State-of-the-Art Imaging and Staging of Plasma Cell Dyscrasias

Behrang Amini, MD, PhD[a], Sarvari Yellapragada, MD[b], Shetal Shah, MD[c], Eric Rohren, MD, PhD[d], Raghunandan Vikram, MD[e,*]

KEYWORDS

• Plasma cell dyscrasias • Monoclonal gammopathy of unknown clinical significance • Smoldering myeloma • Multiple myeloma • Solitary plasmacytoma • Imaging

KEY POINTS

- Monoclonal gammopathy of unknown significance (MGUS) is a clinically asymptomatic premalignant clonal plasma cell or lymphoplasmacytic proliferative disorder.
- Smoldering multiple myeloma (SMM), also called asymptomatic multiple myeloma (MM), is an intermediate stage between MGUS and symptomatic MM.
- As the name implies, extraosseous or extramedullary myeloma refers to the presence of myeloma deposits outside the skeletal system.
- Waldenström macroglobulinemia (WM) is a distinct subtype of plasma cell dyscrasia characterized by lymphoplasmacytic lymphoma (LPL) in the bone marrow with an associated IgM monoclonal gammopathy.
- Amyloidosis is a condition characterized by extracellular deposition of fibrils composed of a variety of normal serum proteins.

INTRODUCTION

Plasma cell neoplasms, characterized by clonal proliferation of plasma cells in the bone marrow, comprise a wide spectrum of tumors of variable clinicobiological behavior. They are typically associated with secretion of monoclonal immunoglobulins or immunoglobulin fragments (M-protein, myeloma protein, or paraprotein).[1] These M proteins classically consist of 2 heavy polypeptide chains of the same class (IgG, IgA, and less commonly IgD, IgE, and IgM) and 2 light polypeptide chains of the same type (kappa and lambda).

Plasma cell neoplasms have been challenging to classify in a way that is both biologically correct and clinically useful.[2] The current World Health Organization (WHO) classification places plasma cell neoplasms under the broad category of mature B-cell neoplasms and includes MGUS, solitary plasmacytoma of bone (SPB), plasma cell myeloma (PCM) or multiple myeloma (MM), extraosseous plasmacytoma, and monoclonal immunoglobulin deposition diseases as subcategories.[3]

[a] Musculoskeletal Imaging, Diagnostic Radiology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA; [b] Hematology & Oncology, Medicine, Michael E DeBakey VA Medical Center, Baylor College of Medicine, 2002 Holcombe Boulevard, Houston, TX 77030, USA; [c] Diagnostic Radiology, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA; [d] Nuclear Medicine, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA; [e] Abdominal Imaging, Diagnostic Radiology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA
* Corresponding author.
E-mail address: rvikram@mdanderson.org

Radiol Clin N Am 54 (2016) 581–596
http://dx.doi.org/10.1016/j.rcl.2015.12.008
0033-8389/16/$ – see front matter

From a clinical perspective, classification aims to separate patients who do not require systemic therapy (those with MGUS, asymptomatic PCM, and SPB) from those who do (those with symptomatic PCM and MM). This classification is predominantly laboratory based (**Box 1**); however, imaging plays an important role in evaluating the disease burden as well as its complications. Performance of laboratory tests, such as total serum protein, serum albumin, serum and urine protein electrophoresis, quantitative immunoglobulins, immunofixation in serum and urine, and for detection of immunoglobulin free light chains, allows accurate diagnosis of patients with suspected plasma cell dyscrasias. In addition, complete blood cell count, serum creatinine, and electrolytes, including calcium, lactate dehydrogenase, and β_2-microglobulin are obtained. In a patient with suspected MM, a bone marrow aspirate and biopsy should be obtained to determine the percentage of plasma cells and for prognostic studies, such as fluorescence in situ hybridization (FISH).

Box 1
Diagnostic criteria for plasma cell myeloma and related disorders

Monoclonal gammopathy of undetermined significance

M protein in serum <30 g/L

Bone marrow clonal plasma cells <10% and low level of plasma cell infiltration in a trephine biopsy (if done)

No evidence of other B-cell proliferative disorders

No related organ or tissue impairment (see **Box 2**)

Asymptomatic (smoldering) myeloma

M protein in serum ≥30 g/L and/or ≥10% clonal plasma cells in bone marrow

No related organ or tissue impairment (see **Box 2**)

Solitary plasmacytoma (solitary plasmacytoma of bone; solitary extraosseous plasmacytoma)

Single area of bone destruction due to clonal plasma cells or single extraosseous deposit

No M protein in serum and/or urine

Bone marrow not consistent with MM

Normal skeletal survey (and MR imaging of spine and pelvis if done)

No related organ or tissue impairment (see **Box 2**)

Symptomatic multiple myeloma

M protein in serum or urine (no levels specified)

Clonal plasma cells in bone marrow or plasmacytoma (>60%)

Related organ or tissue impairment heavy chain disease

Once a diagnosis of symptomatic MM is made, its staging under the International Staging System is entirely laboratory based, which relies on serum β_2-microglobulin and serum albumin to classify the disease into a 3-stage system to indicate different levels of projected survival rates and point to increasingly aggressive treatment strategies.[4] Recently, the revised ISS has also been published, which incorporates the FISH data and lactate dehydrogenase level creating a more robust prognostic model.[5]

An important point is that the number of bone lesions on skeletal survey is not included in the current diagnostic or prognostic models. A minimum of 2 or 3 lytic bone lesions has been erroneously propagated in radiology literature as required for the diagnosis of symptomatic PCM; however, as noted by other investigators,[6] cutoffs for bone lesions on skeletal survey do not appear in the myeloma literature. As evident in **Box 1**, a single bone lesion in the setting of the appropriate laboratory findings is sufficient for a diagnosis of MM. A more recent staging system, the Durie/Salmon PLUS staging system,[7] uses the number of bone lesions on PET-CT and MR imaging in categorizing the severity of disease; however, this system has failed to gain widespread acceptance.

MONOCLONAL GAMMOPATHY OF UNKNOWN SIGNIFICANCE

MGUS is a clinically asymptomatic premalignant clonal plasma cell or lymphoplasmacytic proliferative disorder. It is the most common type of plasma cell dyscrasia and is seen in more than 3% of the general population aged 50 years or older.[8] It is 2 to 3 times more common in Africans and African Americans compared with whites and the incidence increases with age. It is clinically important because it is considered a premalignant condition, a precursor to MM. Patients with MGUS are associated with an overall 1% per year risk of progression to MM (**Fig. 1**). MGUS can further be stratified into risk categories based on the type and quantity of the M protein and the serum free light chain, helping define the risk of evolution per year into symptomatic MM. MGUS, by definition, should have no symptoms that can be attributable to the underlying plasma cell disorder