Treatment of IgM Related Neuropathies

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There are a number of lymphoproliferative disorders which seem to have an increased incidence of peripheral neuropathies associated with them. These include monoclonal gammopathies of unknown significance, multiple mylemoa, Waldenstroms macroglobulinemia, B cell lymphoma, and chronic lymphocytic leukemia. Many of the patients with these neuropathies have readily identifiable autoantibodies against antigens present on peripheral nerve. These include myelin associated glycoprotein (MAG), sulfatide, and gangliosides such as GM-1. However, many patients with peripheral neuropathy and waldenstrom's macroglobulinemia have no identifiable autoantibody. In these cases the neuropathy may be due to a vasculopathic process caused by increased serum viscocity or by indirectly recruiting complement or through cell mediated destruction. In still other cases there may be an elevated amount of light chains present leading to amyloidosis and direct nerve destruction. Regardless of the mechanism, the common link is the presence of elevated amounts of antibody. In the past the only therapeutic measures consisted of high dose cytotoxic chemotherapy or plasmaphresis. We have treated a number of patients with waldenstroms macroglobulinemia and other neuropathies with elevated levels of IgM antibodies with Rituxamab. With sustained depletion of circulating B-cells levels of autoantibodies and IgM have dropped by as much as 70% with an associated improvement in their neuropathy. In addition, we have identified several cases where there was no identifiable autoantibody, but in whch treatment with Rituxamab has still improved their neuropathy. This argues that elimination of circulating B cells, in addition to directly reducing IgM autoantibodies, may reduce secondary recruitment of the immune system.