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ELDER CARE

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Multiple Myeloma: a Disease of Older Adults

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Multiple myeloma (MM) is disorder in which an abnormal clone of plasma cells proliferates in the bone marrow. Plasma cells make antibodies (immune globulins) and in MM a clone of abnormal plasma cells produces large amounts of an abnormal immune globulin-like paraprotein, resulting in a "monoclonal gammopathy." This paraprotein is found throughout the body and leads to end-organ damage.

MM occurs predominantly in older adults with a median age at diagnosis of 70 years. It is twice as common among African Americans than in other racial/ethnic groups. With the growing aging population, the annual incidence of MM is projected to nearly double over the next 20 years.

Clinical Presentation

About 30% of patients with MM are asymptomatic at the time of diagnosis. They are diagnosed incidentally as a result of abnormalities found during routine laboratory testing.

The remainder of patients present with one or more clinical and/or laboratory findings referred to with the acronym "CRAB" which stands for hyper**C**alcemia, **R**enal failure, **A**nemia, and **B**one abnormalities. Bone abnormalities such as lytic lesions occur in about 90% of MM patents, about one-third of patients with MM are diagnosed after sustaining a pathologic fracture.

Other manifestations of MM may include infections (commonly pneumococcal infections, often related to suppression of normal immunoglobulin production by MM plasma cells in the bone marrow); hyperviscosity-related symptoms (malaise, paresthesia, headaches); and occasionally thrombocytopenia.

Diagnostic Evaluation

Tests used in the evaluation of patients with suspected MM are summarized in the Table 1. Although not all of these tests are essential to establish the diagnosis, test results are useful for disease staging and establishing prognosis.

When interpreting test results, it is important to realize that MM is actually part of a spectrum of monoclonal gammopathies. On one end of the spectrum is monoclonal gammopathy of unknown significance (MGUS). MGUS is a common condition, occurring in 3% of more of older adults. Of patients with MGUS, only about 1% develop overt MM each year.

Further along the spectrum is smoldering multiple myeloma (SMM), which has a much higher progression risk (10% per year). On the far end of the spectrum is MM itself. The criteria used to diagnose MGUS, SMM, and MM are shown in Table 2.

Table 1. Diagnostic Evaluation for Multiple Myeloma

Laboratory studies:

- Complete blood count with differential
- Comprehensive metabolic panel
- Serum protein electrophoresis (SPEP) and immunofixation
- Quantitative immunoglobulin levels (IgG, IgA, IgM)
- Serum free light chain assay
- Serum beta-2 macroglobulin
- Lactate dehydrogenase (LDH)
- Urine protein electrophoresis (UPEP) and immunofixation
- Bone marrow aspirate/biopsy with flow cytometry, cytogenetics, and fluorescent *in situ* hybridization (FISH)

Imaging:

- Radiographic skeletal survey, whole-body MRI, or whole-body PET/CT scan

Staging

A new staging system for MM was released in 2015. It is based on lab test results including beta-2 macroglobulin level, cytogenetics, albumin level, and lactate dehydrogenase levels. Staging criteria and 5-year survival rates for each stage are shown in Figure 1.

TIPS FOR DEALING WITH MULTIPLE MYELOMA (MM) IN OLDER ADULTS

- Use current diagnostic criteria and staging for MM provide more accurate diagnosis and risk stratification.
- Use the IMWG frailty scoring system to help select the optimal therapy based on a patient's level of fitness to tolerate treatment.
- Collaborative interdisciplinary care is the optimal way to provide care for older adults with MM.

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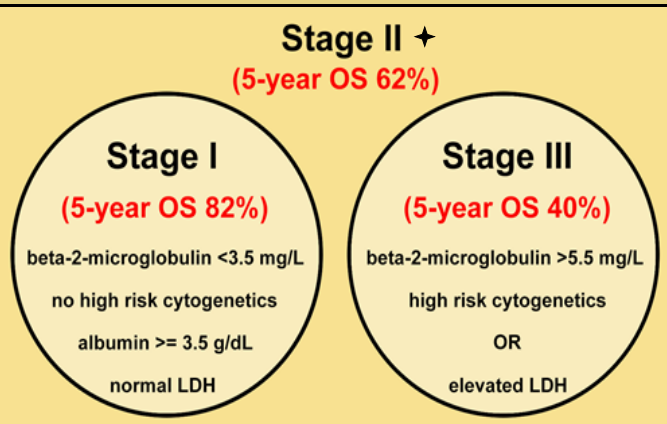
Table 2. Diagnostic Criteria for MGUS, SMM, and MM	
MGUS	<10% clonal plasma cells in bone marrow AND Serum monoclonal protein <3 g/dL AND No myeloma-defining CRAB events
SMM	10-60% clonal plasm cells in bone marrow AND/OR Serum monoclonal protein ≥3 g/dL or ≥500 mg per 24 hours AND No myeloma-defining CRAB events
MM	≥10 % clonal plasma cells in bone marrow and occurrence of myeloma-defining CRAB events OR ≥60% clonal plasma cells in bone marrow, or >1 focal skeletal lesions, or ratio of involved-to-uninvolved serum free light chains ≥100
CRAB events include: hyper**C**alcemia, **R**enal failure, **A**nemia, or **B**one abnormalities	

Figure 1. Staging of Multiple Myeloma



OS = overall survival, LDH = lactate dehydrogenase
✦ Stage II refers to patients with MM who do not meet criteria for Stage 1 or III

Approach to Treatment of MM in Older Adults

There has been a growing awareness of how frailty can affect treatment tolerance and prognosis in older adults with MM. Studies show that about one-third of patients with MM are frail at the time of diagnosis, but MM therapy has largely been based on studies involving non-frail patients.

In 2015, the International Myeloma Working Group (IMWG) developed a frailty scoring system that predicts risks of toxicity and death in older adults with MM. The scoring system categorizes patients into three fitness levels (fit, intermediate fitness, and frail). The overall 3-year survival rates vary from 84% in fit patients, to 76% in those with intermediate fitness, to only 57% in those categorized as frail. A calculator for computing the frailty score is at http://www.myelomafrailtyscorecalculator.net/.

Using the calculator to categorize patients allows clinicians to better match therapies to a patient's ability to tolerate them. More aggressive therapies with multiple pharmaceutical agents and autologous peripheral blood stem cell transplantation can be considered for fit patients regardless of age. Conversely, the classification scheme can help avoid complications that might occur if those Less aggressive therapy regimens are often tolerated and can provide benefit to less fit older adults.

Discontinuing Treatment

Even though recent advances in treatment have resulted in longer survival times, MM is still an incurable disease. As a result, one challenge is determining when to consider discontinuing treatments aimed at prolonging survival and instead, turning to end-of-life (EOL) care, including hospice care. The decision is not always easy because disease progression in MM is less predictable than with other kinds of cancer.

Although there are no formal consensus guidelines, experts have identified factors that influence when to initiate EOL care in patients with MM. Advanced age with frailty is one factor. For those receiving treatment, factors that suggest the need to discontinue treatment and initiate EOL include treatment-refractory disease, shorter progression-free intervals during treatment, and worsening functional status.

Given the complexity of patient factors and the variety of therapy options, selecting optimal treatment regimens, and knowing if and when to discontinue treatment, requires the expertise of a medical hematologist/oncologist in collaboration with the patient's primary care clinician and other members of an interdisciplinary team.

References and Resources

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