Abstract

Diagnostic and Treatment Criteria for Waldenstrom's Macroglobulinemia

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Waldenstrom's macroglobulinemia (WM) is characterized by the proliferation of B lymphocytes that produce an IgM monoclonal protein. The incidence of WM is 0.5/100,000 with almost 1,500 new cases each year in the United States. The incidence increases with age with a rate of 36/100,000 at age 75 years or older for males. Weakness and fatigue are the most common initial symptoms. Blurring of vision or bleeding from the oronasal area may also occur. Enlargement of the liver occurs in approximately one-fourth of patients at diagnosis, while splenomegaly and lymphadenopathy are slightly less frequent. Funduscopic evidence of hyperviscosity may be seen.

Anemia is a frequent finding. Leucopenia and thrombocytopenia may be present initially. The serum cholesterol level is frequently very low. Renal function is usually normal. Electrophoresis always reveals a spike of the IgM type. Approximately 75% have kappa light chains. Monoclonal light chains (Bence Jones proteinuria) are found in about three-fourths of patients, but it is usually small in amount. Macroglobulins may precipitate in the cold (cryoglobulin) in about 10% of patients, but they are rarely symptomatic. The bone marrow aspirate may be hypocellular, but the biopsy is usually hypercellular and extensively infiltrated with lymphoid or plasmacytoid cells. They express CD19, CD20, CD22 and, of course, a single light chain type. CD9 and CD10 are usually negative, while CD5 is expressed in about 10% of patients. The most common chromosomal abnormality is deletion of 6q21 which is found in almost one-half of patients. Mast cells may be increased and help differentiate macroglobulinemia from other lymphoproliferative disorders. Lytic bone lesions are uncommon. Peripheral neuropathy is present in approximately one-fifth of patients.

A complete history and physical examination including funduscopic examination is necessary. Determination of the serum viscosity should be performed initially. The diagnosis depends upon the demonstration of a monoclonal IgM protein in the serum and monoclonal lymphocytes or plasmacytoid lymphocytes in the bone marrow. It must be differentiated from monoclonal gammopathy of undetermined significance (MGUS) of the IgM type, lymphoma, primary amyloidosis, and chronic lymphocytic leukemia. The presence of an IgM monoclonal protein level of < 3.0 g/dL; the absence of anemia, hepatosplenomegaly, or lymphadenopathy; mild lymphocytic infiltration of the bone marrow; and no constitutional symptoms are suggestive of MGUS of the IgM type.

The initiation of therapy should not be based on the IgM level per se or on the basis of a pathology report indicating significant infiltration of the bone marrow with lymphoid cells. Treatment is indicated if the patient has constitutional symptoms, anemia, hepatosplenomegaly, or lymphadenopathy. Some patients may have symptoms due to the biological effects of the monoclonal IgM protein. Such patients may have symptomatic peripheral neuropathy, cryoglobulinemia, cold agglutinin disease, or primary amyloidosis (AL). These patients may need treatment to control complications from the monoclonal IgM produced by a small clone of lymphocytes. If one is undecided about initiating therapy, the patient should be reevaluated in two or three months. The patient should be advised to return to the physician in the event of any symptoms or untoward problem.