Session X: Disease Related Morbidities in

Waldenström's Macroglobulinemia

Abstract 155

Presenter: S. Berentsen

Cold Agglutinin mediated Autoimmune Hemolytic Anemia in Waldenström's macroglobulinemia. Sigbjorn Berentsen Department of Medicine, Haugesund Hospital, Haugesund, and Institute of Medicine, University of Bergen, Bergen, NORWAY.

In primary chronic cold agglutinin disease (CAD), the autoimmune hemolytic process is initiated by cold agglutinins encoded by the VH4-34 gene segment. These monoclonal immunoglobulins are of the IgM class in at least 90% of the patients, with kappa light chain restriction in 95%. Monoclonal CD20+,kappa+ lymphocytes can be detected by flow cytometry of bone marrow aspirates in 90% of the patients, and a clonal lymphoproliferative bone marrow disorder can be verified by histology and immune histochemistry in 75%. Lymphoplasmacytic lymphoma is found in 50%. Thus, CAD represents a spectrum of clonal lymphoproliferative bone marrow disorder in which approximately 50% of the patients can be classified as having Waldenström's macroglobulinemia (WM) according to current criteria. The prevalence of CAD is 16 per million inhabitants and the incidence rate 1 per million per year according to a Norwegian study. Hemoglobin levels are below 8.0 g/dL in one-third of the patients; 50% are considered transfusion dependent at some time during the course of the disease; acrocyanosis and/or Raynaud symptoms are present in more than 90%; and exacerbations during febrile illnesses occur in a majority. Conventional therapies are ineffective; e.g., less than 20% of the patients respond to corticosteroids. Two prospective phase 2 trials and one population based retrospective study, however, have shown partial response to rituximab single agent therapy in 50-55%, using strict response criteria. Median response duration is 11 months. We are currently running a prospective, uncontrolled trial of rituximab and fludarabine combination therapy. Some preliminary results will be presented and may indicate a higher frequency of complete responses, but superiority over rituximab monotherapy remains to be proven. CONCLUSIONS: 50% of CAD patients have WM. CAD is not an "indolent" disease in terms of clinical symptoms and quality of life. The most established therapy is rituximab infusions, but response rates and duration are not optimal. Patients with CAD requiring therapy should be included in clinical trials.