorders

Abstract 111

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Cytogenetic aberrations in polyneuropathy associated with IgM monoclonal gammopathy. Eurelings M, Lokhorst HM, Notermans NC, Krijtenburg PJ, Kessel B, Eleveld MJ, Bloem A, Wokke JH, Poot M, Buijs A, NETHERLANDS.

The relation of polyneuropathy and IgM monoclonal gammopathy of undetermined significance (MGUS) is well supported. MGUS is characterised by the presence of a monoclonal protein (M-protein) without an underlying haematological malignancy. In patients with MGUS and polyneuropathy malignant transformation occurs more frequent than in patients with MGUS without polyneuropathy. The knowledge of cytogenetic aberrations in IgM MGUS is limited. To determine the occurrence and nature of cytogenetic aberrations we applied interphase fluorescence in situ hybridization (FISH) in 22 patients with polyneuropathy associated with IgM monoclonal gammopathy including 12 patients with MGUS and 10 patients with indolent Waldenström's Macroglobulinemia, multiplex ligation-dependent probe amplification (MLPA) assay in 18 of these patients and genome-wide-array-based comparative genomic hybridization (CGH) in eight of these 18 patients. No cytogenetic aberrations were found in 12 patients with IgM MGUS. Of the 10 patients with LPL four patients had 10-20% and one patient had 30% B cells with IgH translocations; one patient had additional loss of 14qter; one patient had amplification of 6p and loss of 6q. Cytogenetic aberrations may be found in one third of the patients with neuropathy associated with IgM monoclonal gammopathy and are mainly associated with indolent Waldenström's Macroglobulinemia. We also studied V(H)DJ(H) and V(L)J(L) gene use in monoclonal B cells by clonal analysis in 20 of these patients with polyneuropathy and IgM monoclonal gammopathy. V genes associated with bacterial responses appear over-represented and V(H)3-23 was preferentially used.