Plasma Cell Disorders

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KEYWORDS

• MGUS • Multiple myeloma • Waldenström macroglobulinemia • Amyloidosis • POEMS

KEY POINTS

- Monoclonal gammopathy of undetermined significance is a premalignant condition with an incidence of 3% in the general population and a rate of progression to myeloma of 1% per year.
- Myeloma patients can present with anemia, bone lesions, renal dysfunction, and/or hypercalcemia. There are now multiple treatment options for myeloma, which have improved survival.
- Waldenström macroglobulinemia can present with anemia, hyperviscosity, and/or neuropathy. The US Food and Drug Administration has approved ibrutinib to treat Waldenström macroglobulinemia.
- Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes syndrome is a rare disease with a prolonged survival but high rates of disability due to progressive neuropathy.

INTRODUCTION

Plasma cell disorders are a heterogeneous group of blood disorders characterized by the detection of a monoclonal paraprotein in the serum or urine and/or the presence of monoclonal plasma cells in the bone marrow space or, rarely, in other tissues. Plasma cell diseases include monoclonal gammopathy of undetermined significance (MGUS), multiple myeloma (MM), lymphoplasmacytic lymphoma/Waldenström macroglobulinemia (LPL/WM), amyloidosis, and POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, and Skin changes).

MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE

MGUS is a clinically asymptomatic premalignant clonal plasma cell, and in some cases, lymphoplasmacytic disorder that is typically identified incidentally while

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patients are being worked up for other reasons, such as anemia, neuropathy, or hypercalcemia, among others.

MGUS has been identified in 1% to 2% of individuals in studies from the United States and Europe.[1–3] The incidence and prevalence of MGUS increase with age, are higher in men than women, and are higher in individuals of African descent.[4,5] Limited data suggest the incidence of MGUS in Asians and Hispanics is lower than in Caucasians.[6,7] First-degree relatives of patients with MGUS have a higher risk of developing other plasma cell disorders.[8,9]

Current population-based data support that about half of individuals diagnosed with MGUS at age 70 had had a monoclonal paraprotein for 10 years.[10] Patients are typically diagnosed due to the presence of a monoclonal paraprotein in serum or urine protein electrophoresis (SPEP and UPEP, respectively). Immunoglobulin G (IgG) MGUS is the most common type (70% of the cases), followed by IgM (15%) and IgA (12%).[11] IgD, IgE, and light chain–only MGUS have been reported.

The diagnosis of MGUS is made when a monoclonal paraprotein less than 3 g/dL is found in an asymptomatic patient. The minimum initial evaluation for patients with MGUS should include the following:

- Complete blood count (CBC)
- Serum calcium and creatinine levels
- SPEP/UPEP with immunofixation
- Serum free light chain (FLC) levels and ratio
- Quantitation of immunoglobulins
- Skeletal survey (radiographs)

A bone marrow biopsy is indicated in patients with an IgG monoclonal paraprotein greater than or equal to 1.5 g/dL, patients with non-IgG (IgM, IgA, IgD, light chain–only) monoclonal paraprotein of any size, patients with an abnormal FLC ratio, and in patients with abnormalities of the CBC, creatinine, calcium, or radiographs. Therefore, a bone marrow biopsy can be deferred in patients with IgG MGUS with monoclonal protein less than 1.5 g/dL, normal FLC ratio, and with no clinical concerns for myeloma. In patients with IgM MGUS, computed tomography (CT) scans should be considered to evaluate for the presence of lymphadenopathy and/or hepatosplenomegaly.

The diagnostic criteria for MGUS are as follows[12]:

Diagnostic criteria for non-IgM MGUS
- Presence of a serum monoclonal protein (IgG, IgA, or IgD) less than 3 g/dL
- Fewer than 10% clonal plasma cells in the bone marrow
- Absence of lytic bone lesions, anemia, hypercalcemia, and renal insufficiency related to the plasma cell disorder.

Diagnostic criteria for IgM MGUS
- Presence of a serum IgM monoclonal protein less than 3 g/dL.
- Fewer than 10% clonal plasma cells in the bone marrow
- Absence of anemia, constitutional symptoms, hyperviscosity, lymphadenopathy, hepatomegaly, or splenomegaly related to the plasma cell disorder

Diagnostic criteria for light chain MGUS
- Abnormal FLC ratio (ie, kappa to lambda ratio <0.26 or >1.65)
- Increased level of the appropriate involved light chain
- No monoclonal immunoglobulin heavy chain (IgG, IgA, IgD, or IgM)
- Fewer than 10% clonal plasma cells in the bone marrow