

Waldenström's Macroglobulinemia

Jennifer A. McKenna, RN, MSN, CS, ACNP

Waldenström's macroglobulinemia (WM), first described in 1944, is an uncommon disease caused by abnormal production of monoclonal immunoglobulin M (IgM) macroglobulin (Syms, Arcila, & Holtel, 2001). WM affects approximately 1,500 people in the United States annually and represents 2% of all hematologic malignancies. The median age at diagnosis is 63, a slight male preponderance exists, and the disease is more common among Caucasians than African Americans (Dimopoulos, Galani, & Matsouka, 1999; Dimopoulos, Panayiotidis, Mouloupoulos, Sfrikakis, & Dalakas, 2000; Owen, Johnson, & Morgan, 2000).

WM is a monoclonal gammopathy, a type of disorder that is characterized by a clone of plasma cells or lymphocytes that is capable of producing homogenous immunoglobulin or its components (Alexanian, Weber, & Liu, 1999). Other monoclonal gammopathies include monoclonal gammopathy of undetermined significance, multiple myeloma (MM), and amyloidosis (Alexanian et al.). Although the exact cause of WM is unknown, researchers have suggested the role of genetic predisposition and occupational exposure to leather, rubber, dyes, and paints has been associated with the disorder (Dimopoulos et al., 1999). Radiation exposure and chronic stimulation of the immune system also have been suggested as possible etiologies (McDermott & Bell, 1999).

WM is a B cell lymphoproliferative disorder that resembles MM and chronic lym-

phocytic leukemia (CLL) but is distinguished by its overproduction of monoclonal IgM (Alexanian et al., 1999; Dimopoulos et al., 1999). WM also has been described as a low-grade lymphoplasmacytic lymphoma characterized by the overproduction of IgM. Specific properties of monoclonal IgM and direct tumor infiltration lead to the symptoms and complications of the disease (Dimopoulos et al., 1999).

Pathology and Biology

To understand WM, a brief review of hematopoiesis of the B cell line is essential. Single pluripotent stem cells either self-replicate or differentiate into the lymphoid or myeloid line. The lymphoid cells further differentiate into T or B lymphocytes. B lym-

phocytes mature into immunoglobulin-producing plasma cells. Immunoglobulins are divided into five classes: IgG, IgA, IgM, IgD, and IgE (Sommers, 1998). WM is a disease of late-stage B (i.e., plasmacytoid) cells that overproduce monoclonal IgM (McDermott & Bell, 1999).

WM always involves the bone marrow, but the degree of infiltration varies highly (Dimopoulos et al., 1999, 2000; Owen et al., 2000). The cells of WM express CD19, CD20, and CD52 antigens, but the lack of CD5 and CD23 antigen expression differentiate the immunophenotype of WM from that of other B cell malignancies (Dimopoulos et al., 1999; Owen et al., 2000). The phenotype of WM

has implications for specific, targeted treatments.

Clinical Features

The most common presenting symptoms of WM are weakness and fatigue; abnormal bleeding, particularly from the nose and

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