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A Bone to Pick Regarding Use of Magnetic Resonance Imaging to Begin Treatment in Patients With Asymptomatic Multiple Myeloma

TO THE EDITOR: On the basis of results from recent studies, some patients with asymptomatic multiple myeloma (AMM) have been reassigned to a category of early myeloma in need of treatment because of a high risk (> 80%) of progression in 2 years. Two findings at the time of diagnosis that support consideration of immediate therapy for patients are bone marrow plasmacytosis of greater than 60% and a high involved-to-uninvolved free light chain ratio of greater than 100.[1] Early identification and treatment could prevent disease-related morbidities in a group for whom the disease almost inevitably is destined to progress. Findings from a recent study also suggest a survival advantage with treatment for high-risk asymptomatic patients.[2]

The article by Dimopoulos et al[3] suggests that a third finding when AMM is diagnosed, that of greater than one focal lesion on magnetic resonance imaging (MRI) of the spine and pelvis, should also prompt immediate treatment. This recommendation is predominantly based on previous studies by Hillengass et al[4] and Kastritis et al.[5] However, it is not clear that the data presented justify the recommendation. Hillengass et al[4] identified 23 patients with greater than one focal lesion on MRI, but 13 of the 23 patients also had evidence of a diffuse marrow abnormality, itself a significant independent risk factor for progression in multivariable analysis. Only 10 patients had greater than one focal lesion in the absence of diffuse marrow abnormality, and a grouping together of all patients with greater than one lesion seemed certain to overestimate the severity of a few lesions by assigning these patients the same risk as those who had more extensive disease. Numbers count in symptomatic multiple myeloma, and greater than seven focal lesions is associated with a worse outcome. It seems likely that the same would hold true in patients with AMM.[6]

Kastritis et al[5] found that nine of 67 patients had greater than one focal lesion and that 69% of patients with more than one lesion experienced progression to symptomatic multiple myeloma within 2 years.[5] However, six of the nine patients with greater than one focal lesion on MRI had other high-risk features, such as marrow plasmacytosis greater than 60% or an abnormal involved-to-uninvolved free light chain ratio greater than 100. Therefore, only three of nine patients had focal bone lesions without other features that would have led to immediate treatment.

Strangely, a study from Heidelberg by Merz et al[7] was referenced to suggest that patients with at least two small and equivocal lesions should undergo repeat MRI in 3 to 6 months. Treatment would be advised for those with new or expanding lesions on the second imaging study. However, in the series by Merz et al,[7] MRI was generally repeated approximately 1 year after the first study, and only 10 of 31 patients who experienced disease progression underwent repeat studies within 6 months of the first examination. Importantly, although patients with an abnormal first MRI were more likely to undergo a second MRI study within 1 year, they were not more likely to experience progression, as demonstrated on the second or subsequent MRI, than patients who had a normal initial MRI. Conversely, patients with stable MRI findings on the second examination were not at increased risk of disease progression regardless of the presence or absence of abnormal findings on the first examination. On multivariable analysis, the presence of at least two focal lesions on the first study was not associated with an increased risk of disease progression.

The recent literature regarding the identification of higher-risk patients with AMM for treatment, including the study by Dimopoulos et al,[3] is dominated by disease characteristics and biomarkers at the time of diagnosis, as if there are no additional opportunities to intervene before the development of CRAB (hypercalcemia, renal insufficiency, anemia, lytic bone lesions). Indeed, in a recent randomized study that showed the superiority of lenalidomide and dexamethasone versus observation, patients in the observation group were followed until they developed CRAB.[2] However, several studies have shown that evolution of the M protein is associated with a high incidence of subsequent CRAB.[8,9] Indeed, in a recent preliminary study, patients with bone marrow plasmacytosis greater than 20%, progressive paraproteinemia, and immunoparesis had an 82% chance of developing CRAB at 2 years,[10] which fulfills recent criteria for beginning treatment. Because most patients with AMM are examined at 3-month intervals, when blood and urine samples are checked, patients with asymptomatic-but-progressive disease can be advised to begin therapy. Therefore, analogous to the results of sequential MRI by Merz et al,[7] biologic or radiologic evidence of progression may be a stronger indication for beginning treatment than an MRI finding of greater than than one focal lesion at the time of diagnosis.

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AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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