Monoclonal Gammopathy of Undetermined Significance and Multiple Myeloma in Older Adults

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KEYWORDS

• MGUS • Multiple myeloma • Older adult • Elderly • Geriatric • Cancer • Neoplasm

KEY POINTS

- Monoclonal gammopathy of undetermined significance and multiple myeloma (MM) are plasma cell disorders of advanced age.
- Unexplained anemia, hypercalcemia, renal insufficiency, or bone pain, among other symptoms, should prompt a work-up for a plasma cell disorder.
- Chemotherapy is standard of care for MM and, although incurable, survival in MM is progressively improving thanks to new drugs.
- Treating MM in older adults requires careful monitoring, dosing, and management of toxicity to attain good outcomes.
- Geriatric assessment and other novel instruments may soon enable personalization of MM therapy for older adults.

INTRODUCTION AND EPIDEMIOLOGY

Monoclonal gammopathy of undetermined significance (MGUS) and multiple myeloma (MM) are disorders on the spectrum of plasma cell dyscrasias that are diseases of aging. In multiple population-based studies, the prevalence of MGUS increases with age; 5.3% of people greater than or equal to 70 years old and 7.5% of people greater than or equal to 85 years old.[1] The median age at diagnosis of MM

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is 69 years, with half of deaths from MM occurring in patients aged 75 years and older (Fig. 1).[2] MM accounts for about 10% of all hematologic malignancies and 1.6% of all new cancer cases in the United States.[2,3] It is estimated that there will be 26,850 new cases of MM in 2015. MGUS and MM are more common in men than in women, and in African Americans than in white people.[1,2,4,5]

Five-year overall survival in MM has increased from 29.7% in 1990 to 45.1% in 2007,[2] largely attributable to novel therapies.[6]

Given the anticipated growth in the older adult population and presumably static prevalence rates as a function of age, the raw numbers of older adults with plasma cell disorders will increase over time. Therefore, a familiarity with MM and MGUS is, and will remain, important for geriatricians.

BIOLOGY AND CAUSE

MM is a malignancy of plasma cells, terminally differentiated B lymphocytes that secrete antibodies when exposed to specific antigens. The exact pathogenesis of MM and MGUS is not well understood. Virtually all cases of MM are thought to arise from MGUS, a premalignant, asymptomatic proliferation of plasma cells.[7,8] The initiation of MGUS is likely an abnormal plasma cell response to antigenic stimulation that leads to primary cytogenetic abnormalities and other genomic changes; the resultant derangement of plasma cell biology ultimately causes plasma cell clonal expansion and in some cases clinically significant disease. The expanded plasma cells usually overproduce a complete monoclonal immunoglobulin or some part thereof (eg, light chain only).[9,10] The transition in some cases from MGUS to MM is thought to be caused by additional biological abnormalities (eg, genomic, bone marrow microenvironmental) that lead to further clonal proliferation.[9] Once MGUS has progressed to MM, end organ damage begins because of infiltration of the neoplastic plasma cells into the bones and organ systems, damage mediated by circulating monoclonal

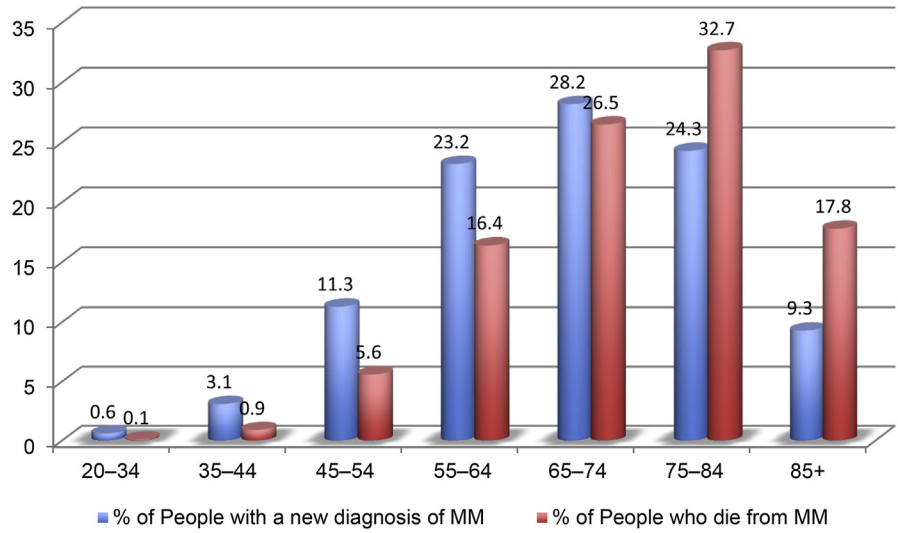

Fig. 1. Age distribution of patients with MM and deaths from MM. (*Data from* Institute NC. SEER stat fact sheets: myeloma. 2015. Available at: http://seer.cancer.gov/statfacts/html/mulmy.html. Accessed May 18, 2015.)