Incidence and Predispositions to WM

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Increased prevalence of monoclonal gammopathy, abnormal immunoglobulin levels, and recurrent infections in family members of patients with Familial Waldenström's Macroglobulinemia. Z. R. Hunter, L. Ioakimidis, J. Soumerai, C. J. Patterson, L. Xu, X. Leleu, B. T. Ciccarelli, A. Sacco, S. Adamia, E. Hatjiharissi, S. P. Treon. Dana-Farber Cancer Institute, Boston, MA; Dana-Farber Cancer Institute, Boston, MA, USA.

Background: Waldenström's macroglobulinemia (WM) is a B-cell malignancy characterized by IgM secreting lymphoplasmacytic lymphoma. Recurrent sinus infections are commonly observed in WM patients. Familial prevalence of B-cell disorders is seen in up to 20% of patients with WM (Treon et al, Ann Oncol 2006).

Methods: We sought to delineate familial predilections for WM by examining a large cohort of first and second degree family members of WM patients with and without familial histories for B-cell disorders. One hundred forty five family members were enrolled, of whom 87 were in a family with a familial history. Prior medical history, complete blood counts, serum laboratories, immunoglobulin levels, serum immunofixation studies, peripheral blood and cheek cell DNA were collected as part of this IRB approved study.

Results: An increased incidence of recurrent sinusitis (32.9% vs. 12.1%; p=0.004), abnormally low IgA (18.5% vs. 1.9%; p=0.003), elevated total IgM (25.9% vs. 9.4%; p=0.03), and presence of a monoclonal gammopathy (22.9% vs. 1.9%; p=0.0004) were observed among family members of WM patients with a familial B-cell disorders history. Seventeen of the 19 family members with a monoclonal gammopathy within the familial cohort had an IgM monoclonal protein, and 2 had an IgG monoclonal protein. No significant differences in complete blood counts were observed among cohorts.

Conclusions: Among family members of patients with WM with a familial B-cell disorders history, a significantly higher incidence of recurrent sinus infections, abnormally low IgA and elevated IgM levels were observed, along with a ten-fold increased incidence of monoclonal gammopathies. These observations may have important implications in the pathogenesis of WM, and screening efforts for family members of WM patients. Molecular studies to elucidate the underlying genetic basis for these observations are currently underway in our laboratory. An update of this analysis will be presented at the meeting.