

[Abstract 56]

IGM MYELOMA: EVALUATION OF IMMUNOPHENOTYPE, CYTOKINE AND MOLECULAR FEATURES.

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A 58 year-old male (JH) presented with hyperviscosity syndrome due to Waldenström's macroglobulinemia (WM) in March 2000. One year later he developed lytic bone lesions not present initially. Biopsy of one of these lesions showed 39% atypical plasma cells which were IgM, kappa positive with no evidence of IgG. Flow cytometry of bone marrow disclosed mu (μ), kappa (κ), CD19, CD38 and CD138-positive cells; CD20 was borderline.

Experience to date regarding osteoclast activating factors (OAFs) known to be important in lytic bone disease has been mainly restricted to typical isotype-switched multiple myeloma (MM). We evaluated the following cytokines in our patient: macrophage inflammatory protein-1 alpha (MIP-1 α), receptor for the activation of NF-Kappa B (RANKL) and osteoprotegerin (OPG) in CD38, κ -positive cells. Intracellular expression of MIP-1 α (7.6%) and RANKL (8.7%) was noted. By contrast, OPG was expressed in only 0.7% of those cells. Serum levels of OPG by ELISA were significantly reduced (3.43 ± 0.20 pmol/l) in JH compared to sera from 13 patients with IgM (6.49 ± 0.77 pmol/l, $p < 0.0005$) and 17 patients with IgG monoclonal gammopathies (4.8 ± 0.45 pmol/l, $p < 0.02$). Cytogenetic studies on the marrow disclosed t(11:14)(q13:32) translocation by FISH, a finding typically associated with IgM MM but not WM. Ig variable (V) gene analysis revealed usage of VH3 (V3-7) donor gene by tumor cells with somatic mutation evident, in the absence of any intraclonal variation. By using signature VH probes, tumor-derived variant isotype-switched transcripts (IgG/A) were identified, indicative of origin from a post-follicular B-cell which arrests during switch events.

In conclusion, this case confirms the cytogenetic and molecular features distinguishing IgM myeloma from WM and MM. To our knowledge, these data provide the first measurements of OAFs and OPG in IgM myeloma. Further studies to analyze these cytokines may aid in understanding the pathogenesis of lytic bone lesions in this unusual disorder.